Hybrid Health Systems Simulation Modelling: Controlling COVID-19 Infections in Care Homes

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Declaration

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Chapters 2, 3, 4, 7, 8, and 9 were conjoint work with Dr Itamar Megiddo (IM), Professor Susan Howick (SH), Dennis McLafferty (DM), Gillian Anderson (GA), Professor Robert Van Der Meer (RV), and Dr Josephine Pravinkumar (JP) as described in Table 1.

Table 1: Contributions to conjoint work

Paper (Corresponding Section/Chapter)	**The PhD author**	**The co-authors**
1 (Section 2.4)	• Conceived the study • Conducted the analysis • Drafted the paper and led the submission and revision process for conference publication	• Supervised the study: IM and SH • Commented on the draft paper: IM and SH
2 (Chapter 3)	• Designed the study • Conducted the analysis • Drafted the paper and led the submission and revision process for conference publication	• Conceived and supervised the study: IM and SH • Contributing to designing the study • Commented on the draft paper: IM and SH
3 (Chapter 4)	• Conceived the study • Conducted the analysis • Drafted the paper and led the submission and revision process for conference publication	• Supervised the study: IM and SH • Commented on the draft paper: IM and SH
4 (Early version of Chapter 7)	• Conceived the study • Conducted the analysis • Developed the conceptual framework	• Supervised the study: IM and SH • Contributed to developing the framework: IM and SH

Paper (Corresponding Section/Chapter)	The PhD author	The co-authors
	• Drafted the paper and led the submission and revision process for conference publication	• Commented on the draft paper: IM and SH
5, 6 (Chapter 8)	• Conceived and designed the study • Developed the conceptual model • Collected data • Programmed and parametrized the model • Conducted the analysis • Drafted the paper and led the submission and revision process for journal publication	• Contributed to designing the study: IM and SH • Supervised the study: IM and SH • Contributed to developing the model: IM, SH, DM, and JP • Facilitated data collection: GA, RV, DM, and JP • Commented on the draft paper: IM, SH, DM, GA, RV, and JP
7 (Chapter 9)	• Conceived and designed the study • Developed the conceptual model • Collected data • Programmed and parametrized the model and conducted the analysis • Drafted the paper and led the submission and revision process for journal publication	• Contributed to designing the study: IM and SH • Supervised the study: IM and SH • Contributed to developing the model: IM and SH • Commented on the draft paper: IM and SH

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Abstract

Although healthcare-associated infections have caused significant burdens in care homes, the evidence for controlling infection spread in this setting is extremely limited, and the Coronavirus disease 2019 (COVID-19) pandemic highlights this limitation. Plenty of evidence exists for controlling infection in hospitals and especially in ICU settings, but care homes are unique in that they are a home rather than purely a health facility. The understanding of how a care home interacts with other care homes and the resulting transmission dynamics within and between homes is also incomplete. This research addresses these issues by combining system dynamics (SD) and agent-based modelling (ABM) to capture the complexity of the transmission dynamics of COVID-19 within a care home and across a heterogeneous network of care homes. Various approaches adapted from both SD and ABM practices are used to build confidence in the models.

This research makes several theoretical, methodological, empirical, and practical contributions. The theoretical contributions to the infectious disease dynamics and modelling fields include the conceptualization of the care home environment with characteristics important for infection control that provides a basis for future research and the development of a multi-layer simulation that can be tailored and applied in different contexts. From a methodological perspective, this research contributes to the modelling and simulation field by proposing a detailed and practical framework for developing a conceptual hybrid simulation model, describing new practices for modelling interfaces between SD and ABM modules, and demonstrating the confidence-building approaches for a hybrid model. Lastly, this research makes two empirical contributions. This research helps understand the transmission dynamics of COVID-19 and the relative impact of interventions that mitigate the spread of COVID-19 within and across care homes. It has been instrumental for policymakers in making evidence-informed decisions and policies during the COVID-19 pandemic. Opportunities for future research are proposed.

Table of Contents

List of Figures

List of Tables

List of Abbreviations

ABM	Agent-Based Modelling
CI	Confidence Interval
COVID-19	Coronavirus Disease
DES	Discrete-Event Simulation
HAIs	Healthcare-Associated Infections
HCWs	Health Care Workers
HICs	High-Income Countries
HSCP	Health and Social Care Partnership
ICU	Intensive Care Unit
IPC	Infection Prevention and Control
IQR	Interquartile Range
KS	Kolmogorov–Smirnov
LHS	Latin Hypercube Sampling
LMICs	Low-Middle-Income Countries
MDROs	Multi-Drug Resistant Organisms
MRSA	Methicillin-Resistant *Staphylococcus Aureus*
MS/OR	Management Science/Operational Research
NHS	National Health Service
ODD	Overview, Design concepts, and Details
PPE	Personal Protective Equipment
PRCC	Partial Rank Correlation Coefficient
RR	Relative Risk
SARS-CoV-2	Severe Acute Respiratory Coronavirus Virus 2
SCWG	Social Care Working Group
SD	System Dynamics

Chapter 1. Introduction

1.1 Research Overview

Healthcare-associated infections (HAIs) are a global health burden because of their significant impact on patient health and health care systems. Systems simulation modelling that captures the dynamics between patients, pathogens, and the environment is increasingly being used to improve understanding of epidemiological patterns of HAIs and to facilitate decisions on infection prevention and control (IPC). However, researchers/practitioners using single simulation modelling approaches can face significant challenges representing the multi-dimensional nature of complex healthcare systems composed of interactive and interconnected constituents with dynamic behaviours. Combining different simulation methods offers an opportunity to overcome these challenges and to capture important characteristics and behaviours of such systems. This thesis is about developing and utilising simulation models, including a hybrid model, to provide support to decision-makers involved in controlling HAIs and to explore frameworks to inform the design of hybrid simulation models. This chapter aims to introduce the research project by providing the background of the research (section 1.2) and discussing why it is of interest and relevance and what it aims to achieve (section 1.3). This chapter will conclude with an overview of the structure of this thesis (section 1.4).

1.2 Research Background

The World Health Organization defines HAIs as infections occurring in a patient as a direct result of any healthcare intervention or interaction in a hospital or other healthcare facility which was not incubating or present at the time of admission (World Health, 2011). This includes infections acquired in the hospital but appearing after discharge and also occupational infections among the staff of the facility (World Health, 2011).

HAIs pose a serious risk for patients and providers as they cause increased morbidity and mortality, prolonged length of stay in healthcare facilities, increased prevalence of multi-drug resistant organisms (MDROs), and psychological and financial burdens to patients, their families, and the healthcare system. The risk of HAIs is universal and pervades every healthcare facility, setting, and system globally. In Europe, the prevalence of HAIs was estimated at 5.5% (Suetens et al., 2018), and about 2.6 million new patients with HAIs have been identified annually (Cassini et al., 2016). These infections accounted for an estimated 33,000 attributable deaths and 900,000 disability-adjusted life-years (Cassini et al., 2019). In the US, the estimated prevalence of HAIs in hospitals was between 2.9% and 3.5% in 2015 (Magill et al., 2018). In Scotland, an estimated 55,500 (1 in 22) adults in acute care settings suffer from at least one HAI annually (Cairns et al., 2017). In Scotland, the increased length of hospital stay caused by HAIs is approximately eight extra days; and the cost attributable to HAI treatment in the National Health Service (NHS) Scotland is £46.4 million per annum (Manoukian et al., 2021). Cash cost is a small proportion of the total cost of HAIs, contributing 2.4% of total costs, which include capital, overheads, staff, pharmacy, and laboratory costs. The burden is even higher in low- and middle-income countries (LMICs). A systematic review and meta-analysis reported that the pooled prevalence of overall HAIs in Southeast Asia, where most countries are middle-income, was 9.1% (Ling et al., 2015). The reported prevalence in Africa varies significantly: in Ghana, it ranged between 3.5% and 14.4% across healthcare facilities, and the prevalence values in tertiary hospitals in South Africa and Ethiopia were 7.67% and 19.4%, respectively (Labi et al., 2019; Nair et al., 2018; Ali et al., 2018). Data on the impact of HAIs at the national level in LMICs, especially in African countries, is scanty and fragmented, generating difficulty in assessing the true scale of the problems of HAIs. The actual figure is assumed to be higher due to the lack of a functioning HAI surveillance system in these countries (World Health, 2011).

Since its emergence, the Coronavirus disease 2019 (COVID-19) has placed enormous pressure on healthcare systems worldwide, which increases the risk of healthcare-associated COVID-19 infections among non-COVID-19 patients. Estimates of the prevalence of healthcare-associated COVID-19 in China were as high as 41% (Zhou et al., 2020; Wang et al., 2020b). In a study involving 314 UK hospitals, 9.7% of patients with COVID-19 became infected after admission to hospitals providing acute and general care (Read et al., 2021). This study also found that resident community care hospitals and mental health hospitals had substantially higher hospital-acquired infection proportions (i.e., 61.9% and 67.5%, respectively). The risk of mortality was 1.3 times greater in patients with healthcare-associated COVID-19 infections compared to community-acquired (Ponsford et al., 2021). Immunosuppressed patients with healthcare-associated COVID-19 infections were twice as likely to decease in hospital as those admitted with community-acquired infection. Healthcare workers (HCWs) who contract COVID-19, or are required to isolate, can be absent from work for prolonged periods, causing strain on the workforce. The anxiety of acquiring COVID-19 in hospitals and the subsequent risk of mortality can deter people with medical needs from attending hospitals.

Many studies have demonstrated that comorbidity, fragility, and old age were associated with poor outcomes amongst COVID-19 infected people, explaining the significant impact of COVID-19 outbreaks seen in care homes (Wang et al., 2020a; Chen et al., 2020; Yang et al., 2020; Williamson et al., 2020; Hewitt et al., 2020). The case-fatality rates for over-80-year-old infected patients in China and Italy were 21.9% and 20.2%, respectively. The rates were significantly lower for younger age groups and individuals without comorbidities (Onder et al., 2020). In the first wave of the pandemic, around 70% of the total deaths in Scotland were people of the 75-or-over age group (NRS, 2021). Such evidence contributes to explaining why care homes, where the majority of residents are elderly and have complex medical and care needs, have suffered devastating outcomes (McMichael et al., 2020; Comas-Herrera et al., 2020).

1.3 Research Motivations

Assessing the effectiveness of interventions for controlling and preventing HAIs, as well as their costs and cost-effectiveness, requires understanding the healthcare system as a whole. A substantive body of literature has shown that within a healthcare facility measures such as contact isolation, environmental decontamination, hand hygiene, and active case detection and surveillance can reduce the prevalence of HAIs. However, the healthcare system is an interconnected ecosystem where patients encounter multiple providers both within and across facilities. The effectiveness of an intervention, therefore, depends on the actions of other units, facilities, and providers. Implementing combinations of strategies to prevent HAIs without understanding their potential outcomes, knock-on effects, and overlapping impacts and effects, including unexpected ones, can be costly.

Historically, randomized control trials, cohort studies, and case-control studies were commonly used methods to investigate the epidemiology of diseases in general and the epidemiology of HAI in particular (Barnes et al., 2010). Additionally, researchers performed cluster randomized control trials or quasi-experimental studies to examine the effectiveness of various measures for infection prevention and control (IPC) (Harris et al., 2006). However, performing large cluster randomized control trials across various health facilities to achieve generalizability and sufficient power to address important research questions is difficult. Furthermore, although quasi-experimental studies are more feasible and practical to conduct, the lack of randomization is a threat to the internal validity and limits the generalizability of the results to larger populations (Harris et al., 2006). Therefore, a more comparable, reliable, and easy-to-use planning tool is needed to assess interventions and their impacts (Schinaia and Parisi, 2014).

Evaluating the effectiveness of interventions is challenging due to the inherent complexity and dynamics of HAI transmission and the healthcare contexts in which the interventions are implemented. Simpler modelling approaches such as Markov models and decision trees are not sufficient for analysing complex healthcare systems although they have been standardized as methods to evaluate healthcare interventions (Marshall et al., 2015). Simulation models can help identify the critical functional and relational aspects of a system and, therefore, provide an understanding of how the organization and relationships among components of the system cause the system to behave the way it does. Simulation models can also capture patient characteristics and preferences to simulate patient and provider behaviours and anticipate the outcomes of their behavioural interactions.

Modelling is increasingly being used to improve understanding of epidemiological patterns of HAIs and to facilitate decisions on IPC. Simulation modelling that captures the dynamics between patients, pathogens, and the environment is particularly useful for studying complex systems like the healthcare system (Marshall et al., 2015). Simulation modelling provides a risk-free environment where ideas on IPC strategies can be tested systematically without the time, costs, and risks associated with experiments conducted in a real-world setting. It is a valuable tool to guide the selection of the most appropriate empirical research to pursue and examine the effects of IPC strategies, serving as a “virtual policy laboratory” for decision support by researchers, policymakers, public health officials, hospital managers and administrators, and other health care decision-makers (Lee et al., 2012).

Simulation modelling can help understand the relative effectiveness of different interventions, identify the risk of HAIs for different population groups, provide confidence intervals on the epidemic behaviours and, therefore, aid decision making. Like other modelling methodologies that try to predict outcomes, simulation modelling does not necessarily provide precise results that are completely reliable (e.g., the exact number of infections or the precise course of an epidemic). Perfect prediction using simulation can rarely be achieved as it is impossible to build a model that fully replicates the real world; particularly when we describe a stochastic system as complex as infection transmission, which is influenced by human behaviour, pathogen, host biological characteristics, and the health facility structure among many factors. IPC decision-makers using simulation models for decision-support must consider model assumptions and their relevance to the particular context in addition to carefully weighing the predicted benefits of interventions against the inconvenience, stigmatization, and costs they might engender.

Three key simulation approaches which have been used in healthcare include discrete-event simulation (DES), system dynamics (SD), and agent-based modelling (ABM) (Mohiuddin et al., 2017; Soh et al., 2017; Palmer et al., 2018; Vieira et al., 2016; Gul and Guneri, 2015; Isern and Moreno, 2015; Currie et al., 2018; Carey et al., 2015; C and Appa Iyer, 2013; Fakhimi and Probert, 2013; van Lent et al., 2012; Hulshof et al., 2012; Katsaliaki and Mustafee, 2011; Salleh et al., 2017). Although each simulation method has previously had success in supporting decision-makers in a healthcare context, each method considers a problem from a different perspective and some problems can benefit from the complementary view gained from using multiple simulation methods together. A combination of different methods of simulation (i.e., hybrid simulation models) can be particularly useful for understanding the impact of interventions in one part of the system on other components of that system or on the system as a whole (Marshall et al., 2015).

The motivation of this research is to develop a hybrid simulation framework that considers how different types of simulations may be combined to provide support to decision-makers involved in controlling HAIs in care homes, a high-burden setting. We are also motivated to develop useful, relevant models to support decision-makers in assessing the relative effectiveness of various IPC strategies and policies and to utilize these models in the context of the Scottish healthcare system. These motivations have led to the three following research questions, which we will consider through a review of literature which we will address in Chapter 2 (Q1), Chapter 3 (Q2), and Chapter 4 (Q3).

Q1: How have HAIs in care homes been controlled and prevented? What have been the challenges of IPC practice in this setting?

Q2: How have simulation modelling methods been used on their own and together to understand and solve the problems of HAIs?

Q3: What benefits do simulation modelling and hybrid simulation modelling methods offer to study the problems related to HAIs? What are the challenges of mixing methods?

1.4 Structure of the Thesis

This thesis consists of 10 chapters illustrated in Figure 1.1. To conclude this introduction, this section provides an overview of each chapter.

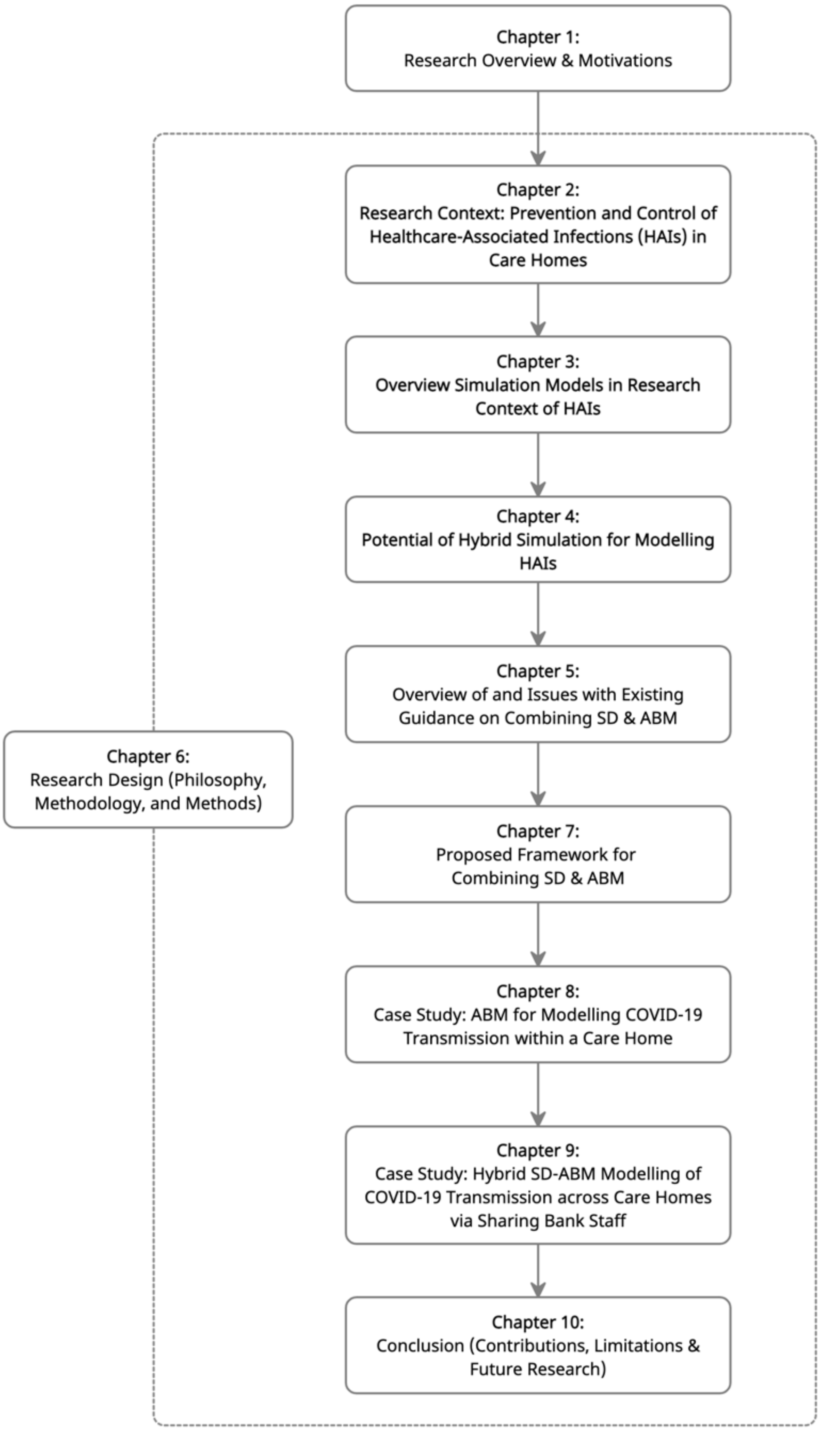

Figure 1.1: Structure of the thesis

Chapter 1 introduces the research background and presents the research motivations.

Chapter 2 provides a review of the burden of HAIs and COVID-19 in particular and discusses the current IPC evidence and practice in the focused setting, which is the care home setting. This chapter also reveals the knowledge gaps in IPC in care homes, which have become an urgent problem during the COVID-19 pandemic.

Chapter 3 introduces and compares different simulation modelling methods, focusing on SD and ABM which are the two commonly used methods in infectious disease modelling. The comparison of SD and ABM provides a ground for consideration of why and when they can be mixed. This chapter also presents a review of how simulation models have been used to investigate HAIs and their mitigation and how these models have evolved. This review enables the identification of the research gaps that are of concern and relevance to this research.

Chapter 4 discusses the benefits of mixing SD and ABM in-depth and highlights challenges in the development and use of hybrid simulation models.

Chapter 5 focuses on one of the challenges of developing hybrid simulation models highlighted in Chapter 4. This chapter reviews the literature that guides the combination of SD and ABM and identifies the unsolved problems in this field.

Chapter 6 presents the philosophical standpoint of this thesis and the methodology undertaken to address the research gaps highlighted in Chapter 4 and Chapter 5. This chapter may be viewed as an overarching chapter for the thesis.

Chapter 7 introduces a proposed framework for combining SD and ABM in the conceptual model development process with an example of a hybrid model of inter-facility transmissions in networks of heterogeneous care homes to demonstrate the use of the framework. This framework is based on the review of the existing guidance on combining SD and ABM in Chapter 5 and the researcher's reflection on the modelling process of the case study discussed in Chapter 9. It responds to the lack of methodological clarity on mixing SD and ABM revealed in Chapter 5.

Chapter 8 presents an ABM that explores the spread of COVID-19 within a care home and the effectiveness of different mitigation interventions and, therefore, addresses the gap about IPC in care homes identified in Chapter 4. This model provides insight to refine the research question about inter-facility transmissions and contributes to informing the experiment design of the hybrid model presented in Chapter 9. It also helps build confidence in one of the modules constituting the hybrid model.

Chapter 9 presents the case study of hybrid simulation modelling of networks of heterogeneous care homes and the inter-facility spread of COVID-19 by sharing staff. The model findings add to knowledge about the spread of epidemics across care homes, for which a gap has been identified in Chapter 4. This chapter explains the choice of simulation modelling methods and describes the hybrid model structure informed by the proposed framework for combining SD and ABM discussed in Chapter 7.

Chapters 8 and 9 describe the historical situation in the spring/summer of 2020 before COVID-19 vaccines and lateral flow tests were available. Further analyses can be found in Nguyen et al. (2021b) and Nguyen et al. (2021c). The alpha SARS-CoV-2 variant was the dominant variant in the UK before December 2020.

Chapter 10 concludes the thesis with a discussion of the key contribution of the research. These are followed by reflections on the limitations of the research and consideration of future work in this field.

Chapter 2. HAIs in Scottish Care Homes: Burden and IPC Challenges

2.1 Introduction

This chapter aims to provide a comprehensive description of the research context. It presents a review of the burden of HAIs in care homes, the current IPC practice, and the challenges faced by care homes to prevent and control HAIs, addressing Q1 raised in Chapter 1. This review identifies the gaps in evidence of effective IPC practice in this setting. This chapter also discusses how the COVID-19 pandemic has highlighted care homes' vulnerability to outbreaks and the existing issues of IPC practice in this setting.

Section 2.4 was published as

Nguyen, L. K. N.[a], Megiddo, I.[a], & Howick, S.[a] (2020). Challenges of infection prevention and control in Scottish long-term care facilities. *Infection Control and Hospital Epidemiology*, *41*(8), 943-945. https://doi.org/10.1017/ice.2020.113

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The introduction of section 2.4 is the abstract of the above-published paper. Sub-headings have been added for each of the discussed challenges of IPC in Scottish care homes to improve the clarity of the discussion.

It should be noted that footnotes are used to highlight the sections of this thesis that have been taken from a published paper.

2.2 The Burden of HAIs in Scottish Care Homes

Due to the Scottish population becoming older and frailer, the country is increasing demand for health and social care (NRS, 2017; Audit-Scotland, 2016). Changes in the demographics of residents living in care homes and the resulting increase in their needs for health and social care pose challenges for prevention and control of HAIs in vulnerable and already frail populations (NSS, 2017; Audit-Scotland, 2016). To accommodate these emerging healthcare needs and challenges of the aging population, in 2011 the Scottish Government set out the strategic 2020 Vision for health and social care reforms to develop a more sustainable model in healthcare delivery across the country. Its objective was to ensure a longer healthier life for everyone who lives at home, or in a homely setting (Scottish-Government, 2013; Scottish-Government, 2015). In this 2020 Vision, care homes played an important role as they are responsible for the wellbeing and care of vulnerable populations in need of assistance with medical issues or daily activities over a long period of time (Scottish-Government, 2013). In order to pursue this strategic plan, IPC interventions need to be evaluated and best practices identified with consideration for the distinct characteristics of care homes and the changing healthcare delivery in this type of setting.

As the residents living in care homes are older, more likely to have chronic and multiple diseases, and require more care than the general population, they are more vulnerable and at an increased risk of HAIs (Strausbaugh and Joseph, 2000; Strausbaugh, 2001). People over 65 years of age are the main resident group of nearly three-quarters of care homes in Scotland (ISD, 2018). The frequency and severity of infections observed in this geriatric population are attributed to many factors, including easily overwhelmed immunity systems, altered physiology, impaired liver, and renal function (Bajaj et al., 2021; Yoshikawa, 2000). Delays in diagnosis and treatments, which often make the infections more severe and take longer to recover, may also result from the absence or vague presentations of signs and symptoms in the elderly and/or their impaired communication capability. Symptoms like dysuria with urinary tract infection, cough, and sputum with pneumonia that may manifest as a decline in functional independence, falls, urinary incontinence, anorexia, and cognitive impairment may complicate the clinical assessment and diagnosis of HAIs among care home residents. Data suggested frequent misinterpreting of clinical clues of infection in the elderly (High et al., 2009). Additionally, the majority of residents in care homes (approximately 70%) are disorientated, nearly half are immobile, and more than two-thirds have urine and/or faecal incontinence (NSS, 2017). As a result of such fragility and comorbidity, they are more likely to have invasive devices such as catheters and frequent visits to hospitals which lead to rising risks of contracting infections. Furthermore, residential adults with cognitive impairment, mental health issues, and physical disabilities, who are the other main client groups for which care homes provide care services, may be unable to follow basic hygiene practice to prevent HAIs. The causative pathogens of the same HAI seem to be more diverse in elderly than in younger patients, which requires the therapy consisting of broad-spectrum antimicrobials (Yoshikawa, 2002). The frequent use of these drugs with activity against both gram-positive and gram-negative bacteria promote colonization and spread of MDROs among care home residents (Gruber et al., 2013; Lin et al., 2017).

The 2017 national point prevalence survey of HAIs reported that approximately one in 17 residents in care homes contracted at least one infection relating to the care received in the facilities, and approximately one in 15 received at least one antimicrobial (NSS, 2017). The former figure is higher than the corresponding figure in adult hospitals (1 in 22 inpatients) (Cairns et al., 2017). Additionally, the rate of antibiotics prescribed for Scottish care home residents who are older than 65 years old was 5.6 antibiotic items/1000 people/day, nearly double that reported in all people older than 65 (3.1 antibiotic items/1000 people/day) (HPS, 2015). The level of antibiotic use remains the same as the level seven years ago. The predominant proportion of HAIs originated in those currently residing care homes, comprising 97.5% of all infections, while HAIs initiating in hospital and other care homes constituted only small percentages of 1.7% and 0.8%, respectively (NSS, 2017). As only a small proportion of the facilities (15.4%) reported having a registration system to record colonization of HAIs in general and MDROs in particular among residents, data on the prevalence of colonization is not available (NSS, 2017). Also, HAIs can result in increased hospital admissions and readmission (Emerson et al., 2012). Twenty-six to 50% of hospital admissions from care homes were due to the onset of infection, and deaths among residents were mainly caused by pneumonia (Gavazzi and Krause, 2002; Strausbaugh, 2001; Schulz et al., 2011). Furthermore, multivariate analyses of the point prevalence survey also indicate that a number of risk factors independently associated with a higher prevalence of HAIs include older age, hospital admission in the last three months, having an inserted urinary catheter, and any wounds (NSS, 2017).

2.3 Infection Prevention and Control in Scottish Care Homes

While all hospitals have IPC committees and approved annual IPC plans and guidelines in place (Cairns et al., 2017), the IPC resources and strategies for tackling HAIs currently available in Scottish care homes are not well established. Internal or external infection control committees exist in less than a third of care homes (27.5%). Local health protection teams and local hospital IPC teams are the two main sources from which care homes obtain external IPC recommendations. The majority of care homes report having staff who have received IPC training (approximately 67%) or having access to IPC experts (75%). Eighty percent of care homes provide IPC training for nurses and care staff, with a higher proportion reported in care homes with nurses (approximately 90%) compared to those without nurses (nearly 50%). Although most care homes (approximately 98%) are aware of the availability of the NHS Education for Scotland IPC educational resources, only approximately 70% of care homes use them for training.

Hand hygiene, surveillance, isolation, and antimicrobial stewardship are the IPC interventions that have been implemented in care homes in Scotland. Firstly, hand hygiene is the most commonly used and important IPC measure in care homes. Although data on staff compliance with hand hygiene is not yet reported, liquid soap is available in all of the care homes and alcohol-based hand rub is ready for use in more than 80% of the care homes. However, only a small proportion of care homes in Scotland (15.4%) and other European countries (5.0 – 12.5%) used alcohol-based hand rubs as the most frequent measure for hand hygiene. More than half of the care homes had alcohol wipes for hand hygiene. Although the information is not available to identify whether this is a popularly used method of hand hygiene, it contradicts the recommendation found in the National IPC Manual, which states that the products should only be adopted where running water is unavailable (NSS, 2017). Secondly, slightly above half of the care homes confirmed having an HAI surveillance program, but only a quarter provided feedback on surveillance outcomes to their staff members. Approximately 85% of care homes had designated staff members who take responsibility for reporting and managing HAI outbreaks. Although residents with the colonization of MDROs were considered for isolation and taking additional precautions in more than half of the care homes, a much smaller proportion of the facilities (approximately 15%) had a registration system that enables the recording of colonized or infected residents. Furthermore, therapeutic guidelines were available in all care homes for prophylaxis and treatment of urinary tract infections, and in 90% and 80% of the care homes for skin and soft tissue infections and respiratory tract infections, respectively. However, the availability of an MDRO surveillance program was only found in a minority of the care homes (approximately 16%), and none reported annual data on the consumption of different classes of antimicrobial.

The 2017 Point Prevalence Survey revealed the variation in IPC policies across Scottish care homes, reflecting the difference in care services delivered in these facilities, the ownership, the sources of IPC advice, and surveillance/audit and feedback activities. Several surveys undertaken in various countries also reported limitations and gaps in the existing IPC strategies and policies in care homes (Zoutman et al., 2009; Gamage et al., 2012; Donlon et al., 2013).

2.4 Challenges of Infection Prevention and Control in Scottish Care Homes[1]

2.4.1 Introduction

Residents living in care homes are at high risk of contracting HAIs. The unique operational and cultural characteristics of care homes and the currently evolving models of healthcare delivery in Scotland create significant challenges for IPC. Existing literature on the challenges of infection control in care homes focuses on operational factors within a facility and has not explored the challenges associated with higher levels of management and the lack of evidence to support IPC practices in this setting (Yoshikawa et al., 2019; Dumyati et al., 2017; Travers et al., 2015; Mavrodaris et al., 2014; Montoya and Mody, 2011; Longo et al., 2002; Nicolle, 2001). This section will provide a broader view of challenges faced by care homes in the context of the current health and social care models in Scotland (Table 2.1). Care homes in the rest of the UK and internationally also face many of these challenges.

2.4.2 Mismatch between Demand and Funding for Health and Social Care

The mismatch between demand and funding for health and social care provided in Scottish care homes, which also occurs in other parts of the UK, is likely to negatively influence the priority of IPC, which is a key element for safe care (Table 2.1). Most care homes in Scotland serve a mix of state-funded and self-funded residents (CMA, 2017). Councils and NHS boards in Scotland who fund nursing and personal care services provided in care homes for entitled residents are encountering increasing financial pressure caused by an aging population with

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increasingly complex health and social care needs (Audit-Scotland, 2016). Currently, the shortfall in public funding (UK-wide) for care homes is around 5-10%, equivalent to approximately £200-300 million (CMA, 2017). The facilities that are most exposed to local-authority-funded residents are most affected. As a result, they have to charge self-funded residents higher fees to maintain services.

Table 2.1: Summary of the challenges of IPC, the causes and impacts of these challenges in Scottish care homes

Challenges	Causes	Impacts
Mismatch between demand and funding for health and social care.	• Aging population with increasingly complex health and social care needs • Delay in shifting to more sustainable models of health and social care • Reduced health and social care budgets • Difficulty in shifting resources from NHS to non-NHS settings	• Low priority for improving IPC practice over other nursing and care services • Restricted access to publicly funded health and social care, leading to increases in avoidable infections
Staffing shortage	• Competition with the NHS for staff • Migration policies for HCWs • Brexit	• Heavier workload, increased time pressure, leading to low compliance to infection IPC standards and measures • Reducing capability to handle threats such as outbreaks or epidemics
High turnover of staff	• Less attractive working terms and conditions and career development opportunities compared with the NHS's offers • Perceived unsafe working conditions due to staffing shortage	• Less familiar with the facilities' IPC protocols and programs, resulting in lower compliance • Requiring more frequent IPC education and training, associated with increasing costs
Difficulty in establishing regional or national guidelines for IPC	• Heterogeneity of care homes and their resident populations • Lack of evidence for effective IPC practice in care homes • Guidance on IPC practices in hospitals are not transferrable to care homes	• Inconsistency in IPC practices across care homes

Additionally, the shift to more sustainable models of health and social care, which reduce costs, employ sufficient staff with the right skills, and meet growing demand, is not occurring rapidly enough to address this issue. Cutting health and social care budgets and the difficulty in agreeing on integrated budgets between councils and NHS boards also obstruct the shift of resources to non-NHS settings such as care homes. Furthermore, due to lower thresholds in the financial assessment for eligibility to access publicly funded health and social care, fewer people can benefit from nursing and care services provided in care homes. The financial restriction to access timely and appropriate care in care homes has led to an increase in avoidable infections and increased use of NHS services among people aged 65 and over (Thorlby et al., 2018). Due to restricted financial resources, the Scottish government is more likely to prioritise other health and social care needs for the growing elderly population than investing to implement improved models of IPC practice. Service providers in care homes, most of whom are in the private sector, may also not be eager to prioritize IPC over other nursing and care services that improve resident satisfaction more directly.

2.4.3 Staffing Shortage and High Turnover of Staff

Significant staffing shortages and high turnover of staff can reduce compliance to IPC practices and make it more difficult and costly to provide IPC training, thereby promoting the spread of HAIs. The 2017 survey data from Scottish Social Care Councils, Care Inspectorate, and Scottish Care estimated that the nurse vacancy rate for care homes is at 14 – 20%, and two-thirds of the facilities are struggling to recruit nurses as they have to compete with the NHS that offers better terms and conditions and career development opportunities (Scottish-Government, 2019; Thorlby et al., 2018). Migration policies[2], including the decision to retain the minimum salary threshold at £30,000 for applicants seeking a Tier 2 visa and the minimum salary threshold requirement for permanent residence (£35,000) also prevent the recruitment of HCWs from overseas to fill the workforce gaps in care homes (Scottish-Government, 2019). HCWs working in this setting, even those with many years of post-qualification experience, often earn less than £30,000. Additionally, the possibility of limited European Union migration

[2] There has been a change in migration policies since this was published. As of 1 December 2020, the Tier 2 minimum salary requirement threshold was lowered to £25,600. Details are available at: https://www.gov.uk/government/publications/statement-of-changes-to-the-immigration-rules-hc-813-22-october-2020

following Brexit may exacerbate the pressure of scarce HCWs, both in general and in care homes, by a projected shortfall of more than 70,000 nursing and social care workers by 2025 (Dayan, 2017). The shortage of HCWs, which causes heavier workloads, increased time pressure, and stress, is associated with lower compliance with IPC interventions and standards and the resulting increased spread of HAIs (Burnett, 2018; Stone et al., 2004). The nurse shortage is also a major factor that constrains healthcare facilities' capability to handle possible future threats such as outbreaks and epidemics (Travers et al., 2015). In addition, the insufficient number of HCWs in care homes hinders the implementation of many IPC procedures such as screening and surveillance. The perception of unsafe working conditions in care homes caused by staffing shortfalls also impedes the retention of qualified HCWs in this setting, worsening the current situation (Stone et al., 2004). In addition to the staffing shortage, high turnover rates of HCWs in care homes and the reliance on temporary employees can undermine efforts to implement IPC policies and provide IPC education and training to HCWs in this setting. The annual turnover rate of 33.8% for nursing and care workers in care homes is substantially higher than the rate of 6.4% for NHS staff (Thorlby et al., 2018; Audit-Scotland, 2017). These high staffing turnover rates imply that care homes bear additional costs to provide more frequent in-service training sessions on IPC practices and to ensure that new staff are familiar with the facility's IPC practice protocols and annual IPC programs.

2.4.4 Difficulty in Establishing Regional or National Guidelines for IPC in Care Homes

The heterogeneity of care homes and their resident populations makes it complicated to establish regional or national guidelines for IPC approaches in this setting. The heterogeneity in ownership across Scottish care homes (NSS, 2017) creates variations in services provided, operational structures, business plans, and budgets which affect the development of annual IPC programs in care homes. Although some NHS Boards across Scotland set IPC guidelines and policies prior to the introduction of the Final Standards for infection control in care homes in 2005, they were not consistent, and regulated substances were not established (NSS, 2017). The standards focus on addressing the operational structures and processes in care homes with the provision of audit tools for self-auditing to support effective IPC rather than providing direct guidance on the best IPC practices in this setting (NHS-Scotland, 2005). Nonetheless, almost 15 years of implementation have not guaranteed consistency in compliance with the Final Standards; in fact, compliance rates remain low. For example, standard 2 requires that care homes have an infection control group that endorses all IPC policies, guidelines, and procedures and provides advice and support for implementing and monitoring the progress of annual IPC programs. However, a low compliance rate with standard 2 was evident as internal or external infection control committees were available in only 27.5% of care homes (NSS, 2017). Clearly, there is no easy solution for IPC in this setting and the establishment of the Finals Standards is only a starting point.

Most evidence that guides IPC practice and decisions implemented in care homes has been adapted from IPC validated in hospitals, despite evidence in one setting not directly translating to the other. For example, the National Infection Prevention and Control Manual is a practice guide mandatory for Scottish NHS employees to follow in order to reduce the risk of HAIs (NHS-Scotland, 2015). Although it is considered as the best IPC practice guidance in care homes, the suitability and practicality of this manual and the extent to which staff in this setting comply have neither been examined nor reported. Additionally, this manual covers only basic IPC practices such as hand hygiene, safe management of equipment and environment, and the use of personal protective equipment (PPE). Other IPC measures, such as surveillance, screening, and decolonization, are not included. The effectiveness of IPC interventions, programs, and program components have not been rigorously evaluated in care homes (Hughes et al., 2013; Uchida et al., 2013) due to challenges of conducting research in this setting (Lam et al., 2018). IPC strategies and policies used in hospitals may not be appropriate or effective to address the distinct problems of HAIs in a care home environment that serves as both a healthcare setting and a residential home because of the differences in infrastructure, management, and culture between care homes and acute care settings. For example, isolation and contact precautions are considered effective and commonly used IPC interventions in hospitals; however, they may not be preferable measures in care homes where social interaction is important for resident welfare (Furuno et al., 2012; Cohen et al., 2015). Additionally, residents in care homes are at as high a risk of contracting HAIs from HCWs as patients in acute care settings, and they also have frequent contacts with other residents and visitors in communal areas. Consequently, interventions such as hand hygiene that target HCWs alone may not be sufficiently effective to control the spread of HAIs; thus, the active participation of residents and visitors is also required.

2.4.5 Summary

HAIs have been a burden in care homes. Prevention and control of HAIs in care homes is complicated, and these facilities face several challenges. Although these challenges have been discussed in the context of the Scottish health and social care system, the rest of the UK and other countries across the globe are facing similar challenges. Apart from the barriers caused by the unique operational and cultural characteristics of care homes, other issues that challenge IPC in this setting originate from gaps in knowledge and resources. These gaps characterise the entire Scottish health and social care system and cannot be addressed by individual facilities. Therefore, a broad picture of challenges in IPC in care homes is useful to seek effective solutions that can both improve IPC practice and uphold the comfort and quality of life for care home residents.

2.5 Impact of the COVID-19 Pandemic on Care Homes

The COVID-19 pandemic has highlighted care homes' vulnerability to infectious disease outbreaks and the lack of context-specific best practice IPC guidance for this setting. As of January 2021, the cumulative number of COVID-19 deaths in over 30,000 care homes in the US was approximately 140,000 deaths (Comas-Herrera et al., 2021). The rate of COVID-19 deaths among residents was estimated to be over 7%. As of 22 January 2021, 75% of all COVID-19-associated deaths in Australia were among care home residents (Australian-Government, 2021). Many provinces in Canada also reported that high proportions of death among confirmed cases were residents living in care homes in the early pandemic (e.g., 47% in British Columbia as of 12 April; 62.5% in Alberta; 37% in Ontario; 70% in Quebec as of 14 April 2020) (Hsu and Lane, 2020). The Public Health Agency of Canada indicated that care homes continued to account for the greatest proportion of COVID-19 cases and deaths, representing about 7% of all cases and 59% of all deaths as of early March 2021 (Clarke, 2021). Infections among staff in care homes represented more than 10% of Canada's total cases. Furthermore, as of November 2021, there have been over 800,000 COVID-19 deaths in Europe with more than 88% occurring in people aged over 65 years (ECDC, 2021). Residents in care homes across Europe comprised large proportions of the total number of COVID-19 deaths (e.g., 55.2% in Ireland as of 13 April, 49.4% in France, 63.9% in Norway, and 33% in Portugal as of 15 April) (Comas-Herrera et al., 2021).

Similar to care homes in other countries worldwide, COVID-19 has had a disproportionate impact on care home residents and staff in Scotland. The Care Inspectorate revealed that 42% of the total care homes in Scotland had recorded confirmed/suspected COVID-19 cases in the first wave of the pandemic (Scottish-Government, 2020a).

Additionally, more than 90% of care homes with more than 90 residents had an outbreak. According to the National Records of Scotland data, 44% of all excess deaths in Scotland were attributed to COVID-19 deaths among care home residents as of January 2021 (NRS, 2021). COVID-19 also led to the loss of significant years of life in residents aged 70 and over (Burton et al., 2021). The staff has also been significantly impacted. In April 2020, 10% of all care home staff were reported as absent. This absence rate declined steadily in October 2020, before increasing again to over 4% in January 2021 (Comas-Herrera et al., 2021). Staff absence due to reasons relating to COVID-19 aggravated the long-standing staff shortfall in the health and social care sector. Furthermore, Pautz et al. (2020) reported that pre-existing issues for care home staff in Scotland were amplified during the first wave of the COVID-19 outbreak. These issues relate to terms and conditions, supportive managers, a safe work environment, decent pay, and job security.

It is essential that care homes, which are integral and vital to the wider healthcare system, continue to function safely and effectively amidst COVID-19 to avoid increasing the pressure on the acute care sector. If care homes stop admitting patients discharged from hospitals, patients have to stay in hospitals longer than medically necessary, which puts them at greater risk and adds pressure on hospitals by filling up hospital beds. Prolonged hospital stay also causes distress for many individuals with dementia. However, unsafe transfers will increase the risk of outbreaks in care homes that will increase the return of residents with severe COVID-19 symptoms back to hospitals. Controlling outbreaks of COVID-19 within care homes and transmissions across settings are vitally important to protect the vulnerable residents and staff in the ongoing pandemic.

2.6 Chapter Summary

This chapter has discussed the burden of HAIs, current IPC practice, and challenges to implementing IPC in care homes. It has highlighted care homes' vulnerability to HAI outbreaks and the lack of context-specific evidence for best practice IPC guidance for this setting. The lack of evidence has been especially problematic during the COVID-19 pandemic, contributing to a devastating impact on care home residents and staff. Guidance for care homes has been adapted from the acute care setting and, therefore, has not accounted for the unique characteristics of care homes. Therefore, there is an urgent need to address the following research question to inform effective responses to the pandemic to protect residents and staff.

Q4: How can we prevent and control the spread of COVID-19 within and across care homes?

In order to apply simulation models to address this research gap in IPC knowledge in care homes, we first need to understand the broader picture of how simulation models have been used to solve the problems of other HAIs before the COVID-19 pandemic. This is in line with question Q2 raised in Chapter 1.

Chapter 3. Simulation Models for Transmission Dynamics of HAIs

3.1 Introduction

This chapter presents a systematic review that addresses research question Q2, i.e. *How have simulation modelling methods been used on their own and together to understand and solve the problems of HAIs?*, noted in Chapter 1 and highlighted again in Chapter 2. We conducted this systematic review early in this research and, at the time, we considered the three simulation methods, namely SD, ABM, and DES.

Section 3.3 was published as

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Section 3.3.1 consists of the last two paragraphs of the Introduction section in the above paper. Section 3.3.2 includes the Methods section of the paper and the Study Selection section. Section 3.3.3 has been amended from the Discussion section of the paper to clarify the gaps in the research. Each gap is supported with evidence from relevant parts of the Results section in the paper. The summary (section 3.3.4) has been taken from the Conclusion section of the paper.

As this research evolved, DES was found to be less appropriate than SD and ABM for modelling the research problems relating to COVID-19 transmission dynamics. This will be explained further in section 3.5. This chapter will therefore focus on the use of SD and ABM in modelling the problems of HAIs and mention DES where relevant. In this chapter, only the results and discussions from the paper detailed above that are of relevance to this thesis are included. First, this chapter provides an overview of the origins, features, and practical applications in healthcare for SD and ABM. The chapter then discusses the similarities and differences between SD and ABM. This comparison provides an understanding of the strengths and limitations of both methods, explores how they might complement one another, and, therefore, determines why and when to mix these methods. This chapter continues to discuss how simulation models have been used to investigate HAIs and relevant mitigation actions, especially in the context of care homes. The chapter concludes by identifying and discussing the gaps in the literature that are of relevance to this research.

3.2 Overview of Different Simulation Modelling Methods

3.2.1 System Dynamics

3.2.1.1 Origins of SD

Jay Forrester developed SD at the Massachusetts Institute of Technology in the 1950s (Forrester, 1958). He aimed to use engineering and science to identify the core factors vital for the success of corporations. His work emerged from tackling managerial problems in General Electric (New York). Forrester incorporated the existing decision-making rules for hiring and layoffs in the production plants into manual simulations that captured the internal stock-flow-feedback structure of the firm. This work demonstrated that the internal structure of the firm, not external forces such as business cycles, was the root cause of the employment instability (Forrester, 2007). Under the direction of Forrester, his team at the Massachusetts Institute of Technology Computation Centre developed the first computer SD simulator, DYNAMO, followed by the publication of the first book in the field, Industrial Dynamics, in 1961 (Forrester, 1964).

3.2.1.2 Features of SD

From an SD perspective, interactions among the elements within a system and their interactions with the environment generate the characteristic behaviour of that system (Pidd, 1998). SD is a top-down continuous simulation modelling method that represents the structure of complex systems as accumulations (stocks), rates (flows), feedback, and time delays, and examines their behaviour over time (Sterman, 2000). Stocks (or “levels”) are defined as aggregation or accumulations of inflows and outflows over a period of time. Feedback exists when a change in a variable in the system impacts other variables in the system and these variables then, in turn, influence the initial variable. Delays represent the time it takes to measure and report information, make decisions or update stocks that cause outputs to lag behind inputs. SD abstracts from the fine details of the system (Sterman, 2000). This thesis also considers compartmental models from the mathematical epidemiology and ecology literature that describe the disease transmission dynamics and links them to aspects of healthcare facilities and the provision of services that affect health outcomes. These models similarly take a top-down approach that often assumes continuous time, and they are implemented using differential equations (Anderson, 1991).

3.2.1.3 Practical Applications of SD in Healthcare

SD has proven to be an appealing simulation method as it offers a participatory approach to developing models (Atkinson et al., 2015). SD allows for the elicitation and alignment of "mental models" from various stakeholders involved in the process of model-building via discussions. This promotes a better understanding of the underlying mechanism and cause of a problem and greater insight into the system at a strategic level than other simulation methods. This also helps achieve agreement on action plans and, therefore, facilitates the adoption and successful implementation of broader policy (Atkinson et al., 2015).

SD has been implemented in the healthcare sector in various ways since the 1970s (Homer and Hirsch, 2006). It has been adopted to improve operational perspectives of healthcare delivery and capacity, including but not limited to patient flows in extended care and emergency, population-based health maintenance organization planning, the influence of terrorist acts and natural disasters on healthcare delivery and capacity, service demands, and workforce needs (Homer and Hirsch, 2006; Atkinson et al., 2015). SD has also been used to understand the epidemiology of many complex health issues such as substance abuse (Homer, 1993; Roberts et al., 1982; Tengs et al., 2001), infections (Royston et al., 1999; Homer et al., 2000), heart disease (Luginbuhl et al., 1981; Homer et al., 2004), diabetes (Jones et al., 2006) and cancer (Katsaliaki and Mustafee, 2011). In addition, this simulation modelling method has improved the understanding of interactions between disease epidemiology and healthcare capacity (Hirsch and Immediato, 1999; Hirsch et al., 2004). SD models of infection control have simulated the population as aggregates of sub-populations representing different states of infection rather than individuals with distinct characteristics and behaviours. Therefore, these SD models provide a cross-sectional view, patterns, and trends of the system over time rather than longitudinally tracking specific individuals.

3.2.2 Agent-Based Modelling

3.2.2.1 Origins of ABM

ABM stems from ideas and methods in many different fields. The history of ABM can be traced back to the concept of cellular automation, a collection of cells with specific rules on a grid, in Von Neumann and Burks (1966) and Gardner (1970). Many authors viewed cellular automation as a simple ABM where agents are stationary (Wilensky and Rand, 2015). Thomas Schelling's segregation model developed in 1971 was one of the earliest ABM models. He developed an ABM used for explaining the persistence of racial segregation despite the growing tolerance of the cultural and legal environment (Schelling, 1971). The model specified agent actions with a sequence of if-then statements. Individuals will tolerate racial diversity, but they will not tolerate it if they are in a minority in their locality. He used coloured squares on a matrix to illustrate that complete segregation is a stable equilibrium despite increased tolerance. At that time, coins and graph paper rather than computers were used to develop the model. However, it still embodied the core principle of ABM, as the interactions of autonomous agents in a shared environment produced observed aggregate, emergent outcomes. In ecology, Gross and DeAngelis (1992) developed individual-based modelling independently, alongside ABM. They highlighted the importance of unique individuals' biological characteristics and behaviours, as opposed to assuming that many individuals may be aggregated into a single state variable. They also discussed the role of individuals' spatial-temporal neighbourhood, in contrast to ignoring spatial dependence. In the field of political science, Axelrod (1984) created the tournament of prisoner's dilemma strategies and had them employ the strategies and interact with other agents multiple times to determine a winner. Axelrod (1997) also developed many other ABMs to study phenomena from ethnocentrism to the dissemination of culture.

3.2.2.2 Features of ABM

ABM is a bottom-up simulation method for modelling autonomous, dynamic, and adaptive systems and is formed on the basis of three key concepts which are agency, dynamics, and structure (Gunal, 2012; Borshchev and Filippov, 2004). Agency means that agents are autonomous entities with specific properties, actions, and possibly goals. Dynamics is the development, change, and evolvement of both agents and their environment over time. Structure is emergent as a result of agent interaction. Agents live in the environment, sense it and decide what action to employ at a certain time on the basis of the current state of the environment and their own state and defined decision rules. Agents can have explicit targets to minimize or maximize, and they can also learn and adapt based on their experiences. Such interactions result in the updates of agents' internal states or decisions on their next actions. The lower-level autonomy and interaction lead to the concept of dynamics at the system level. The system changes and patterns emerge as agents and their environment evolve or co-evolve over time. The core idea of ABM is that a model composed of agents that interact with one another and their environment can effectively demonstrate many (if not most) phenomena and real-world systems (Wilensky and Rand, 2015). This thesis also views similar microsimulation and individual-based models from the mathematical epidemiology and ecology literature as ABMs, though in these models the entities are often only reflexive and do not make autonomous decisions.

3.2.2.3 Practical Applications of ABM in Healthcare

In the context of health care systems, ABM has proved to be a rapidly maturing health modelling tool that is suitable for addressing many public health policy and planning needs, as well as care infrastructure and healthcare investment decisions. First, ABM offers a more realistic approach to modelling than SD and DES for many problems of healthcare in which multiple classes of actors often interact in various ways (Barnes et al., 2013). For example, different types of HCWs which have distinct sets of characteristics and behaviours can be modelled without assuming how each type would affect the healthcare system. The visualization and animation that ABM produces make it easier to communicate and explain the model to healthcare professionals who may not be trained in computational and mathematical disciplines. This helps gain healthcare professionals' confidence in the model and ultimately supports impact. In addition, ABM enables the system to be simulated at the individual level and in a more detailed fashion than SD or DES. Consequently, it provides insights into the system and captures the emergence of the system which may not be observed using other types of simulations or traditional research methodologies (e.g., cohort studies, randomized controlled trials).

ABM has been applied to many areas of health research. In healthcare delivery, ABM has been used to study the effect of different configurations of staffing and economic forces on healthcare system performance and patient safety (Kay Kanagarajah et al., 2008; Jones and Evans, 2008). In ABM, responses of physicians and nurses in the healthcare system are adaptive and evolve according to the needs of patients that are heterogeneous with a unique set of medical requirements, and the state of the entire system. The adaptive behaviour is a distinct characteristic of ABM that other modelling methods cannot replicate. In addition, ABM has expanded on the infectious disease epidemiological research primarily established by SD or compartmental models (Willem et al., 2017; Miksch et al., 2019). By simulating complex individual interactions and behaviours and spatial heterogeneity in the healthcare system, ABM has provided more details about the underlying mechanism and nature of pathogen transmission (Hunter et al., 2018; Miksch et al., 2019; Stephenson et al., 2020; Perez and Dragicevic, 2009). The method has also enabled the explicit implementation of various infection control strategies such as cohorting, contact tracing, and social distancing (Hotchkiss et al., 2005; Thompson et al., 2020; Farthing and Lanzas, 2021; Ferguson et al., 2005; Enanoria et al., 2016). In contrast to SD, capturing stochastic effects resulting from heterogeneous populations is a key feature of ABM. Accordingly, it has significantly enhanced our understanding of epidemics. The increasing recognition of the importance of interdependence between individuals and feedback over time on non-communicable diseases has led to increased applications of ABM in this area (Tracy et al., 2018; Ness et al., 2007). ABM has provided insight into individual health behaviours that increase the risk of diseases such as alcohol consumption, smoking, unhealthy eating, and physical inactivity, and the roles of socioeconomic status and social influence on these behaviours (Chao et al., 2015; Schaefer et al., 2013; Scott et al., 2016; Auchincloss et al., 2011). Health economics and policy applications of ABM include the models that have simulated the interactions between different health facilities at local, regional, and national levels which are often hard to observe or predict from the view of any individual setting (Ringel et al., 2010; Slayton et al., 2020; Liu and Wu, 2016).

3.2.3 Comparing SD and ABM

The first publications discussing the differences between SD and ABM methods appeared in the late 1990s and early 2000s (Phelan, 1999; Phelan, 2004; Scholl, 2001a; Scholl, 2001b). According to Phelan (1999), "reality" is revealed by associating rationality with careful observation conducted using both deductive and inductive approaches. This view concurs with the one proposed earlier by Lane (1994), who asserted the need to have a range of tools and approaches to support the expansion of systems thinking. Phelan (1999) also compared systems theory with complexity theory associated with SD and ABM respectively, and they identified three differences between the methodologies, including agenda, techniques, and epistemology. Firstly, the agenda for systems theory is confirmatory contrasting with explanatory in complexity theory. Secondly, system theory tends to use "circular flows" as its technique as opposed to agent-based modelling in complexity theory. Finally, the epistemology (the theory of method) of system theory concentrates on a holistic view and understanding of the structures of a system while complexity theory focuses on emergence arising from simple interactions among individuals. Furthermore, Phelan argued that the exploratory agenda in complexity science (ABM) will continue to thrive and proceed to confirmatory studies and that this school of thought seems to be moving towards a more constructivist stance. He also argued that ABM will become a familiar technique in systems scientists' toolkit following the widespread availability of artificial intelligence methods that allow agents to learn, make an inference, and plan. Moreover, as both modelling techniques (i.e., circular flows models and agent-based models) can capture "some of the essence of the conceptual categories of complexity and emergence", Phelan believed that the efficacy of each method and the resulting selection of method will be context-dependent. He concluded that systems theory and complexity theory will have some overlapping areas in terms of their agenda and techniques. However, friction between the two theories continues to exist due to differences in their underlying epistemological assumptions (Phelan, 1999). Scholl (2001a) agreed with the notion that more thorough research on comparing SD and ABM is essential as the theories underlying these methodologies share similarities and can be complementary. Phelan and Scholl continued their dialogue by exploring the benefits of studying the same problem with both systems and complexity theories (Scholl, 2001b; Phelan, 2004).

Many researchers have compared the main characteristics of SD and ABM. The early works were credited to Kim and Juhn (1997) and Parunak et al. (1998). These works have then been expanded by other authors (Kim and Juhn, 1997; Pourdehnad et al., 2002; Schieritz and Milling, 2003; Borshchev and Filippov, 2004; Martinez-Moyano et al., 2007; Siebers et al., 2010; Rahmandad and Sterman, 2008; Scheidegger et al., 2018). These works have then been expanded by other authors. From a pedagogical point of view, Pourdehnad et al. (2002) identified six categories of differences between these two simulation modelling methods. Additionally, Scholl investigated the differences between the two schools of thought and later between simulation models based on differing simulation methods but studying the same behaviour (Scholl, 2001a; Scholl, 2001b). He noted that studying the same phenomena in different contexts can differentiate features that are context-dependent from those that are always present. Table 3.1 consolidates the discussions on the comparison between SD and ABM from several publications and provides an overview of the assumptions, stochasticity, inputs, outputs, data dependency, and typical case uses in healthcare for each method. In the literature review, we consider compartmental models from the mathematical epidemiology and ecology literature, equation-based models, and macrosimulation similarly take a top-down approach that often assumes continuous time, and they are implemented using differential equations (Anderson, 1991). We also view similar microsimulation, individual-based model, multi-agent modelling, and cellular automata as ABMs, although in these models the entities are often only reflexive and do not make autonomous decisions. The table provides a starting point to support understanding of the strengths and limitations of both methods in order to identify why and when to mix these methods.

Table 3.1: Overview of the assumptions, inputs, outputs, data dependency, and typical use cases of SD and ABM

Feature	SD	ABM
Similar Models	Compartment model (mathematical epidemiology and ecology), equation-based modelling, macrosimulation	Microsimulation, individual-based model, multi-agent modelling, cellular automata
Assumptions	Entities within each stock are mixed homogeneously	Entities can be heterogeneous and autonomous decision-makers, who can learn and adapt to their environment; entities can interact with each other
Stochasticity	Ordinarily deterministic, but stochasticity could be incorporated	Typically, stochastic but could be deterministic
Inputs	Stock and feedback and accumulation structures; initial levels of stock/sub-populations aggregated by particular characteristics; rates, which characterize the inflows and outflows of a stock	Agent types and definitions in terms of their characteristics, possible actions and rules of behavior; initial number of agents; environment characteristics and rules; definition of agent-agent (e.g., network), agent-self, and agent-environment interactions
Outputs	Deterministic time series of population/stock levels and flows and insight into behavior of the system	Stochastic (typically) time-series of population and sub-population outputs such as number of entities in a specific

Feature	SD	ABM
		state, frequency of actions, and frequency of events as well as state of the environment; insights into the system emergence behavior; tracking individual entities
Data dependency	Objective data at aggregate levels supplemented by judgmental, subjective data, and informational links	Depending on simulation aims, these methods can be highly data-dependent because they model entities at the individual level and try to describe variations in their characteristics and other inputs
Typical use cases	Model transmission dynamics of infections and evaluate impact of strategic interventions at global/national/regional level (e.g. public health policies) Provide a strategic overview of the system, accounting for competing demands and feedback effects (e.g. workforce planning for health and social care sector at a national level to cope with future epidemics)	Model transmission dynamics of infections and evaluate impact of interventions at organizational/ individual level affected by social and spatial networks, demographic and health characteristics (e.g., age and underlying conditions), and behaviors (e.g., compliance to hand washing, self-isolation practice) Determine how interventions (e.g., screening/testing and vaccination) can be tailored/targeted to specific groups of individuals at high-risks due to their characteristics (e.g., elderly, individuals with comorbidity), contact patterns (e.g. bank/agency staff working at multiple care homes who can spread the infection) and/or behaviours (e.g., ancillary workers with low compliance to hand hygiene)

3.3 Simulation Models for Transmission Dynamics of HAIs

3.3.1 Introduction[3]

A number of reviews have been conducted on the mathematical modelling of HAIs in the 21st century. Grundmann and Hellriegel (2006) wrote the first literature review on HAI modelling; they focused on explaining the capacity of models to enhance epidemiological understanding in hospitals, and thus their work was restricted to the detailed description of a number of publications. Nelson and his colleagues carried out a similarly in-depth and limited in-breadth literature review on economic analysis applied to HAIs using dynamic transmission models (Nelson et al., 2017). In contrast, van Kleef et al. (2013) published a systematic review on the overall trends in the application and development of mathematical models of HAIs over time. Lastly, Opatowski et al. (2011) illustrated the overall progress of mathematical and simulation modelling of multi-drug resistant bacteria spread in both the community and hospital settings.

Since these reviews were conducted, a significant number of simulation models, including ABM and hybrid models, exploring the dynamics of HAIs have been published. The application of simulation modelling of HAIs has grown rapidly, possibly due to the recognition of this methodology's advantages and the increasing capabilities of computers. The current adoption and application of HAIs simulation modelling needs to be consolidated and updated to facilitate further development of appropriate models, enabling the investigation and evaluation of the best practice for IPC under different healthcare settings from clinical and economic perspectives. Therefore, we conducted a systematic review to establish i) how simulation models have been utilized to investigate HAIs and their mitigation, ii) how these models have evolved, and to identify iii) gaps in their adoption, and iv) useful directions for their future development. The next section briefly summarises the approach to the systematic review and the identified research gaps.

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[3] Section 3.3.1 is the last two paragraphs of the Introduction section in Nguyen et al. (2020c).

3.3.2 Methods of Conducting the Systematic Review[4]

Information Sources and Search Strategy

Pubmed, EMBASE, Cochrane Library, ABI/INFORM Collection via ProQuest, Business Source Complete and Scopus were searched from the date of inception to the 19rd of February 2019. Results were restricted to peer-reviewed publications written in English. Search terms for HAIs were combined with search terms for simulation models as follows:

- *Infection OR infections*

AND

- *Health care associated OR hospital acquired OR nosocomial OR HAI* OR HCAI**

AND

- *System dynamic* OR compartmental OR agent based OR microsimulation* OR discrete event* OR simulation**

All databases were searched identically. Reference lists of the previous literature reviews (Grundmann and Hellriegel, 2006; Nelson et al., 2017; van Kleef et al., 2013; Opatowski et al., 2011) were also searched for relevant citations.

Eligibility Criteria

We included studies that had fulfilled all of the following criteria: i) simulation modelling of the dynamics of HAI transmission, clinical and economic evaluation of preventions for HAIs, and/or the dynamics of antimicrobial resistance, ii) simulation models including SD, DES, and/or ABM, and iii) a primary focus on HAI transmission in healthcare settings including hospitals, care homes (e.g., residential homes, nursing homes), and/or medical centres.

[4] This section includes the Methods section and the Study Selection section in Nguyen et al. (2020c).

Exclusion Criteria

We excluded studies which did not involve: either i) human-to-human transmission or ii) human-environment-human transmission, or did involve: iii) animal transmission of HAI, or iv) pharmacokinetics and/or pharmacodynamics of antimicrobial drugs and/or molecular biological perspectives within hosts (e.g., molecular mechanisms of antibiotic resistance within hosts, efficacy and/or side effects of antibiotics, mode of action of drugs), or v) within hosts immunity or strain competition only, or vi) community transmission of pathogens spread in the healthcare environment as well, where the focus of the papers was community spread (e.g., SARS epidemics), or vii) literature review which did not contain new primary studies. Furthermore, we did not include editorials or letters to editors.

Data Collection Process

Data was extracted for the included studies, categorized and summarized in tabular format (Table A.1 in Appendix A).

Data Items

We extracted key data to address the objectives of this review. Firstly, this contained the basic information of the studies (study title, authors, year of publication). Secondly, as the main objective of the review was to explore the existing use of simulation modelling for understanding HAI transmission and improving IPC in various healthcare settings from clinical and economical perspectives, we looked for the following codes: country of research, setting, type of simulation model, research theme, aim of the simulation model, pathogen, and inclusion of economic analysis. Additionally, because we were interested in how models of HAI transmission in healthcare settings were simulated to evaluate the effectiveness of IPC strategies, data on the type of intervention and the type of interactions (i.e., patient-HCW, HCW-HCW, patient-patient, patient-visitor, environment reservoir for transmission, interactions between health facilities and interactions between health facility and community) were also extracted. Furthermore, to explore how different types of simulation models and hybrid models have been utilised, we looked into the technical perspectives of these models, including whether sensitivity analysis, software used for simulation, calibration, validation and verification, and transferability and generalizability were performed and how they were performed.

Study Selection

Figure 3.1 shows the process of identification, screening, and selection using the PRISMA[5] flowchart (Moher et al., 2009). There were 606 records identified from electronic database searches and 25 records from other sources. After removing duplicates and reviewing the title and abstract of the remainder, full-text articles were retrieved for the retained 109 records to assess their eligibility. Further 54 records were removed as they either did not meet the inclusion criteria. Additional 13 studies were identified via reference screening of the existing systematic reviews (Grundmann and Hellriegel, 2006; Nelson et al., 2017; van Kleef et al., 2013; Opatowski et al., 2011). Overall, 68 publications were included and reviewed in detail.

[5] PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses (http://www.prisma-statement.org/)

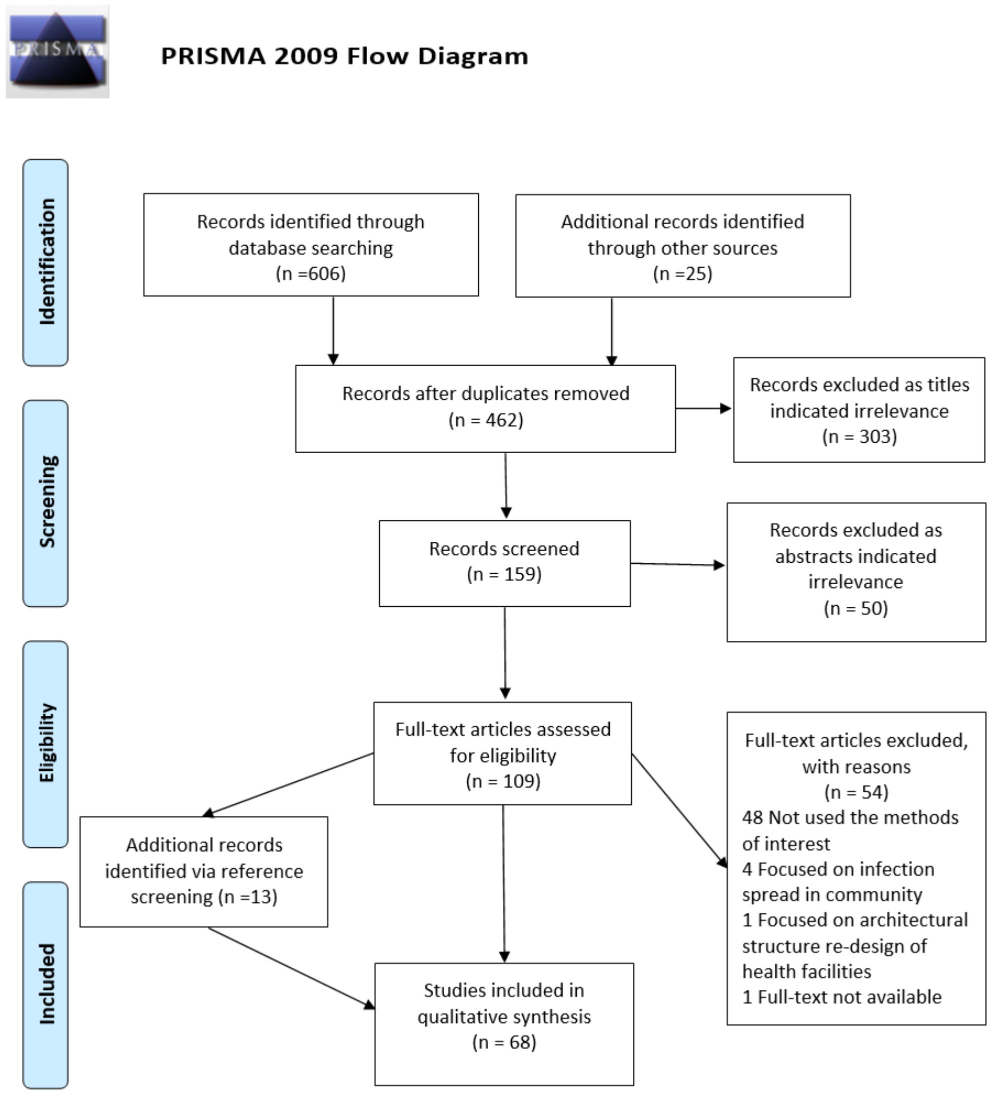

Figure 3.1: PRISMA flow diagram

3.3.3 Gaps in Research Identified from the Systematic Review[6]

The review highlighted a number of research gaps. First, the majority of studies developed simulation models to investigate HAI problems in adult hospital settings (60 studies, 88%). These models depicted an intensive care unit (ICU), a single general ward, or a simplified hospital, of which most lacked any detailed ward structure. Other types of healthcare settings, such as care homes and paediatric hospitals, as well as interactions between settings, were not extensively investigated. In particular, only a small number of studies (5 studies, 7%) modelled

[6] This section has been amended from the Discussion section in Nguyen et al. (2020c) to clarify the gaps in research and each gap is supported with evidence from relevant parts of the Results section in the paper.

the transmission dynamics of HAIs in care homes, including pathogens such as influenza (Nuño et al., 2008; Wendelboe et al., 2015; van den Dool et al., 2008), Methicillin-Resistant *Staphylococcus Aureus* (MRSA) (Chamchod and Ruan, 2012) and viral nosocomial gastroenteritis (Vanderpas et al., 2009). The majority of publications did not take transmissions across healthcare facilities, especially across care homes and between hospitals and care homes, into consideration. Donker et al. (2010) were the first to look at the impact of different referral patterns among various categories of hospitals upon MRSA infection rates. A year later, two other studies examined the interaction between settings for MRSA. Barnes et al. (2011) examined MRSA transmission between a single hospital and a single care home, and Kouyos et al. (2011) studied its transmission between multiple hospitals and the community. Furthermore, Lee et al. (2013b & 2013c) explored MRSA transmission between multiple hospitals, care homes, and the community.

Second, the problems of HAIs in LMICs, where the burden is significantly higher than in high-income countries (HICs), are rarely addressed in the literature and particularly in simulation modelling studies. The prevalence of HAIs in LMICs is at least double the prevalence in Europe (World Health, 2011). Additionally, the incidence of HAIs acquired in ICUs in LMICs triples the incidence in the US (Klevens et al., 2007). However, from the three-quarters of the studies that did specify a particular country: only two (3%) looked at healthcare settings in a middle-income country (South Africa and Thailand), and another three (4%) looked at an upper-middle-income country (China). The majority of publications (68%, 46 studies) concentrated on HICs of which nearly half were in the US (21 studies). The transmission patterns of HAIs in LMICs require further studies as they are likely to be dramatically different from the transmission patterns in HICs. The differences are due to many factors such as poor infrastructure, insufficient environmental hygiene conditions, different staff cohorting, shortage of HCWs, HCWs' knowledge and compliance with IPC measures, overcrowded healthcare facilities, absence of comprehensive IPC guidelines and policies, lack of procedure, and different antibiotic prescribing and referral patterns.

Third, despite the increasing employment of hybrid simulation models in this field, their application is still ad-hoc without explicit rationalization and guidance on how the methods are combined. Few studies included in this review explicitly explain why they choose one method over the others to answer their research questions. The advantages of ABM over other simulation modelling methods were also discussed in four papers, mainly emphasizing its capability to simulate the heterogeneity of patients and behaviours of HCWs in healthcare settings and their contact networks (Hotchkiss et al., 2005; Hotchkiss et al., 2007; Temime et al., 2010; Caudill and Lawson, 2017). These studies indicated that ABM was the most appropriate for modelling an ICU where the population size is small and patient turnover is high. Neither a clearer explanation of the pros and cons of each simulation modelling nor when to combine them and what the benefits of doing so were found in the reviewed studies. Therefore, the rationale underlying the use of different simulation methods in HAIs is still not clear. The choice of simulation method should be problem-driven and depend on the research objectives and data availability. Future modelling studies should be encouraged to include an explicit explanation for selecting a specific simulation method. This would provide insights for researchers and modelers in this field with respect to the different uses for each simulation methodology. Furthermore, a comprehensive framework for choosing a simulation method should be broached in future research.

Fourth, the use of simulation modelling for economic analysis of different IPC measures and strategies has increased but is still relatively scarce (ten studies, 15%). The application of this method to evaluate the cost-effectiveness of various IPC strategies is promising in the sense that it can appropriately guide and prioritize the allocation of limited resources and funds. Hagtvedt et al. (2009) adopted DES to conduct a cost-effective analysis based on actual data from two hospitals in the US. This study strongly suggested the association between length of stay and HAIs, which had been ignored in previous publications (Graves et al., 2003; Roberts et al., 2003). Recently published studies paid more attention to the economic aspect of HAIs. They have estimated the cost-effectiveness of different IPC strategies and investments, mainly for MRSA (Hagtvedt et al., 2009; Hubben et al., 2011; Robotham et al., 2011; Gurieva et al., 2013; Robotham et al., 2016; Luangasanatip et al., 2018) followed by *Clostridium difficile* (Nelson et al., 2016; Stephenson et al., 2017). Economic analyses were carried out for a single intervention (i.e., hand hygiene (Hagtvedt et al., 2009; Luangasanatip et al., 2018), isolation (Hagtvedt et al., 2009), vaccination (Greer and Fisman, 2011; Stephenson et al., 2017), patient room design (Shin et al., 2017)), combinations of two (Hagtvedt et al., 2009; Gurieva et al., 2013) or three interventions (Robotham et al., 2011; Robotham et al., 2016), and a bundled strategy (Nelson et al., 2016). It can be seen that most studies focused on the cost-effectiveness evaluation of hand hygiene, screening, and isolation.

Fifth, there is insufficient understanding of other interaction types in a healthcare setting apart from interactions between doctors/nurses and patients. Only a limited proportion of the models simulated transmission caused by HCWs other than doctors and nurses (8%, six studies), which included peripatetic HCWs (Temime et al., 2009; Temime et al., 2010), rogue HCWs (Barnes et al., 2010), respiratory therapists, occupational therapists, speech therapists, physical therapists (Jiménez et al., 2013), admission personnel, auxiliary personnel and cleaning staff (Jaramillo et al., 2015), and volunteers (Wang et al., 2011). Additionally, Jiménez et al. (2013) created one of the most comprehensive social networks among patients and different types of HCWs in a simulated hospital in which individuals had their own activity schedules. Simulation modelling studies have hardly considered direct HCW-to-HCW contacts or interactions between visitors/caregivers and patients. Visitors/family caregivers can play a very important role in infection transmission in a health facility, especially in settings such as paediatric or geriatric health facilities where patients often need extra care. In many cultures, including Asian countries and LMICs, regular visits by visitors and caregivers are common practice and sometimes encouraged due to a considerable shortage of staff and a need to reduce medical costs to patients (Shin et al., 2017). As visitors and caregivers are also more mobile than patients, they are both highly susceptible to contracting infections and potentially able to transmit pathogens to various locations inside and outside of a health facility (Jiménez et al., 2013).

Last, the evaluation of clinical and cost-effectiveness was only conducted for a number of commonly used interventions like hand hygiene, isolation, and screening; further investigation on other IPC measures and a combination of different strategies is imperative to determine best practice in various healthcare settings. The intervention strategies investigated in the studies included in this review were: hand hygiene (39%, 23 studies), patient isolation (27%, 15 studies), screening, and antibiotic stewardship (22% for each type of intervention, 13 studies), decolonization (19%, 11 studies), and HCW cohorting (17%, ten studies). Some studies assessed the effectiveness of integrating two different IPC strategies, including the effect of combining hand hygiene and decolonization for MRSA (Webb et al., 2010), isolation and screening for MRSA (Bootsma et al., 2006), and screening and contact isolation (Lee et al., 2012). A study published in 2015 used simulation modelling to conduct a more intensive assessment of the impact of mixing four different interventions (Codella et al., 2015). Similarly, another publication released a year later assessed the benefits of a "bundle" IPC strategy (Nelson et al., 2016). Researchers have not extensively explored IPC measures such as vaccination, patient cohorting, barrier precaution, environmental disinfection, and referral patterns. Models can also be developed to simulate coordination and collaboration among health facilities to assess the impact of a regional IPC program.

3.3.4 Summary[7]

The review aims to consolidate and update the development and application of systems simulation modelling in studying HAIs. It can help guide further development of simulation models, especially hybrid models, to target gaps in knowledge in this field of research. In summary, the results of this review indicate that the complexity of simulation models for HAIs, in terms of the level of details of healthcare settings and interactions modelled and methodological designs, significantly increased over time. However, the context predominately remained focused on the transmission dynamics of MRSA in hospitals in HICs, rather than in other types of healthcare settings such as care homes or LMICs. Furthermore, the overview of existing simulation models in HAIs can facilitate and direct researchers to gap areas for further research, such as the transmission of HAIs in healthcare settings other than hospitals and across different types of settings. Future development and application of hybrid simulation models could help to secure further insights into HAIs.

3.4 Simulation Modelling for HAIs in Care Homes

Due to the many distinct characteristics of HAI transmission in care homes, the insights gained from simulation models for HAIs in hospitals may not be applicable in this setting. First, while HCW-patient contacts are the main driver of transmission described in most simulation models of HAIs in hospitals, these models have not captured other types of contacts that are important for driving transmission in care homes, including patient-patient and patient-visitor contacts. Although the majority of residents in care homes have their own room (NSS, 2017), they tend to spend a lot of time aggregating in common areas, including dining rooms, rehabilitation areas, and family visitation rooms. Sharing objects and space for a prolonged length of stay implies longer exposure to infectious pathogens carried by residents and HCWs (Strausbaugh et al., 2003; Utsumi et al., 2010). The resulting frequent contacts among residents, staff, and visitors can increase the risk of HAI spread. Second, ABM models for HAIs in hospitals have

[7] Taken from the Conclusions section in Nguyen et al. (2020c)

captured heterogeneous social and contact networks between patients and different types of HCWs, but these models have not accounted for heterogeneous individual characteristics such as age, morbidity, and mobility that are important to reflect variations in residents' susceptibility to infection, disease progression, and mortality (Hotchkiss et al., 2007; Barnes et al., 2012; Jiménez et al., 2013; Rubin et al., 2013; Jaramillo et al., 2015). Last, hospital model findings on the effectiveness of interventions such as patient isolation and cohorting are not applicable to care homes. Although many studies found that patient isolation was effective to control HAIs in hospital settings (Robotham et al., 2011; Cooper et al., 2004; Hagtvedt et al., 2009), this intervention is not practical in care homes. Care homes provide accommodation and support to elderly and frail residents with many having dementia, learning disabilities, and people with severe and enduring mental illness (ISD, 2018). These residents need to wander and benefit from wandering, making the effective implementation of resident isolation impractical (Halek and Bartholomeyczik, 2012). Also, significant staff shortages in care homes and the use of bank/agency staff (SSSC, 2020; Shembavnekar, 2020; Van Houtven et al., 2020) are likely to undermine the effect of cohorting.

Researchers have rarely applied systems simulation modelling to investigate the problems of HAIs in care homes. The systematic review we conducted identified only five publications (7%) that used this methodology to model HAI transmission within a care home and three (4%) papers that modelled inter-facility transmission between care homes and hospitals (Nguyen et al., 2020c). Three of the studies focusing on within-home transmission adopted SD and divided residents into compartments that represented different states of infection and mixed homogeneously within each compartment (Nuño et al., 2008; Chamchod and Ruan, 2012; Vanderpas et al., 2009). van den Dool et al. (2008) and Wendelboe et al. (2015) used DES to model stochastic transmission events in which individuals acquired infection at pre-defined probabilities. However, these models did not describe interactions between individuals explicitly, and individuals were homogeneous. Modellers have not taken advantage of ABM's ability to capture the heterogeneity of individual residents and HCWs in care homes, the stochasticity and complexity of their contacts, and the spatially explicit environment of this setting. These features are important for transmission dynamics occurring in a small, intricate care home environment.

DES models have contributed to our understanding of vaccination in the context of influenza in care homes but have not considered other infectious diseases. van den Dool et al.

(2008) developed a simulation model to investigate the impact of vaccination on influenza infections in care homes. Wendelboe et al. (2015) later reconstructed this model and compared its outputs with surveillance data from New Mexico . Both studies concluded that increasing the vaccination coverage among HCWs in care homes decreases the prevalence of influenza infection among residents. While the former asserted that a threshold for herd immunity could not be identified (van den Dool et al., 2008), the latter found that herd immunity can be achieved when outbreaks are defined as the presence of a single infected resident instead of as an attack rate among residents (Wendelboe et al., 2015).

SD models have explored non-pharmaceutical interventions in care homes, but to a limited extent and in an abstract manner that does not describe the interventions' details. Nuño et al. (2008) also studied the effectiveness of non-pharmaceutical interventions in preventing and controlling influenza transmission in care homes without a detailed description of the interventions. The study found that non-pharmaceutical interventions can prevent residents living in care homes from influenza pandemics without having to use pharmaceutical measures like vaccines and antivirals. This finding informs IPC practice in the scenarios in which pharmaceutical products are not readily available such as at the beginning of pandemics. The major constraint of implementing non-pharmaceutical interventions is that they require significant social change and high corporation and motivation from HCWs working in care homes. Chamchod and Ruan (2012) indicated that various IPC measures, including screening at admission, decolonization, hand hygiene improvement in both staff and residents, and increasing staff: resident ratio, are effective for MRSA prevention and control in care homes. Researchers have not studied other IPC interventions such as antibiotic stewardship, surveillance, cohorting, restricted or banned visitation, and bundled strategies nor the economic evaluation of such measures.

The application of single methods and hybrid simulation to explore transmission across settings has been limited (Barnes et al., 2011; Lee et al., 2013b; Lee et al., 2013c). Barnes et al. (2011) simulated MRSA transmission between a care home and a hospital via patient/resident transfers. This study used SD to model transmission dynamics within both the care home and the hospital. Lee et al. (2013b) and Lee et al. (2013c) investigated the impact of regional contact precaution measures on the prevalence of MRSA in a network of different healthcare settings, including hospitals and care homes via patient transfers. Other routes of inter-facility transmission via sharing staff and healthcare professional visitors have not been explored. Furthermore, researchers have not utilized the benefits of hybrid simulation to explore the dynamics between intra-facility and inter-facility transmission.

In conclusion, only a few simulation modelling studies have evaluated the clinical effectiveness and cost-effectiveness of IPC interventions in care homes in order to identify best practices in this setting. In particular, the heterogeneity of interactions between residents, HCWs, and visitors has not been modelled, and therefore, they are not well understood. Additionally, as care homes possess distinct features in terms of transmission dynamics within and across the settings and between hospitals and themselves, contact patterns, and the knowledge and perceptions of HCWs, these factors need to be taken into account when developing IPC strategies and policies for this type of setting.

3.5 Discrete Event Simulation and Infectious Disease Modelling

DES is a process-based simulation method used for modelling the operation of a system as a discrete sequence of activities and events in time, characterizing and analysing queuing processes and networks of queues, and solving problems of resource utilization (Pidd, 2004). Events, entities, attributes, and resources are the key components in DES. Entities are passive individual objects that possess attributes. These attributes are unique characteristics or features such as age and health status. Resources, as defined in DES, require time to provide a service to an entity, making other entities wait and form a queue. Entities consume resources while they experience events. However, the consumption of those resources does not depend on individual-level entity behaviour. As entities use up resources, they are indirectly competing with other entities in the queue (Karnon et al., 2012). DES can capture the effect of variability, stochasticity, and randomness of multiple elements within a system, but it does not explicitly model feedback or interactions between entities (Morgan et al., 2017).

The need for DES studies to model human behavioural aspects has been recognised for some time (Juran and Schruben, 2004; Brailsford and Schmidt, 2003), but the use of DES for this purpose is less common than ABM. Baines et al. (2004) indicated that DES studies that simulated manufacturing problems rarely included human aspects. A systematic review also showed the limited use of DES to model human behaviour in operations management (Greasley and Owen, 2018). In modelling HAIs, although ABM and DES models were introduced nearly concurrently, ABM has been used much more frequently to model HAIs than DES.

ABM is a more natural approach than DES to model populations of diverse individuals having a variety of attributes, behaviours, and interactions (Siebers et al., 2010). These features are important for epidemic models as individuals whose attributes, behaviours, and interactions drive the epidemic dynamics are the focus of interest. Problems concerning the spread of infectious diseases often do not focus on processes and, therefore, do not favour using DES. As an example, although Brailsford et al. (1992) developed a DES model to test different strategies for controlling HIV infections, some of the interventions examined were behavioural interventions and modelled in the essence of an ABM approach. In this model, the people's own behaviour determined what happened to them next. Furthermore, although DES has been recognized as a powerful tool to support decisions on health and social care services planning, Penny et al. (2022) suggested utilising a hybrid DES-ABM approach to model disease progression in a more natural and intuitive way than representing it as a series of queues and activities.

Applying DES to model complex behaviours such as interactions, movement, and proactive behaviour is problematic, while ABM offers more straightforward solutions for modelling such behaviours. Similar to ABM, DES allows the incorporation of detailed patient attributes and is well-suited to modelling the procedure of activities that patients progress through. However, unlike ABM, DES does not consider social contacts and interactions among individuals. Therefore, the transmission of infections needs to be simulated indirectly in a DES epidemic model by determining the next event to occur (Chhatwal and He, 2015). DES is also inappropriate to model human movement patterns as entities in a DES model are not independent and self-directed and are restricted to pre-determined routes (Brailsford et al., 2006; Baysan et al., 2009). By contrast, ABM with autonomous, self-directed agents makes it easier to model different movement patterns that are useful for capturing individual movements across settings or geographical locations in epidemic models and, therefore, to understand how pathogens spread (Manout and Ciari, 2021; Perez and Dragicevic, 2009; Simoes, 2005).

3.6 Chapter Summary

This chapter has provided a review of the application of single-method and hybrid simulation models in studying HAIs. It has revealed that the use of simulation models for studying IPC in care homes is scanty although the methods have been widely used in modelling HAI transmission in acute care settings. The chapter has also discussed why the findings of HAI models in acute care settings do not apply to the care home environment, and therefore, developing models that capture transmission characteristics specific to care homes is necessary. The need to develop novel models for addressing our research problem has led to the following research questions, which will be explored in Chapter 8 and Chapter 9.

Q5: How do we choose appropriate simulation modelling methods to tackle our research problem?

Q6: How do we design a hybrid model (if appropriate) to address our research problem?

Furthermore, this chapter indicates that the adoption of hybrid simulation models in HAIs has become increasingly common in recent years, but the areas of application are still limited. As only a few studies included in our review explain the rationale underlying the decisions to combine different simulation methods, the next chapter seeks to understand the benefits and challenges of combining methods (aligning with research question Q3 noted in Chapter 1).

Chapter 4. Hybrid Simulation for Modelling HAIs: Promising but Challenging

4.1 Introduction

The previous chapter presented a review of how simulation models have been used to study HAIs. The review showed a recently growing but still limited use of hybrid simulation models in studying HAIs. This chapter discusses the benefits in more depth but also highlights some challenges associated with the development and use of hybrid simulation models. The discussion in this chapter answers research question Q3 raised in Chapter 1.

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The overview (Section 4.2.1) has been adjusted to maintain the flow of the thesis and avoid repetition.

4.2 Benefits of Hybrid Simulation Models in HAIs[8]

4.2.1 Overview

The systems simulation community has found that combining systems simulation methods into hybrid simulation models (i.e., combining the methodological strengths of at least two of SD, DES, and ABM) can provide richer insights, answer questions that are difficult to answer with one simulation method, and improve the balance between simulation efficiency and accuracy, and these benefits are useful for modelling HAIs (Brailsford et al., 2013; Mustafee et al., 2015; Bobashev et al., 2007). For example, the combination of different systems simulation methods will be particularly useful for understanding the impact of IPC interventions in one part of the system on other components of that system or on the system as a whole because each method considers problems from a different perspective. Additionally, hybrid simulation modelling can help improve decision-makers' acceptance of a model by enabling modellers to incorporate greater details of particular model components. For example, modellers can integrate an ABM component into an SD model that represents the transmission of HAIs in a hospital to provide greater details of the transmission occurring in a hospital ward to address credibility concerns. Increasing the model's credibility can lead to increasing acceptance and adoption of the model by decision-makers in HAIs.

Despite hybrid system modelling's significant potential, it has had limited application to HAIs. A systematic review indicates that healthcare is the largest application area for hybrid simulation, even though this included only 31 papers, representing 22% of the total publications in hybrid simulation (Brailsford et al., 2019). Furthermore, our systematic review identified that only nine out of 68 publications modelling HAIs use hybrid simulation; the others use single simulation methods (Nguyen et al., 2020c). The scant application of this method implies that the systems simulation community and researchers in infection control should work together to increase awareness of hybrid simulations' potential benefits. Although a few published papers have discussed the need to consider health systems using systems modelling (Verguet et al., 2019; Rutter et al., 2017), none describe the advantages of combining methods, and none consider HAIs.

[8] Section 4.2 includes the adjusted introduction and the first three sections in Nguyen et al. (2020b).

4.2.2 A Method to Promote Richer Insights beyond Single Simulation Approach

Combining the strengths of different simulation modelling methods can provide richer insights for specific questions than using a single simulation method. As SD, DES, and ABM have distinct benefits, limitations, strengths, and weaknesses, combining them can overcome the drawbacks faced by using a single approach. Hybrid simulation can also provide a more plausible explanation and, therefore, richer insights into a problem than a single simulation approach.

The hybrid model in Barnes et al. (2011) provides an example that demonstrates how a hybrid method can generate richer insights compared to using a single simulation method. This study adopted a hybrid SD-ABM model to investigate the impacts of transferring patients between different healthcare facilities upon the prevalence of HAIs at each facility (Barnes et al., 2011). Each healthcare facility was modelled as an agent in a network of various facilities with a predefined configuration of directed links representing patient movement from one facility to another at a specific rate. An SD model embedded within each healthcare facility agent represents the transmission dynamics within the facility. Like traditional epidemiological compartment models (e.g., Susceptible-Infected-Recovered models) (Anderson, 1991; Daley and Gani, 2001), stocks of the SD model represent corresponding susceptible patients, persistently and transiently asymptomatic carriers. Proportions of patients in different infection states constitute a unique state that characterizes each facility agent. The hybrid model helps understand the impact of the heterogeneity and stochasticity of different configurations of patient transfer on the transmission of HAIs within each facility. Reshaping this model to use ABM alone requires the researchers to remove the SD component within each agent health facility or replace this component with an ABM, which models each facility in the network at an individual entity level. The former approach does not capture the dynamics of HAI transmission within each facility and thus the impact of inter-facility connections upon this intra-facility transmission dynamics. The latter approach will obfuscate this impact since both the interconnectivity between facilities and the heterogeneity among individuals in each facility would concurrently influence the transmission of HAIs in this approach. It is important to separate these effects to identify whether heterogeneity/interactions within facilities or heterogeneity/interactions across facilities primarily cause the spread of HAIs. This understanding can help inform whether interventions such as active screening and decolonization of all transferred patients are required. Another way to reshape this model is to use SD alone. However, this would provide poorer insights on the heterogeneity and stochasticity in the interconnections between facilities and, thus, their impact on the transmission of HAIs within each facility. There are other examples of hybrid models taking similar approaches in literature (Vincenot and Moriya, 2011; Banos et al., 2015; Bradhurst et al., 2015).

4.2.3 A Method to Support Decision-Makers at Different Levels of Management

Another benefit of hybrid simulation modelling is that it permits healthcare decision-makers and policy-makers to study a problem at different levels of abstraction. SD often deals with high abstraction levels, whereas DES is used for low to middle abstraction levels, and ABM can be applied across all levels but is preferably used for low levels (Borshchev and Filippov, 2004). The modeller will find SD useful to quickly evaluate an IPC program implemented in a large population and provide an integrated and holistic view of feedback systems that can affect outcomes of the program years or decades later without knowing how processes take place at the micro-level within each healthcare facility. Health policymakers at a high level would find this type of simulation modelling helpful to inform their decisions at a strategic-level decision that influences a large-sized population in the long run. By contrast, ABM is well-suited for evaluating the operational level of the program. It can be used when agents, their characteristics, behavioural rules, and interactions are well understood, but the emergent and stochastic behaviours of the system are unknown. ABM can also be used to explore and understand unknown characteristics, behaviours, and interactions of individuals at the operational level when the system outcomes for particular scenarios are known.

For example, a hybrid simulation model that combines an SD and ABM approach can be used to evaluate an IPC intervention such as hand hygiene in hospitals at both strategic and operational levels. Modellers can develop SD and ABM models in parallel, which provide two representations of the same system, offering complementary insights into the system. The SD model can generate a general view of the long-term impact of hand hygiene upon the dissemination of HAIs. This would be of interest to decision-makers at a high level who are responsible for developing general guidelines or standards for infection control in hospitals. However, ABM is the most appropriate method to capture the spatial intricacies of a hospital ward. It accounts for the stochasticity of transmission events due to individual variations in characteristics (e.g., HCW profile, daily schedule, and patient allocation) and the time and space heterogeneity of their behaviours (e.g., hand hygiene compliance and efficacy) and interactions. Additionally, ABM allows adaptive behaviours of individual HCWs to be incorporated, such as increasing hand hygiene compliance when performing high-risk medical procedures and providing care for infected patients. The flexibility to explicitly model all of these factors simultaneously also makes ABM more appropriate to address questions for which they are all important. Individual heterogeneity and the interactions of these factors affect the transmission dynamics (Rahmandad and Sterman, 2008); for example, it can cause super-spreading events in which cross-transmissions to a large number of patients are mediated via a single HCW (Temime et al., 2009). Identifying super-spreaders can help inform the target groups for interventions that aim to improve hand hygiene compliance at the operational level.

Brailsford et al. (2010) argued that although using one simulation method is possible to represent problems at a macro- and micro-level at the same time, they described this approach as “a case of hammering in a screw” because it forces modellers to use a simulation method that may not be suitable for all components of the problem. Morgan et al. (2011) also agreed that it may not possible to develop a model using one method to obtain all of the intended objectives without the need for additional assumptions which risks making the model less representative of reality.

4.2.4 A Method to Balance Simulation Performance and Result Accuracy

Hybrid simulation modelling is helpful for handling trade-offs between simulation performance and the accuracy of results, which is the degree to which the model results/predictions conform to the actual outcomes (macro-level predictions), and avoids the need for an excessive amount of input data (Mustafee et al., 2017). The accuracy of results, in this case, could be measured using methods such as hypothesis statistical testing, mean absolute scaled errors, root mean square error, and mean absolute error (Hyndman and Koehler, 2006). As deterministic models yield a single outcome for each parameter set while stochastic models produce a distribution of possible outcomes, the literature recommends averaging a sufficient number of simulations to assess the accuracy of stochastic models’ results (Hassan et al., 2013). In addition to the single-valued forecast, probabilistic forecasting, which aims to quantify the inherent uncertainty in predicting the future in stochastic models, can be assessed by methods such as marginal calibration plots, probability integral transform histograms, sharpness diagrams, and proper scoring rules (Funk et al., 2019; Gneiting et al., 2007).

Running SD models is extremely quick because they are deterministic and do not need several replications to gain insights into a system's behaviour. Also, the data requirements of SD models are generally less than those of DES models or ABMs as they are typically used at a higher and more aggregated level. However, Forrester (1960), who first introduced SD, contended that SD models are "learning laboratories" (Forrester, 1960), and later research even argued that outcomes produced by SD models are seldom greater than 40% accurate (Lane, 2000). DES and ABM are capable of modelling a problem in much more detail than SD, providing the flexibility for a closer representation of reality. However, they require a vast amount of data and several simulations to generate reliable results, which is time-consuming to collect and run. Hybrid simulation modelling offers a top-down approach where researchers can model a problem at a macro-level using SD and then zoom in on certain aspects of the problem that require microscopic understanding, using DES or ABM. Modellers often try to keep their models as simple as possible whilst seeking to still produce reasonably accurate results. An abstract SD model that represents a system at a macro-level, where causal relationships and feedback effects are revealed, is often faster to run and requires fewer data inputs compared with a micro-level DES or ABM model that represents the spatial details and microstructure of the same system. Hybrid simulation modelling can be used to solve the issue of balancing the simulation performance and the accuracy of results.

Mustafee et al. (2017) used the study of Djanatliev (2015) as an example to demonstrate this benefit of hybrid simulation modelling methods. In this study, three models that represent the same problem in healthcare were developed using a single method of SD and ABM and a hybrid simulation modelling method where SD and ABM were combined. The first model had been developed using only SD, and it took a few seconds for this model to finish running, even for a nationwide population size. By contrast, simulations of the second model, using ABM, took 1.5 hours to run, and the model comprising more than 20,000 agents was not able to complete. However, the author stated that the ABM produced much more accurate results because of a more detailed presentation of the problem. They then developed a hybrid simulation model by using ABM to model and represent specific parts of the SD model whose greater details were of interest to the problem being considered. Agents with similar properties that had been created in the ABM were also aggregated into one super-agent. This hybrid simulation model generated results comparable to those of the ABM in an acceptable runtime. When weighing result accuracy and model simplicity, it is important to emphasize that the level of accuracy is dependent upon the research problems and objectives. For example, estimating the costs of IPC interventions for resource planning and allocation would require a higher level of result accuracy than evaluating the clinical effectiveness of the interventions for directing further research.

The ecology dynamic hybrid SD-AB model in Wallentin and Neuwirth (2017) is another example of the use of hybrid simulation that optimizes the trade-off between the predictive and computational modelling performance. The model dynamically alters among different SD-ABM configurations where, for instance, one entity may be represented by stocks and another entity is represented by agents. The switching point is informed by a threshold determined by the size of the population of interest. This results in heterogeneity and spatial networks among individuals of each entity type having more or less impact on the model's outcomes. A similar approach is adopted in Bobashev and his colleagues' epidemiological modelling study in which the model begins as an ABM when the number of infected people is small, and individual variation is critical, and switches to a SD model after the infected population becomes large enough to apply the population-averaged approach (Bobashev et al., 2007).

4.3 Challenges in Developing and Applying a Hybrid Simulation Model[9]

Developing and applying a hybrid simulation model is a challenging task. First, although there have been some conceptual publications and guidelines on the development of frameworks for combining different simulation methods (Morgan et al., 2017; Swinerd and McNaught, 2012; Chahal and Eldabi, 2008; Mustafee et al., 2017), these works studied hybrid simulation modelling only at a high level and did not provide overarching methodological frameworks that explicitly guide and specify how modellers can apply them to develop their model. Indeed, there is not yet any evidence that these frameworks are comprehensive, useful, and practical enough to apply when building a hybrid simulation model. Zulkepli and Eldabi (2015) also asserted that most attempts to hybridize different simulation modelling methods have been "ad-hoc and pragmatic with no clear methodology". Additionally, although a few studies (i.e., none of these is about modelling in HAIs or healthcare) reported the validation and verification for single-method sub-models in a hybrid simulation model using existing standard approaches for single-method models (Brailsford et al., 2019), more comprehensive propositions to validate

[9] This section has been taken from Nguyen et al. (2020b).

and verify the overarching hybrid models are needed. These barriers make it difficult and time-consuming to develop, verify, and validate a hybrid simulation model, which in turn prevents this approach's wider adoption.

Second, although the selection of a simulation modelling method should be objective-driven, the best modelling approach is often ambiguous. Modeller expertise, experience, and preference may bias the decision on when the use of a hybrid simulation model is needed and beneficial. Thirdly, the reasons for choosing a specific simulation modelling approach are inseparable from the intention of solving a problem more efficiently, requiring less time, effort, and cost inputs. The research community has yet to conclusively determine when using a hybrid simulation model offers a quicker, easier, and cheaper approach to solving a complex problem than using a single simulation modelling method (Mustafee et al., 2017). The development of multi-method simulation modelling tools, which are more user-friendly to modellers and offer a free version for personal learning, can counteract the resistance to use hybrid modelling and help reduce time and effort inputs. Further studies which explore when to use which simulation modelling method (i.e., single or hybrid simulation) in modelling HAIs can guide modellers to choose appropriate methods. Encouraging and requiring modellers to rationalize the simulation method used in published works can help prevent them from selecting a particular method just because they feel comfortable with it. This approach also leads to the availability of case studies of hybrid models in HAIs, which offer an explicit clarification to justify the use of hybrid simulation.

Finally, it can be argued that the need for hybrid simulation models potentially initiates from attempts to model a problem as close to reality as possible to improve the prediction capability of the models. However, this purpose may be achieved at the trade-off of their generalizability, the degree to which they can be validated and verified, and without the guarantee that they will capture more detail that results in more insights (Mustafee et al., 2015). The development of more comprehensive validation and verification approaches, along with promoting the collection of relevant clinical data in HAIs for model inputs and validation, can help address this challenge. Addressing these challenges will facilitate the process of developing valid and credible hybrid models, and therefore, improve the acceptance and adoption of the models among healthcare professionals and policymakers whose decisions will drive impacts on health outcomes such as improvements in HAIs.

4.4 Chapter Summary

Like any other research method, hybrid simulation modelling has both benefits and drawbacks. It can generate richer insights compared with a standalone simulation method for specific questions, allow for modelling a system at different abstraction levels that supports decision-making at different levels of management, and balance simulation performance and result accuracy. Thus, its application in modelling HAIs can improve the understanding of HAIs as well as aid strategy and planning for infection prevention and control. Additionally, it is increasingly recognized that when finding solutions to healthcare problems, it is important to consider the system as a whole rather than focus on individual parts. Therefore, hybrid simulation is promising and potentially beneficial for capturing the links and interdependencies between different parts of the system. However, applying hybrid simulation to HAIs and other healthcare problems is complex and challenging due to the unavailability of comprehensive guidance and technical obstacles. Deciding when and why this method should be chosen for a particular question and judging whether it is worth the challenges it creates will be a subjective decision, depending on the researcher's objective and expectations.

This chapter discussed the promising benefits of hybrid simulation modelling methods. However, the challenges of developing hybrid models restrict their application in practice. One of these challenges is the lack of a comprehensive methodological framework to guide how modellers can combine simulation modelling methods, especially mixing SD and ABM, the two commonly used methods in infectious disease modelling. This gap in the literature has led to the following research questions, which will be explored in Chapter 5.

Q7: What existing theoretical guidance, such as frameworks and toolkits, are available to inform the designs of SD and ABM hybridisation?

Q8: What are the limitations of the existing guidance on mixing SD and ABM?

Chapter 5. Existing Guidance on Combining SD and ABM

5.1 Introduction

Researchers/practitioners using single simulation modelling approaches can face significant challenges representing the multi-dimensional nature of complex systems composed of interactive and interconnected constituents with dynamic behaviours. Combining different simulation methods offers an opportunity to overcome these challenges and capture important characteristics and behaviours of such systems. Despite the growing interest and popularity in this approach, guidance for designing and utilizing hybrid models, especially for those combining SD and ABM, is scanty. This chapter aims to address the two research questions raised in Chapter 4:

i) Q7: what existing theoretical guidance, such as frameworks and toolkits, are there to inform the designs of SD and ABM hybridization and
ii) Q8: what are the limitations of the existing guidance on mixing SD and ABM.

5.2 Overview of Existing Theoretical Guidance on Combining SD and ABM

Although SD and ABM are different in terms of their philosophical approaches, both methods possess strong explanatory capabilities and can be combined (Phelan, 1999; Bobashev et al., 2007). The top-down approach of aggregated feedback of SD and the bottom-up approach of ABM can complement one another in a hybrid simulation modelling design to provide useful insights into complex systems. Combining SD and ABM enables problem owners to deal with different factors of system complexity, including micro, meso, and macro perspectives; strategic, tactical, and operational levels; and detail and dynamic complexity (Morel and Ramanujam, 1999; Begun et al., 2003).

SD and ABM have already been used separately to study the same problem. For example, Scholl (2001b) compared SD and ABM literature on the bullwhip phenomenon, which arises in supply-chain management, and Rahmandad and Sterman (2008) studied literature using these methodologies to model "networking" problems such as innovation diffusion and AIDS dissemination through needle sharing. These reviews indicate differences and similarities between results and explanations of the studied phenomena in the two simulation modelling methods. In addition to supply chain management and diffusion, SD and ABM methods were also compared in areas such as ecology (Norling, 2007) and biology (Wakeland et al., 2004). Applying the two methods separately to study the same problem provides fruitful insights, cross-validation, and triangulation of results (Phelan, 2004). While the early works focus on the use of one simulation modelling method to validate outputs generated by the other and triangulate outputs, a growing number of studies using hybrid SD-ABM approaches have shown the diversity in the designs of hybridization of the two methods. Following a review of literature on the existing theoretical guidance to design a hybrid SD-ABM simulation model, the results of different designs for a hybrid SD-ABM model are summarised in Table 5.1. Although some of the studies included in this table provide guidance on mixing SD and DES, mixing analytic and simulation modelling, or mixing methods in general, the hybrid designs they proposed can inform the mixing of SD and ABM. It should be noted that Lättilä et al. (2010), Onggo (2014), and Djanatliev and German (2015) are not included in Table 5.1 (see Appendix B for the full table). Although these studies provide guidance on mixing simulation methods, they did not describe specific hybrid designs.

Table 5.1: The existing theoretical guidance/frameworks for combining SD and ABM

References	**Designs for a hybrid SD-ABM model**					
	Parallel	**Sequential**	**Interaction**	**Enrichment**	**Integration**	**Dynamic**
(Shanthikumar and Sargent, 1983)	Class I	Class III, IV			Class II	
(Bennett, 1985)	Comparis-on			Enrichment	Integration	
(Kim and Juhn, 1997)				Multi-Agent Dynamics where a hybrid model is constructed with the principles of SD and using array variables to represent the individual agents		
(Parunak et al., 1998)				Agents modeled using the equations of SD. An agent can be part of a bigger SD.		

References	Designs for a hybrid SD-ABM model					
	Parallel	Sequential	Interaction	Enrichment	Integration	Dynamic
(Akkermans, 2001)				Using SD to model the logic of individual agents		
(Schieritz and GroBler, 2003)				Using SD to model the internal decision logic or cognitive structure of the agents in an ABM		
(Borshchev and Filippov, 2004)				SD sub-models inside discretely communicating agents Agents live in an environment whose dynamics is modeled using SD		
(Lorenz and Jost, 2006)				Using SD structures to create entities for an ABM An "active" environment		
(Bobashev et al., 2007)						Hybrid threshold model
(Martinez-Moyano et al., 2007)		Scenario exploration and Crisis response			Intertwined models	
(Chahal and Eldabi, 2008)			Hierarchical format	Process - Environment format	Integration format	
(Brailsford et al., 2010)					The "Holy Grail"	
(Vincenot et al., 2011)				Case 1, 2, and 3		Case 4
(Swinerd and McNaught, 2012; Swinerd and McNaught, 2014)	Interfaced class	Sequential class			Integrated class including: Agents with rich internal structure, stocked agents, parameters with	

References	Designs for a hybrid SD-ABM model					
	Parallel	Sequential	Interaction	Enrichment	Integration	Dynamic
					emergent behavior	
(Chahal et al., 2013)		Cyclic interaction	Parallel interactions			
(Wallentin and Neuwirth, 2017)					“Super-agents”	Dynamically switching hybrid model
(Morgan et al., 2017)	Parallel	Sequential	Interaction	Enrichment	Integration	

5.3 Designs for Combining SD and ABM

We identified and classified the existing combinations of SD and ABM into six designs, including parallel (genuinely independent), sequential (loosely coupled), interaction, dynamic, enrichment, and integration (inseparably coupled). As the literature uses different sets of terminology to describe similar designs, we will not explain all terminology but only the general ideas for each design. Detailed explanations can be found in the referenced papers.

5.3.1 Parallel Design

This design includes Class I in Shanthikumar and Sargent (1983), Comparison mode in Bennett (1985), Interfaced class in Swinerd and McNaught (2012 and 2014), and Parallel in Morgan et al. (2017). In this design, SD and ABM are used to develop independent models either to address different aspects of the same problem which are better suited to one particular simulation method or to represent the same problem for direct comparison. Results of these models are ultimately combined to solve the same problem or compared to enhance confidence in the output produced by each model.

5.3.2 Sequential Design

The sequential design has been described in several publications, including Class III and IV in Shanthikumar and Sargent (1983) (the detailed description of these two classes can be found in Table B.1), Scenario explanation or Crisis response in Martinez-Moyano et al. (2007), Sequential class in Swinerd and McNaught (2012 and 2014), Cyclic interaction in Chahal et al. (2013), and Sequential design in Morgan et al. (2017). The word “sequential” itself already illustrates the logical order of processes. This design also includes two or more separate models embedded in different simulation modelling methods in which one model is used to inform the other. One simulation is run first and produces the required output, which becomes the input for the second simulation. The first simulation then terminates before the second simulation starts to run. Data are strictly passed once from the first simulation to the second one. The output of the second simulation represents the final output of the hybrid model.

5.3.3 Interaction Design

In this design, different sub-models developed using different simulation modelling approaches are considered equally important and interact cyclically during run time. Interactions between sub-models occur several times in two directions. The sequential design can be considered as a special case of the interaction design when the interaction occurs once and in one direction only. Publications that describe the design for a hybrid simulation model aligning with interaction design include Hierarchical format in Chahal and Eldabi (2008), Parallel interaction in Chahal et al. (2013), and Interaction design in Morgan et al. (2017).

5.3.4 Integration Design

Integration is an approach to combining different simulation modelling methods to create one seamless hybrid model in which it is impossible to explicitly distinguish between SD parts and ABM parts and to tell where one simulation approach ends and the other starts (Swinerd and McNaught, 2012; Brailsford et al., 2010). This design offers a coherent view of the problem, which enhances continuous flows of information and feedback and captures interactive effects within a system. Shantikumar and Sargent’s Class II, Bennett’s Integration, Martinez-Moyano et al.’s Intertwined models, Chahal and Eldabi’s Integration mode, Brailsford, Desai and Viana’s “Holy Grail”, Swinerd and McNaught’s Integrated class, and Morgan et al.’s Integration are in essence this integration design. Although several studies concur in the definition of integration design, only Swinerd and McNaught described different ways to develop an integrated hybrid model in detail. They proposed three designs that belong to the integrated class, including agents with rich internal structure, stocked agents, and parameters with emergent behaviour.

5.3.4.1 Agents with Rich Internal Structure

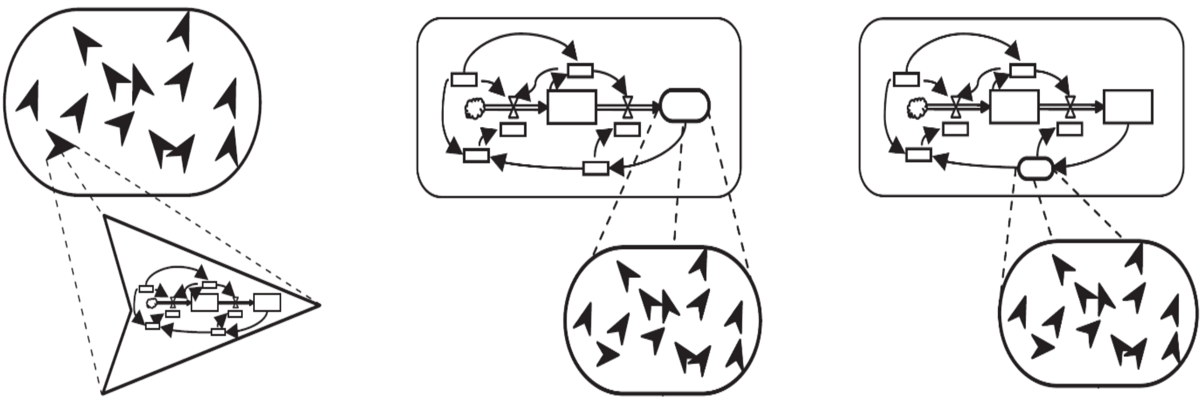
SD is used to model the internal dynamics in decision logic or cognitive structure of agents in an ABM (Figure 5.1A). The output of the SD component will inform behaviours, decision rules, and/or characteristics of agents. Additionally, interactions between an agent with other agents within an ABM can influence the dynamics of the internal SD model within that particular agent. Swinerd and McNaught are not the first investigators who have described this design, but they are the only ones who classify this design as integration. A lot of earlier works have suggested this design consisting of those published by Parunak et al. (1998); Akkermans (2001); Schieritz and GroBler (2003); Borshchev and Filippov (2004); Lorenz and Jost (2006), and Vincenot et al. (2011). More recently, the term “super-agents” proposed by Wallentin and Neuwirth (2017), in which stocks are embedded in agents, also aligns with this design. For example, Schieritz and GroBler (2003) present an integrated model for supply chains with an ABM sub-model representing the connections between companies within the supply chain and SD sub-models describing company decision-making. They chose this integrated design as the interconnected relationships between companies within the supply chain alters with time. Thus, they decided to complement SD with ABM to enhance the model’s flexibility to better capture supply chain connectivity as a function of time.

5.3.4.2 Stocked Agents

Stocked agents and parameters with emergent behaviour are in essence cases 1 and 3 discussed in Vincenot et al. (2011), where individual agents within an ABM interact with a single SD model (Figure 5.1.B). An aggregate measure of an ABM is bounded by a stock level of an SD module. Information tends to flow in one direction from SD to ABM in this case. Robledo et al. (2013) develop a forecasting enrolment model of this design for resource planning. The SD sub-model represents the overall enrolment system of a university, while the ABM sub-model simulates students’ heterogeneous behaviours such as enrolling, dropping a class/course, or transferring to another class at the departmental level. The sum level of stocks for students that have declared their major in Engineering or have not chosen a major bound the headcount of students in that department.

5.3.4.3 Parameters with Emergent Behaviour

In this type of integrated design, a parameter within an SD model is informed using an aggregate observation or measure of an ABM (Figure 5.1C). Opposite to the "stocked agents" design, this design directs the flow of information from the ABM component to the SD component. Kieckhäfer et al. (2009) describe an integrated model for production strategy in the automotive sector with an ABM sub-model representing individual customers with heterogeneous socio-economic characteristics relevant to their preferences and purchase decisions and an SD sub-model modelling feedback relationship in the automotive market. The emergent behaviour of the ABM sub-model resulting from the individual, discrete consumer purchase decisions informs the parameter *the number of sales* which eventually affects the production rate in the SD sub-model.



(A) Agents with rich internal

(B) Stocked agents

(C) Parameters with emergent behaviour

Figure 5.1: Swinerd and McNaught's three concepts of integrated SD-ABM hybrid design
Reproduced from "Design classes for hybrid simulations involving agent-based and system dynamics models", by Swinerd, C., and McNaught, K.R., 2012, Simulation Modelling Practice and Theory, 25, 118-33. Copyright 2012 by Elsevier B.V. Reprinted with permission.

5.3.5 Enrichment Design

Enrichment design has only been discussed in a few papers, including Bennett (1985) and Morgan et al. (2017). Chahal and Eldabi's Process Environment format would be debatably considered as a special case of the enrichment design when the SD component is dominant and the ABM component is relatively minor (Chahal and Eldabi, 2008). This design combines different simulation modelling methods to form one unified hybrid model in which one method dominates and is enhanced by elements of another. As enrichment and integration designs share many similarities, there seems to be a continuum from enrichment to full integration in hybrid simulation modelling designs depending on the relative dominance between the adopted simulation approaches.

5.3.6 Dynamically Switching Design

The dynamic hybrid simulation modelling design illustrated in the work of Bobashev et al. (2007) and Vincenot et al. (2011) (Case 4) allows the dynamic switching between SD and ABM in the structure of a model. This idea was expanded by Wallentin and Neuwirth (2017), in which they suggested four different representations of entities in a system. This results in numerous SD-ABM model configurations where, for instance, one entity may be represented by stocks and another entity is represented by agents. The model dynamically alters among different SD-ABM configurations. The switching point is informed by a threshold at which the size of the population of interest is small or large enough, making the impact of heterogeneity among individuals of each entity type on the model's outcomes become more or less significant, respectively. The authors rationalized the use of this design to optimize the trade-off between the predictive and computational modelling performance. The application of this design in epidemic problems was described in the work of Bobashev et al. (2007), where their hybrid model begins as an ABM when the number of infected people is small and individual variation is critical, and switches to an SD model after infected population becomes big enough to apply the population-averaged approach. The dynamic switching between the two representations of the problem efficiently depicts the process of an ongoing epidemic.

5.3.7 Summary

This section has presented a review of the characteristics of different hybrid SD-ABM designs. Most studies reviewed describe these designs at a high level and emphasize their differences based on the direction of interaction and frequency of interaction over a time window. Enrichment, interaction, and integration designs share many similarities and differ only in terms of the separability and dominance of the SD and ABM sub-models constituting a hybrid model. The relative nature of these characteristics leads to the difficulty in selecting an appropriate design for a hybrid model. In Chapter 7, we will explain how these hybrid simulation designs have influenced the proposed framework.

5.4 Limitations of Existing Guidance for Hybridizing SD and ABM

There are three major limitations of the studies shown in Table 5.1 when providing guidance on combining SD and ABM. Firstly, they do not specify the processes that modellers need to take and which aspects they need to consider to reach a decision on the design of a hybrid model. Secondly, we note that such guidance is established at a high level, and it is, therefore, still quite abstract and not straightforward for problem owners to apply in solving a specific problem. Lastly, most of the existing hybrid simulation modelling studies focus on dealing with issues of particular domains such as inter-organizational network development in Akkermans (2001) or supply chain management in Schieritz and GroBler (2003) rather than offering broader but more detailed guidance specifying when, why, and how to combine SD and ABM approaches.

5.5 Research Gaps

The literature review chapters (Chapters 2 – 5) explored the following research questions:

Q1: How have HAIs in Scottish care homes been controlled and prevented? What have been the challenges of IPC practice in this setting?

Q2: How have simulation modelling methods been used on their own and together to understand and solve the problems of HAIs?

Q3: What benefits do simulation modelling and hybrid simulation modelling methods offer to study the problems of HAIs? What are the challenges of mixing methods?

Q7: What existing theoretical guidance, such as frameworks and toolkits, are there to inform the designs of SD and ABM hybridization?

Q8: What are the limitations of the existing guidance on mixing SD and ABM?

Addressing questions 1 and 2 has helped identify the gaps in the literature with respect to characteristics of transmission dynamics of HAIs and evidence of effective IPC interventions to control the spread of HAIs within and between care homes. It has also revealed the limited use of simulation modelling, especially hybrid simulation modelling methods, in this area of research. As the COVID-19 pandemic has had a devastating impact on the social care sector, especially in care homes, this research will focus on COVID-19 to address the urgent need for support for evidence-based decisions and practice in this setting.

Addressing questions 3, 7, and 8 has provided some guidance on selecting appropriate methods and building our simulation models that study the problem of HAIs in care homes. It has also disclosed gaps surrounding mixing SD and ABM that will be explored by reflecting on our hybrid model and the modelling processes that we will go through. These gaps have led to the following research questions, which will be explored throughout the rest of this thesis. Figure 5.2 provides the flowchart of all research questions covered in this research.

Q4: How can we prevent and control the spread of COVID-19 within and across care homes?

Q5: How do we choose appropriate simulation modelling methods to tackle our research problem?

Q6: How do we design a hybrid model (if appropriate) to address our research problem?

Q9: How do we develop new/improved theoretical guidance on mixing SD and ABM that addresses the limitations of existing guidance?

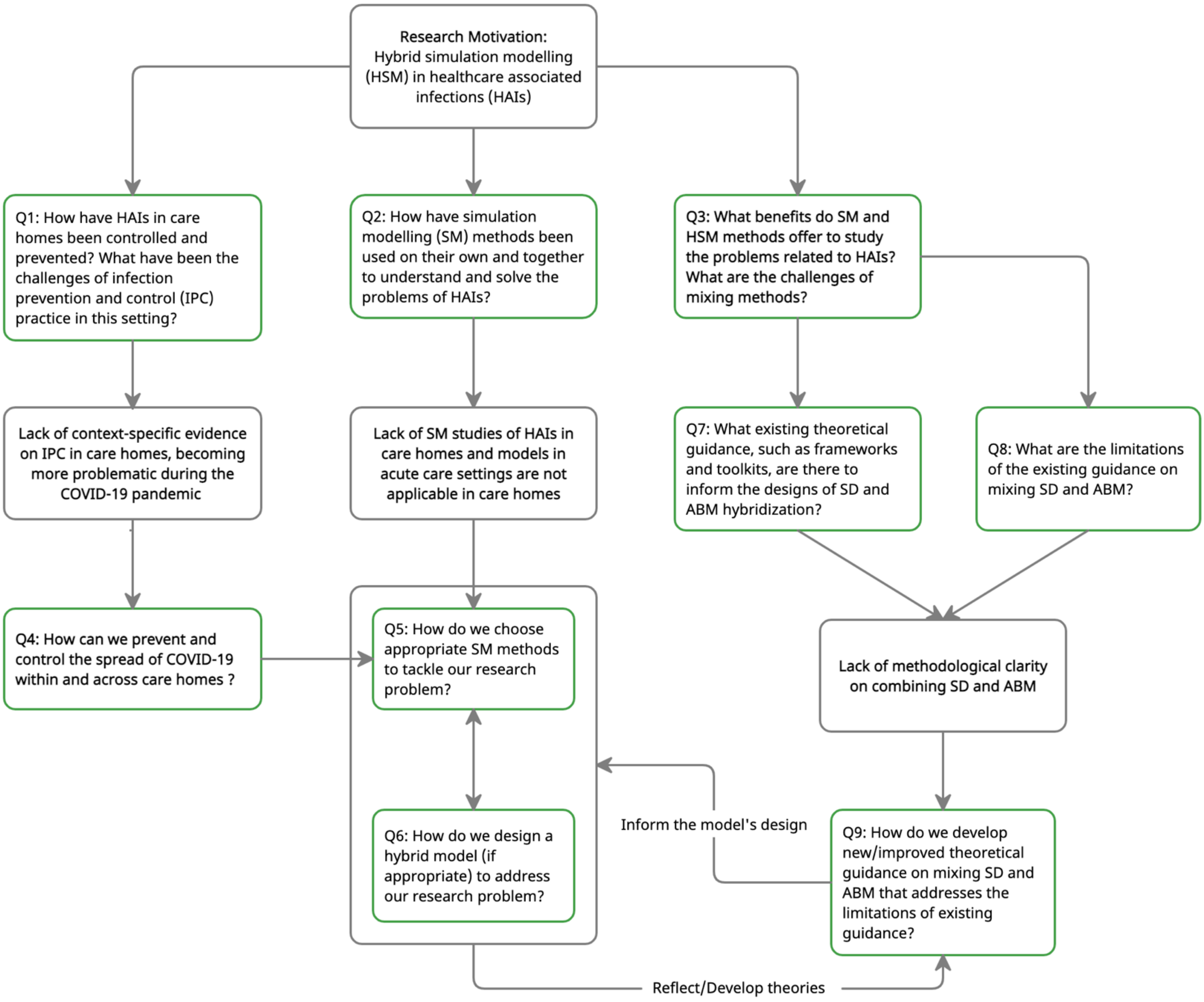


Figure 5.2: Flowchart of research questions

The next chapter discusses the research design given the research aims. It also presents four research objectives summarizing the above research questions identified through the literature review chapters.

Chapter 6. Research Design

6.1 Introduction

Research is experimental and/or theoretical work undertaken on a systematic basis to acquire new knowledge, including knowledge of humans, culture, and society (OECD, 2015). At every stage of research, researchers make different types of assumptions, including epistemological assumptions about what can be known, ontological assumptions about the nature of reality, and axiological assumptions about the extent and ways the researchers' own values influence their research process (Burrell and Morgan, 1979). These assumptions inevitably impact how researchers understand their research questions, how they choose the methods, and how they analyse their results and interpret their findings (Crotty, 1998). Thus, we adopt a consistent and well-thought-out set of assumptions (i.e., a credible research philosophy) that allow us to design a coherent research project.

This chapter presents the design of the research undertaken, which involves the plans and procedures to collect and analyse data in order to answer the research questions (Creswell, 2014). The chapter starts with a discussion about the research philosophy in which we explain why critical realism is a better fit for the nature and context of the research problem compared with positivism. There follows a discussion of the appropriate research methodology for the research problem. This discussion explains why we choose to adopt the case study methodology over the action research methodology. The chapter then discusses the choice and appropriateness of several research methods for data collection informed by the case study methodology. It concludes with the research plan and a note on ethics approval.

6.2 Research Philosophy: Critical Realism

A paradigm can be defined as a dominant ideological or philosophical stance, a system of beliefs about the world's nature and an assumptive base that guides the way we do things, the way we produce knowledge, and the establishment of a set of practices (Rubin and Rubin, 2005). The paradigmatic positioning of a researcher depends upon their epistemological standpoint (their understanding of the nature of knowledge) and their ontological standpoint (their understanding of the nature of reality).

Despite the plethora of academic criticism, positivism remains the dominant paradigmatic basis in the realm of public health research (Kaur, 2016). Its ontological position is that reality is both concrete and external, and objectivity, which exists independent of human perception, is achievable (Sale et al., 2002). Reality can be measured using the scientific method, a process in which a hypothesis is formulated, objective experiments are performed, and data are collected to support sound reasoning. Epistemologically speaking, researchers are independent entities capable of investigating reality without influencing it or being influenced by it. Causal relationships between variables can be measured and analysed within a value-free framework (Denzin and Lincoln, 1998). Randomization and blinding can be taken as examples of the techniques used to ensure a sense of objectivity in research. Under a positivism framework, the preferential "quantitative approach" has been used ubiquitously to define problems (the 'what'), to compute their magnitude with respect to place, time, and people (the 'where', 'when', and 'who') as well as to determine their causes (the 'why' and 'how') (Kaur, 2016). Although positivism takes context into account to some extent, it tends to convert social variables into measurable physical terms (Alderson, 1998), such as how age, sex, and race affect the likelihood of HAI contraction.

Many questions about healthcare are not amenable to positivism. The mismatch between the predominant mechanistic conception of healthcare and the complex social nature of health has proved to be a challenge for innovation in health and health services management research (Plsek and Wilson, 2001) and for the implementation of evidence-based medicine and health policy (Sanderson, 2009). The positivist paradigm gives insufficient attention to the 'human-lived' experience, perception, and belief, which are subjective and embedded in particular historical and social contexts (Broom and Willis, 2007). Therefore, taking an interpretivist point of view of the subject matter as an additional angle is important to provide a complete picture of the complex system. Nevertheless, the difference in ontological assumptions of the two paradigms makes them incommensurable, and a researcher cannot be simultaneously positivist and interpretivist. This requires researchers to take a different philosophical position to address the contradiction between positivism and interpretivism and adopt a different set of research methodologies to help make sense of this complexity.

I adopted critical realism as the philosophical grounding for this research. Critical realism has a similar ontological view to positivism as critical realism maintains the existence of a single objective reality to model independent of the researcher's perspective and belief (Danermark et al., 2005). It differs from positivism in the epistemological domain as critical realists accept the relativism of knowledge as historically and socially situated, conceptually mediated, and consequently concept-dependent (Danermark et al., 2005). It is also important to note that critical realism is neither a compromise nor a conflation between positivism and interpretivism; it represents a standpoint in its own right. In this research, I view the research problem as the reality of which nature is external, fixed, and intransitive and seek to understand that reality. Concurrently, I think that it is important to appreciate, understand, and incorporate social structure when building models and developing frameworks that are aligned with the epistemological aspect of critical realism.

Within critical realism, building simulation models should be based on both observable, tangible facts and subjective, intangible views of a system in order to create a version of the real system. I also aim to develop a framework to combine different simulation modelling methods to inform and facilitate the process of producing such a version of reality. I rely on both the factual information in existing theories and previously developed hybrid models and the subjective experience and reflection during the modelling process to develop a more practical framework for combining simulation modelling methods.

I utilised the research problem as a case study to explore how a modeler can adopt an appropriate simulation modelling approach to understand and address the problem. Unlike positivism, in which the researcher is considered an independent objective observer, the researcher within critical realism is embedded in the research and becomes a part of the research (Mingers, 2000). This means that I should view science as an ongoing process whereby I continuously seek to improve the models I develop to explore and understand the research problem. I should also persist in enhancing the concepts and the approaches that I employ to develop the models. As research in combining different simulation modelling methods, especially those that combine SD and ABM in the context of healthcare, is scant, there are few guidelines that I can rely on to build a hybrid SD-ABM model for this research problem. As a part of the research, I reflected upon the modelling process to create, revise, and adjust the framework for combining SD and ABM. Also, this theoretical framework helped me develop a hybrid SD-ABM model to explore the research problem, revisit, and improve that model.

Critical realists claim that all knowledge about reality is fallible but not equally fallible (Danermark et al., 2005). They claim theories as the best truth at the moment, and this truth can always be surpassed by new theories. Also, the usefulness of the knowledge critical realists attain varies under different conditions (Danermark et al., 2005). Adopting this philosophical position implies that I concur with the notion that all models are wrong, but some are useful. Therefore, in model building, I focus on the usefulness of models in exploring the research question rather than modelling the entire system or incorporating as many characteristics of the system as possible. I also appreciate the usefulness of combining different simulation modelling methods in terms of deepening the knowledge about reality rather than just creating a more realistic model. However, this understanding does not imply that I ignore the reality and its depiction in the model. Furthermore, I do not consider the framework developed for combining SD and ABM static, definitive, and context-free. Rather, it is a guide to assist in designing and developing hybrid SD-ABM models, builds on previous theoretical works, requires modelers' judgment when applied, and is subject to correction by continued research.

6.3 Research Methodology: Case Study

Case study is a research methodology[10] in which the focus is to explore and understand the dynamics present within specific settings or contexts (Eisenhardt, 1989). The contextual conditions are part of the investigation rather than controlled as in experiments (Ridder, 2017). It has historically been used in hybrid simulation modelling research to study the benefit and application of combining different simulation modelling methods within a particular project (Cernohorsky and Voracek, 2012b; Gao et al., 2014; Mackay et al., 2013; Vincenot and Moriya, 2011). These studies presented a single case in which hybrid simulation models were built to explore particular problem(s) within a specific context. They focused on the application of hybrid simulation models in a specific context rather than exploring how the methods are combined. Researchers employed simulation modelling as a means to gain insight into the

[10] The purpose of a research methodology is to rationalize the research approach and strategy that outline how research is undertaken (Howell, 2012).

research problems without going on to discuss and generalize the process of combining different simulation methods.

For the research in this thesis, case study research is a suitable methodology as it enables us to apply hybrid simulation modelling to explore the real-life problem of HAI prevention and control within the specific context of healthcare (i.e., care homes). The case study methodology allows both detailed qualitative and quantitative data relevant to the problem of interest to be collected in real-world settings. It also offers a richer and deeper knowledge of the intricate complexity and the idiosyncrasy of the problem (Rwashana et al., 2009). Furthermore, we can develop a framework for combining SD and ABM through reflection on the modelling process of our case study in conjunction with comparing and analysing previous theoretical hybrid SD-ABM studies and case studies in different fields.

Although reflection on the process of modelling seems to align with the action research methodology, we did not use this methodology for two reasons. Firstly, action research emphasizes the role of participants within a particular research context in defining the problems to be addressed and the criticality of collaboration between the researcher and the participants to the success of a research endeavour (Blichfeldt and Andersen, 2006). This approach might become problematic as the researcher has to rely more on the participants as problem definers and sources of evidence. That also creates a dilemma on whether or not to end an action research project when the focus and interest of participants change. Secondly, action research differs from case study in the resulting action and its responsiveness to evidence, making it a reflexive approach with multiple cycles of action, reflection, and theory building (Coghlan, 2019; Huxham and Vangen, 2003). The constraint of adopting this methodology in this research is the capability and feasibility to repeat the cycle multiple times and to impact practice to then see and reflect on the impact of the changed practice. Therefore, case study is the preferred methodology for this research.

6.4 Setting and Context for the Case Study

The setting of this case study is a heterogeneous network of care homes in Lanarkshire. NHS Lanarkshire is the third-largest health board in Scotland. It serves a population of 661,900 across rural and urban communities in Lanarkshire with over 90 care homes and over 4,400 care home beds. Care homes in Lanarkshire are diverse in terms of resident population size, staff-to-resident ratio, and management and represent the diversity of care homes in the UK (ISD, 2018; CMA, 2017). The large, heterogeneous, and complex nature of the system offers a rich environment to investigate the characteristics of transmission dynamics of infections and the problems related to IPC faced by care homes across the UK. The complex and interconnected nature of the system also provides a potential environment for exploring the possibility, applicability, and benefits of combining SD and ABM.

The widespread COVID-19 in care homes challenged the Health and Social Care Partnerships (HSCP) Lanarkshire in their mission to protect and improve the health of care home residents and staff. Similar to care homes across the globe, COVID-19 hit care homes in Lanarkshire hard. Several care homes in the territory experienced outbreaks and failed to contain the spread of the virus effectively at the start of the pandemic. Care home residents were highly vulnerable to COVID-19: between 10 and 30% who contracted the infection will not survive. Thus, the HSCP and care homes in Lanarkshire were keen to get involved in this research to mitigate the impact of COVID-19 on their residents and population. We worked closely with relevant staff in the local authority and had regular meetings with their managers to ensure that our work was relevant to the challenges faced by the care sector.

We also presented, discussed, and received feedback on our work during regular meetings with other partners over 20 months. Our work was initially intended to support decision-makers at the HSCP and Public Health Lanarkshire and then disseminated to a policy-maker audience in the Scottish Government more broadly, the Scottish Government Care Home Data and Analysis Team, the Scientific Advisory Group for Emergencies (SAGE) Social Care Working Group (SCWG) – the UK Government, and the Department of Health and Social Care – the UK Government. Several external modellers/analysts in these groups also engaged in providing independent feedback on the work.

6.5 Research Methods

Research methods are defined as the tools or techniques by which data are collected (Bell et al., 2018). They define which types of data are obtained and how data are analysed and interpreted. Without the appropriate use of research methods, researchers are unlikely to gather quality data and hence ensure the soundness of the research outcome (Jonker and Pennink, 2010). The section will identify and discuss the research methods used in this research.

6.5.1 Literature Reviews

Literature reviews are essential for: i) developing an understanding of the existing research and debates relevant to an area of study or a specific topic, ii) determining how an area of study or a specific topic has been researched, iii) aggregating findings for a particular research question to identify an interpretable trend or pattern and/or to inform and support evidence-based practice, and iv) identifying areas of study that need further investigation (Paré et al., 2015). This method provides an analysis of ideas, describes relationships between ideas, and demonstrates how the researcher understands the nature and use of argument in the research problems (Hart, 2018).

In this research, we conducted several literature reviews to understand the existing research and debates around i) the situation of HAIs and IPC practice in care homes, ii) the application of single-method and hybrid simulation modelling in this research context, and iii) the potential and methodological guidance for combining SD and ABM and, from that, to identify research gaps. First, we revised literature around the burden of HAIs generally and COVID-19 in particular in the context of care homes, the IPC policies and practice in this setting, and the challenges faced by care homes in respect of IPC (see Chapter 2). This review helped identify a knowledge gap that is the lack of context-specific evidence on IPC in care homes. This knowledge gap became problematic for practice during the COVID-19 pandemic and needed urgent attention.

Second, we conducted a systematic review to explore how researchers had studied the problems of HAIs using single-method and hybrid simulation models (see Chapter 3). We did not restrict this systematic review to HAI models in care homes but included other healthcare settings as there were a limited number of modelling studies in care homes. Learning from the modelling studies in other healthcare settings also helped us understand why these model findings were not applicable to care homes and what features important to transmission dynamics in care homes we needed to capture in our models. Additionally, this review provided insight into how the trend of using single-method and hybrid simulation in this field evolved. The gaps identified in this systematic review then informed areas of research requiring more investigation, helping us decide upon the direction of the research and specify the research questions. We further reviewed emerging epidemic models of COVID-19 in care homes (section 8.2) and other small-scale settings similar to care homes (section 8.3) to refine the research gaps.

Third, we carried out literature reviews on the potential and methodological guidance for combining SD and ABM. The systematic review in Chapter 3 has shown the trend of increasing application of hybrid SD-ABM models in studying HAIs in recent years. We explored the potential of hybrid simulation models and identified the challenges of applying hybrid simulation (see Chapter 4). We also reviewed the existing theoretical guidance on why, when, and how modelers should combine SD and ABM (see Chapter 5). The modelling studies in various application contexts contributed to providing further insight into why, when, and how to combine these simulation methods (see Chapter 7). These reviews served as a basis for us to collate, elaborate, and extend the discussion on combining SD and ABM.

In addition to the literature reviews for problem articulation, we reviewed the literature to obtain the values for parameters characterising the transmission of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) and the COVID-19 disease progression (see Table 8.2 and Table 9.3). We determined the most likely value of each parameter for base-case simulations and its distribution for sensitivity analyses.

6.5.2 Interviews

The modelling process for building ABM and hybrid SD-ABM models within this case study research required us to undertake thorough problem exploration and conceptual model structuring. This step provided in-depth knowledge of stakeholders' perceptions, knowledge, and viewpoints, which minimized the uncertainty and bias of the model developed. We used semi-structured interviews for this step of the model development process to achieve insight from different stakeholders within the investigated system, which assists in constructing a conceptual model. Data collected in interviews helped us capture the experienced-perceived reality and identify which features of the problem are essential to incorporate into the model. This step was also an opportunity for us to reveal any misunderstanding of the problem and seek clarification. All of these benefits brought by interviewing data allowed us to produce a useful model which captured both the objective and subjective reality.

We chose semi-structured interviews over structured and unstructured interviews as this type of interview allowed us to ensure that we consistently asked all essential questions and probed more deeply using open-ended questions. Structured interviews involve a series of closed-form questions without follow-ups to the answers to acquire a greater depth of understanding of the problem (Gall et al., 1996). In contrast, unstructured interviews, which enable an interviewer to ask questions freely without a detailed guideline, are considered highly subjective and time-consuming (Gall et al., 1996). With semi-structured interviews, we had the flexibility to probe emerging areas of interest and tailor the interviews to individual participants.

We identified stakeholders for interviews using the non-probability sampling approach in which we selected samples based on our subjective judgment rather than random selection (i.e., probability sampling). This sampling approach is suitable for qualitative or exploratory research as it enables the exploration of a problem in-depth without requiring a representative sample of the population (Rubin and Rubin, 2005; Patton, 2014). It is cheaper, faster, more conducive, and more practical than the probability sampling approach but is heavily dependent on the researchers' expertise. The three techniques of non-probability sampling we adopted to select participants included purposive, snowball, and convenience sampling (Michalos, 2014; Rubin and Rubin, 2005; Patton, 2014). First, we discussed with the HSCP and Public Health Lanarkshire and used purposive sampling to select participating care home managers, nurses, and senior care workers. This sampling involved identifying and selecting individuals who are knowledgeable about or experienced with the care home environment and IPC in this setting, available, and willing to participate. Patton (2014) suggested selecting interviewees who can communicate experiences and opinions in an articulate, expressive, and reflective manner. We also applied snowball sampling in which we relied on recommendations of participants for others. Managers recommended staff in different roles, including deputy managers, care workers, activity coordinators, and ancillary workers. Managers also referred us to employees at the agencies who supply bank/agency care home staff to their care homes for interviews. Lastly, we used convenience sampling in which we interviewed whoever was able to participate in order to enrich the understanding of the research problem.

We interviewed care-home stakeholders, including managers and staff in different roles across four care homes in Lanarkshire and employees at two care staff agencies (Table 6.1). Our interview questions (Appendix C) covered the following four themes: i) role and responsibility – to gain an overview of the interviewee's role, responsibility, and daily duty, ii) general operation – to understand the care home's operational structure and management, iii) interactions – to understand the contact network between staff, residents, and visitors, and to have an overview of the frequency and nature of contacts, and iv) IPC – to explore IPC practice in the care home before and after COVID-19, focusing on the challenges of IPC interventions implemented to prevent and control COVID-19 outbreaks. The requirements for transmission-dynamic models that can address the research objectives, the gaps revealed by the literature reviews, and the discussions with the HSCP and Public Health Lanarkshire informed the decisions on designing interview question themes. We also carried out follow-up interviews with care home managers, deputy managers, and casual staff, along with interviews with employees at the agencies that provide casual/zero-hour-contract care workers to care homes. The purpose of these interviews was to understand how care homes use bank/agency staff and how bank/agency staff work across care homes (i.e., staff sharing theme).

Table 6.1: Overview of interviewed care home stakeholders

Stakeholders	**Number of interviews**	**Responsibility**	**Interview question themes**
Manager	4 (Full-time) 2 follow-up interviews	Manage the day-to-day operation of the care home	Role and responsibility, general operation, interactions, and IPC Follow-up: Staff sharing
Deputy manager	2 (Full-time) 1 follow-up interview	Lead and manage the care team in their day-to-day duties	Role and responsibility, general operation, interactions, and IPC Follow-up: Staff sharing
Registered nurse	2 (Full-time)	Provide medical care to residents as and when needed	Role and responsibility, interactions, and IPC
Senior care worker	4 (3 Full-time and 1 part-time)	Manage a team of care workers and ensure that the quality of care delivered to residents	Role and responsibility, interactions, and IPC
Care worker (also called as care assistant or support worker)	5 (2 Full-time, 1 part-time, and 2 casual) 2 follow-ups with casual workers	Provide personal care and support to residents with all aspects of daily living	Role and responsibility, interactions, and IPC Follow-up: Staff sharing
Activity coordinator	1 (1 Full-time)	Arrange various events, activities, and trips out to promote residents’	Role and responsibility, interactions, and IPC

Stakeholders	Number of interviews	Responsibility	Interview question themes
		socializing, physical, and emotional wellbeing	
Ancillary worker (Housekeeper or domestic worker)	2 (1 Part-time and 1 casual)	Ensure the cleanness and tidiness of the care home	Role and responsibility, interactions, and IPC
Worker at agency supplying bank staff to care homes.	2 (1 from the booking team and 1 from the recruitment team)	Receive bookings, arrange and assign care workers to care homes	Staff sharing

We conducted 20 interviews between May 2020 and October 2020 and seven interviews between February and March 2021. Each interview lasted between 45 and 60 minutes and was conducted on Zoom, Teams, Skype, and over the phone. Before the interviews, I informed the interviewees that their anonymity and confidentiality would be maintained and then obtained their informed consent (Appendix C). I ensured that the interviewees had understood the aim of these interviews and their role in this study at the start of the interviews. After each interview, I analysed the data to identify what was useful and appropriate for model building and to assess whether I had covered all relevant aspects and whether any questions or themes emerged from the interview. Following the assessment of the data, I made relevant changes, where appropriate, to the interview questions for subsequent interviews.

The data collected in the interviews, along with other data sources, informed different aspects of the modelling study, including conceptual model building, experiment design, and result interpretation. We specified, where relevant, how we used the interview data throughout Chapter 8 and Chapter 9. The data on participants' roles, responsibilities, and daily duties helped us make sense of other interview data and put research findings in context. For example, casual care workers' unfamiliarity with care homes' IPC protocols could be explained by their short time spent at these facilities and frequent movement between facilities. We used the data on the general operations and interactions to design the conceptual model structures, experiments, and uncertainty analyses. The data about IPC practice were useful for designing interventions and research finding interpretation. Furthermore, the data with respect to the use of bank/agency staff informed the interfaces between the hybrid model's modules.

We had considered other research methods, including focus groups, observation, and ethnography but had not been able to adopt these methods. Focus groups would have been another appropriate method to capture stakeholders' views, thoughts, and opinions and enhance the participatory and collaborative process of model building. However, this method was infeasible because of the difficulty of gathering stakeholders. They had a high workload and pressure, especially during the pandemic, and hence limited availability for group modelling discussions. Other research methods that we had also considered for problem exploration and model structuring included observation and ethnography. Although they might have revealed "behind the scenes" characteristics of the problem, there were many barriers that restricted the use of these methods, such as access to care homes, ethical issues with respect to conducting face-to-face research during the pandemic, and time consumption.

6.5.3 Simulation Modelling

Several works have outlined the key activities in a modelling process for single simulation methods (Lieberman and Hillier, 2005; Sterman, 2000; Railsback and Grimm, 2019; Robinson, 2014; Shannon and Johannes, 1976; Law et al., 2007; Hoover and Perry, 1989; Ulgen, 1991; Dietz, 1992; Banks et al., 2005; Gogg and Mott, 1992). Table 6.2 shows that the commonly used examples of modelling processes for SD, ABM, and DES by Sterman (2000), Railsback and Grimm (2019), and Robinson (2014) are generally similar to a generic modelling process described in management science/operational research (MS/OR). As these steps have successfully supported modellers through the modelling process, we adapted them to build our models, as shown in Table 6.3. This modelling process involved several iterations between the modelling phases. We also planned for and carried out the model development and its confidence-building in parallel.

We applied the framework for combining SD and ABM proposed in Chapter 7 to design our conceptual hybrid SD-ABM model. The modelling processes for single simulation methods do not offer sufficient support for dealing with the increased complexity of hybrid simulation models and additional decisions on when, why, and how to combine the methods. The hybrid simulation framework guided the conceptual modelling phase and complemented other modelling phases. The comprehensive design of the conceptual hybrid model, having defined the sub-models, their linkages, and updating rules, facilitated the computer simulation modelling phase and verification. The design of the hybrid model also aided in communicating the model's structure to stakeholders for face validation in the model confidence-building phase. Finally, the detailed and validated design of the hybrid model contributed to the model's reproducibility and methodological rigour.

We worked closely with our stakeholders throughout the modelling process. In the problem articulation phase, discussions with the stakeholders were critical to gain insights, scope the problem, and determine the modelling objectives. We also addressed the issues such as the study timeline, availability and access to data, and challenges in data collection in this phase. The primary data collected in the interviews and discussions with the stakeholders and the secondary data provided contributed to informing the conceptual model's structure. Regular consultation with stakeholders helped justify the modelling assumptions and simplifications emerging from the first three phases of the modelling process, contributing to building confidence in the model. Consulting with stakeholders also provided the contextualised intervention design and analysis, which the previous studies in this field had not adequately addressed. In the implementation phase, we discussed the model results and findings with stakeholders, who were involved in the decision-making process, regularly via several meetings and reports. These activities supported their decisions promptly to handle the rapidly evolving situations in care homes amidst the pandemic. Engaging stakeholders in the modelling process increased the model's credibility and their buy-in, which ensured the implementation of the model's recommendations.

Table 6.2: Comparison of the modelling processes for different single simulation methods

MS/OR (Hillier and Lieberman, 1995)	**SD (Sterman, 2000)**	**ABM (Railsback and Grimm, 2019)**	**DES (Robinson, 2014)**
Define the problem of interest and gather relevant data	Define the model boundary through identifying key variables, time horizon, and the reference modes of key variables	Formulate the research question	Identify the problem within the existing system or the concern about the proposed system
Formulate the conceptual model to represent the problem	Describe the model structure, using stock and flow diagrams or policy structures, to explain the reference modes	Assemble hypotheses for essential processes and structures Choose scales, entities, state variables,	Conceptual modelling (understand the problem situation, determine modelling objectives, design inputs, outputs, and the model content)

MS/OR (Hillier and Lieberman, 1995)	SD (Sterman, 2000)	ABM (Railsback and Grimm, 2019)	DES (Robinson, 2014)
		processes, and parameters	
Develop the computer-based model	Formulate the model (specifying stocks, flows, and causal linkages between stock, flow, and auxiliary variables and parameters, developing equations each component, and determining initial conditions)	Implement the model	Computer model coding
Model validation (retrospective test)	Perform diagnostic simulation for model verification Model testing in terms of dimensions, fit with historical behaviour of key variables, robustness under extreme conditions and sensitivity	Pattern-oriented modelling, sensitivity, uncertainty, and robustness analysis	Verification, validation, and confidence, including conceptual model validation, data validation, verification and white-box validation, experimentation validation, and solution validation
Derive solutions to the problem from the model Prepare for the ongoing application of the model as prescribed by management	Design of policies and experimentation of the model through changes in parameters, feedback processes, what if and decision rules	Analyze, test, and revise the model (patterns)	Experimentation (obtain sufficiently accurate results, search solution space, test solution robustness)
Implementation and learning (communicate the model, monitor experience and system performance, and identify modifications)		Communicate the model to clients, other scientists, and the public	Implement the model, findings, and as learning

Table 6.3: Modelling process for ABM and hybrid SD-ABM models

Modelling process phase	ABM (Chapter 8)	Hybrid SD-ABM (Chapter 9)
Problem articulation	Chapter 1 and Chapter 2	Chapter 1, Chapter 2, and Section 9.2 (Stage 1 of the conceptual hybrid SD-ABM modelling framework in Chapter 7)
Conceptual modelling	Section 8.4	Apply conceptual hybrid SD-ABM modelling framework (Chapter 7) with reference to relevant parts in section 9.3 and section 9.4
Computer simulation modelling	Built in Anylogic PLE 8.7.2	Built in Anylogic PLE 8.7.5
Model confidence building	Section 8.7	Section 9.6
Experimentation, model result analysis, and finding interpretation	Sections 8.6, 8.8, 8.9, and 8.10	Sections 9.5, 9.7, 9.8, and 9.9
Implementation and learning	Section 10.3.4	Section 10.3.4

6.5.4 Introducing the Theoretical Framework from Reflection of Models and Modelling Process

From the critical realist perspective, models only represent parts of reality, and the purpose of research is to explore and understand this reality as much as possible. We appreciated the insights that combining different simulation modelling methods can produce and the importance of making the process of combining the methods easier in contributing to achieving this purpose. We used our systematic review on simulation modelling in HAIs (Nguyen et al., 2020c), our literature review on the existing theoretical studies that guide the combination of SD and ABM (Chapter 5), and the case studies of hybrid SD-ABM models in various application areas (Chapter 7) to understand the development process of hybrid models and identify gaps in this field of combining SD and ABM, respectively. The knowledge and understanding these reviews provided served as a foundation for us to incorporate new elements and build a more practical theoretical framework for combining SD and ABM in the context of healthcare. In our case study, I used the existing knowledge on combining the two methods to inform and guide the process of model building. Throughout this process, I reflected on whether such guidance was practical and helpful to improve its practicality that would facilitate its application in future modelling studies.

6.6 Research Objectives

The purpose of this research is to contribute to how hybrid simulation models can help understand, prevent, and control the spread of COVID-19 in care homes. This section summarizes the research questions resulting from the literature review into the four research objectives.

The first two research questions, addressed in Chapters 2 and 4, were used to derive the first objective:

Objective 1: Obtain an understanding of the research context (i.e., HAIs and COVID-19, in particular, in care homes) and the application of single-method and hybrid simulation models in the context area.

Chapter 4 addressed research question Q3 by discussing the benefits of combining simulation methods in the research context and highlighting the challenges of combing the methods. Chapter 5 focused on one of the challenges that emerged in Chapter 4. It reviewed the existing theoretical guidance for combining SD and ABM to address research questions Q7 and Q8. These questions are summarized as the second objective:

Objective 2: Explore why and how SD and ABM have been combined and what are the limitations of the existing guidance for combining the two methods.

Four further research questions were presented following the literature review (Chapter 2 – 5). Chapters 8 and 9 examined questions Q4, Q5, and Q6, leading to the third objective:

Objective 3: Investigate how to prevent and control the spread of COVID-19 within and across care homes using simulation models.

Question 9 focused on taking the learning on combining SD and ABM from the literature to propose a new/improved framework for combining. This research question is reworded to become the fourth objective:

Objective 4: Develop a framework for combining SD and ABM in the conceptual model development process based on the existing literature and the researcher's reflection upon the modelling.

6.7 Research Ethics

This research was approved by the Departmental of Management Science Ethics Committee in line with the University of Strathclyde Code of Practice on Investigations Involving Human Beings[11] and the University Ethics Committee COVID-19 Guidance[12]. Advice was sought from the NHS senior R&D manager and the Director of Public Health Lanarkshire who confirmed that NHS, Public Health, and HSCP ethical reviews were not required for this study.

6.8 Chapter Summary

Critical realism informs the philosophical foundation of this study. The researcher believes that a rigid reality exists and that individuals involved in the research can contribute their perspectives to develop a comprehensive picture of reality. A critical realist philosophical view of research carries important implications for the modelling process and how the results are evaluated, interpreted, and implemented. This paradigm highlights the involvement of the researcher and stakeholders and encapsulates their perspectives and factual information about the research problem characteristics.

Building on this foundation, this chapter provides an overview of the methodology and methods used to collect and analyse data. The methodology undertaken is the case study that shapes the context and guides the selection of methods for data collection. The methodology and philosophy allow this research to achieve its aims: i) to help solve the empirical problems in a specific health context and ii) to contribute to developing the knowledge on combining SD and ABM. The researcher collates existing research on hybrid simulation modelling and incorporates their view based on experiences and reflections throughout a case study to update the reality.

The generalised value of the hybrid simulation modelling framework is potentially transferable but requires further application beyond the case study in this thesis to confirm. The healthcare setting of the case study represents a rich, complex, and interconnected system for modellers to explore. Therefore, the learning and insights acquired from combining the

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[11] For further information see https://www.strath.ac.uk/professionalservices/media/ps/rkes/Code_of_Practice_eighth_Feb17.pdf

[12] For further information see https://www.strath.ac.uk/coronavirus/staff/universityethicscommittee/

methods of interest (i.e., SD and ABM) to develop a hybrid model within this complex system can be transferable to inform the modelling of other complex systems. In addition, using the context-independent hybrid SD-ABM modelling literature and the case studies of hybrid SD-ABM models in different application areas to inform the development of the framework for combining SD and ABM has also contributed to its generalizability. Nevertheless, the research acknowledges that the hybrid simulation modelling framework should be viewed as a preliminary framework. Developing a hybrid simulation modelling framework is an iterative process, and thus, the framework should be tested and refined in practice beyond this case study for generalizability.

Chapter 7. A Hybrid Simulation Modelling Framework for Combining SD and ABM

7.1 Introduction

Chapter 5 revealed the lack of comprehensive and practical guidance for designing and developing a hybrid SD-AB model. To address this gap in research, this chapter presents a theoretical framework that guides the conceptual modelling phase of a hybrid simulation study. The framework provides practical instructions that specify steps modellers should take to build a conceptual hybrid simulation model. It also suggests the elements that modellers should describe to provide an overarching representation of a conceptual hybrid model for other modellers and stakeholders. These elements include: i) modules, ii) abstraction level, modelling method rationale, and content for each module, and iii) their linkages (i.e., flows of information, interfaces, and updating rules). We define these elements in this chapter. Such a comprehensive illustration of the overall hybrid model is needed at the conceptual model level to i) communicate the model design effectively with stakeholders and the wider research communities for confidence building and ii) facilitate verification and the development of computerized simulation models.

An early version of the proposed framework solely based on the literature review performed in Chapter 5 was published as

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The proposed framework builds on existing guidance on hybrid SD-AB modelling and reflections on existing hybrid SD-ABM studies. It informs the development of the hybrid model described in Chapter 9 and is refined by reflecting on the modelling process. These two activities iterate several times. It aims to assist in the selection of appropriate model designs in future studies, which will facilitate the process of developing hybrid models in addition to improving the models' usefulness. In this framework, we have used the high-level hybrid model designs discussed in Chapter 5 to inform the essential elements for designing interactions between SD and ABM sub-models, including flows of information, interfaces, and updating rules. However, we do not select an interaction, enrichment, or integration design to inform detailed interactions between sub-models as we found an approach that asks the modeller to begin by selecting this design impractical. Instead, we describe the elements for designing interactions between sub-models in detail.

7.2 Framework

The framework to conceptualise a hybrid simulation model consists of four main stages that are presented in Figure 7.1. In stage 1, modellers explore the problem of interest by defining the modelling objectives, scoping the problem, and specifying its characteristics as would normally be done in simulation modelling studies using single methods. After stage 1, modellers can use the framework if they have decided that the problem of interest can be tackled using SD and ABM and that DES is not appropriate (see section 3.5). In stage 2, modellers determine whether an individual SD or ABM or a hybrid SD-ABM is most appropriate to model the problem based on the exploration in stage 1. Stage 3 consists of activities to design the modules comprising the hybrid model, and stage 4 comprises activities to link the modules. The stages are explained in more detail in the following sub-sections. Throughout the description of the framework, we also discuss the confidence-building activities that modellers should plan when conceptualizing the model.

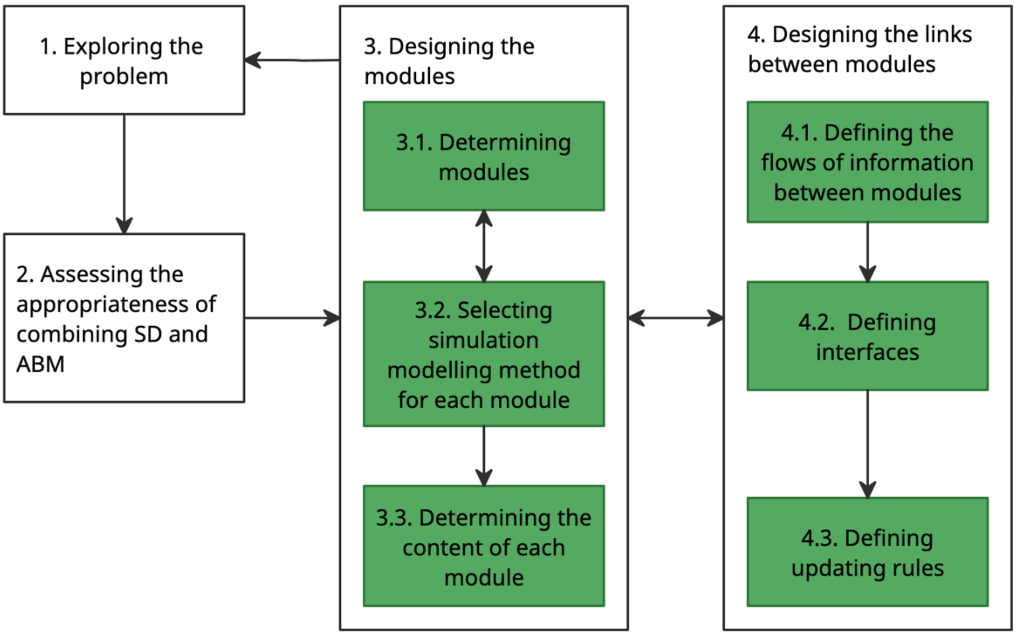

Figure 7.1: The conceptualization stages of the hybrid SD-ABM simulation modelling framework

7.2.1 Stage 1: Exploring the Problem

The first stage is to explicitly define the nature of a problem under investigation and the modelling objectives, similarly to what is normally done in a single modelling method study. This stage is vital to help identify the model scope and the level of detail required and, thus, the selection of appropriate simulation modelling methods (Robinson, 2014; Roberts et al., 2012; Albin, 1997; Randers, 1980; Wilensky and Rand, 2015). Identifying the model outcomes is also useful to inform the content of the model.

In this stage, modellers need to gain a detailed understanding of the problem as it guides modelling decisions. Identifying the problem characteristics that are important to include in the modelling study is domain-specific and requires input from the problem owners and other relevant stakeholders. For example, building a simulation model to explore a public health policy or a health promotion program usually involves defining problem characteristics such as the target population (e.g., age, gender, and risk factors), the target settings, potential interventions, the health outcomes, and the time horizon adequate to capture differences in outcomes across interventions. Gaining an understanding of the problem characteristics builds on the combination of expert knowledge, literature review, and data from, for example, interviews with stakeholders, surveys, focus group discussions, participatory processes, observations, laboratory experiments, or network analysis.

In addition, modellers consulting with the problem owners and relevant stakeholders need to identify and justify the modelling assumptions and simplifications arising from scoping the model. They also need to discuss constraints such as the timeline of the modelling study, difficulties associated with data collection, access to applicable data, and cost constraints (Mykoniatis and Angelopoulou, 2020). If these constraints cannot be reasonably addressed, the objectives and the scope of the model need to be revised.

Modellers should plan for black-box validation at this stage. Black-box validation considers whether the overall behaviour of the model represents the behaviour of the real system with sufficient accuracy for its purpose (Kleijnen and Wan, 2007; Robinson, 1997). Adopting the pattern-oriented modelling approach (Grimm et al., 2005), modellers can identify patterns observed in reality, reported in the literature, and/or based on theories to assess the model's ability to reproduce these patterns. These patterns are identified with the purpose of the model as they serve as criteria for whether the model is realistic enough for its intended purpose. These patterns can also help rationalize critical design decisions of the model (see Black-box Validation in section 9.6.1).

7.2.2 Stage 2: Assessing the Appropriateness of Combining SD and ABM

Once the problem is articulated, modellers need to establish whether a hybrid simulation modelling approach would be more appropriate compared to a single simulation method. Each simulation modelling method has strengths and limitations, making it more or less suited for specific problems (Scholl, 2001b). Therefore, the selection of different simulation modelling methods should be driven by the problem characteristics explored in stage 1. Modellers will choose a hybrid simulation modelling approach that combines the strengths of SD and ABM if one simulation paradigm has difficulty capturing the complexity of the problem on its own. Table 7.1 presents the typical contexts that motivate the application of SD-ABM combinations based on a literature review of hybrid simulation modelling studies. Examples are selected from these studies to demonstrate each contextual application.

It is worth noting that Figure 7.1 indicates that any effort to assess the appropriateness of combining SD and ABM is likely to be iterative. For example, while modellers implement their choice for a hybrid SD-ABM simulation model in stage 3, they may learn new characteristics that lead them to redefine the problem addressed in stage 1 and reassess the method(s) selected in stage 2. Another example is that if a modeller initially selects SD in stage 2 and then finds it difficult to formulate the casual relationships for a highly uncertain variable, they may decide to return to step 1 to explore the variable and then reassess the method selected in stage 2.

In selecting the appropriate simulation modelling approach, modellers also need to consider practical issues that may constrain hybrid simulation modelling work. Building a hybrid simulation model is likely to take more time, especially if modellers lack knowledge and experience in both SD and ABM (Mingers, 2001). Furthermore, modellers may lack access to potentially high-cost software that combines different simulation method modules. Modellers may lack the skills to code from scratch and combine these modules.

Table 7.1: Description of context that motivates the application of hybrid SD-ABM models

Typical context of application of hybrid simulation (When?)	**Example**	**Module design**	**Method often used in previous studies[13]**	**Benefits of hybrid simulation models compared with single modelling methods (Why?)**
Strategic policy decisions with consideration of a wide range of operational/local circumstances	Capacity planning of solar energy resources by modelling the electricity system with a flexible structure that captures energy demands in a region characterized by different households considering different time and seasons (Mazhari et al., 2009)	Using ABM to zoom in one part of the system modelled in SD	SD	Provide richer insight into the interdependences between the behaviours of a system at a macro level and the behaviours of multiple agents involved at the micro level Contribute to explaining why a strategic policy may fail to improve operational performance Offer flexibility to model different operational circumstances or intervention scenarios explicitly
Focusing on causal relationships in the system with stochastic and/or highly uncertain elements	Causal relationships between risk metrics and variables in modelling technological innovation risks that involve uncertainties caused by multiple agents with conflicting information and objectives and that are subject to limited perception and behavioural capacity (Wu et al., 2010)	Using ABM to model uncertain/stochastic elements in the system modelled in SD	Stochastic SD	Help model stochastic/uncertain elements in casual relationships explicitly by entering variation into the appropriate sources/ decision levels of the model Provide richer insight by capturing parameters with emergent behaviours

[13] This column shows the simulation methods that are often used in previous studies to address similar questions. This is based on the literature review provided in the example studies.

Typical context of application of hybrid simulation (When?)	Example	Module design	Method often used in previous studies[13]	Benefits of hybrid simulation models compared with single modelling methods (Why?)
Involving interdisciplinary processes, several organisational factors (e.g., social, economic, epidemiological, and political)	The assessment of innovative health technologies prior to their launch involving interdisciplinary processes: population dynamics, disease dynamics, healthcare financing, and healthcare (Kolominsky-Rabas et al., 2015)	SD and ABM modules represent different disciplines	Both SD and ABM	Model the system in a more natural way Harmonize interdisciplinary expertise of experts whose views may be rooted in either SD or ABM Optimize trade-off between the computational and the predictive performance of the model
Comprising multiple interconnected subsystems	The problem of large infrastructure systems development comprising interconnected sub-systems and involving the partnership of public and private entities with conflicting goals and information asymmetry (Glock et al., 2016; Páez-Pérez and Sánchez-Silva, 2016)	SD and ABM modules represent different sub-systems	Both SD and ABM	Model the system in a more natural way Address and satisfy different views of stakeholders on the system
Social and/or spatial interactions between entities affecting and/or affected by the dynamic global environment	Social-spatial fragmentation and segregation affected by cause-effect chains of urban shrinkage (Haase et al., 2012)	Agents live in an environment represented by an SD module	ABM	The active, dynamic urban environment, where a spatial, social structure of agents live, is characterized by casual relationships and, thus, difficult to model using variables. Provide richer insights into relationships between agents' behaviours and external environment

Typical context of application of hybrid simulation (When?)	Example	Module design	Method often used in previous studies[13]	Benefits of hybrid simulation models compared with single modelling methods (Why?)
Social and/or spatial interactions between entities affecting and/or affected by their internal dynamics	Modelling the complex safety behaviours (e.g., resting decision) of truck drivers in interaction with co-workers (Goh and Askar Ali, 2016)	Embedding an SD module in each agent to represent its internal structure	ABM	Internal dynamics is complex and, thus, difficult to model using state variables Provide richer insights into relationships between agents' internal dynamics and their behaviours

7.2.3 Stage 3: Designing the Modules

A model can consist of several components called “modules”. A module should principally be self-contained and bounded with predefined interfaces (input and output) to the external world, including other modules. In a hybrid simulation model, we find it useful to consider a module as one logical component of a hybrid model developed using one of the simulation modelling methods (Onggo, 2014). In an integrated hybrid model, the boundary between modules is not explicit because the interfaces between modules are intertwined. In this case, we can still dissect the model into smaller components, where each component will be considered as a module that can receive a set of inputs and transform them into a set of outputs.

In this stage, modellers will determine and describe constituent modules of the model, levels of abstraction, and the simulation modelling method used to build each module. Stages 3 and 4 assist in white-box validation, which determines that the constituent parts of the model represent the corresponding parts of the real system with adequate accuracy for its purpose (Kleijnen and Wan, 2007). These stages offer a plausible design of the hybrid model’s structure for presenting to stakeholders and experts for face validation and interface validation (see White-box Validation in section 9.6.1).

7.2.3.1 Step 3.1: Determining Modules

There are several ways to determine modules. It is more of an art than a science; therefore, here we discuss some of the options to perform this task. Djanatliev and German (2015) suggested defining independent problem areas within a specific domain scope and modelling each area using one of the simulation methods. For example, Kolominsky-Rabas et al. (2015) developed a model for assessing innovative health technologies prior to their launch that involves interdisciplinary processes and is divided into modules by these disciplines, including population dynamics, disease dynamics, healthcare financing, and healthcare operation. Defining modules can be specific to a domain. For example, modellers can use a hierarchical breakdown to study the problems in healthcare at the global/national/regional level, institutional level, individual level, and internal level (e.g., internal body processes and disease progression). Modellers can also define modules based on the application contexts described in Table 7.1 (e.g., see section 9.3).

7.2.3.2 Step 3.2: Selecting Simulation Modelling Methods for Each Module

After identifying the modules of a problem, modellers need to determine the level of abstraction and justify the selection of a particular simulation modelling method used for each module (e.g., see section 9.3). Modellers may need to iterate between step 3.1 and step 3.2, splitting or merging modules. While rationalizing the choice of a simulation modelling method for each module, modellers may decide to split a module if they cannot build it using one single modelling method. They may also consider combining modules with the same modelling method to simplify the model structural design while maintaining the "module" principle definition.

7.2.3.3 Step 3.3: Determine the Content of Each Module

Having identified the simulation method for each module, modellers determine the content of each module. SD modules will contain key variables, influencing factors, and feedback interrelations. For ABM modules, modellers identify key agents, their characteristics and behavioural rules, and their interactions. Modellers can adopt section 2 (Entities, state variables, and scales) and section 4 (Design concepts) of the Overview, Design concepts, and Details (ODD) protocol to develop the content for each ABM module (Grimm et al., 2017) (e.g., see sections 9.4.1 and 9.4.2). These sections cover types of agents and their characteristics, and provide an overview of their interactions and behavioural rules and what the model's time steps represent in reality. SD and ABM modules can be described using their own conceptual modelling tools, such as Stock-and-flow Diagram and Causal Loop Diagram (Roberts et al., 1997; Richardson and Pugh 1997; Richardson, 1991; Coyle, 1997; Sterman, 2001; Maani and Cavana, 2000) for SD and Statechart diagrams, Agent-Object-Relationship diagrams for ABM (Scheidegger et al., 2018; Wagner, 2003) (e.g., see Figure 9.2). In the STRESS guidelines for strengthening the reporting of empirical simulation studies, Monks et al. (2019) suggested three checklists for describing the basic conceptual building blocks of SD, ABM, and DES models. In designing the content for each module, modellers must also keep in mind the modelling objectives to justify why they include or exclude particular elements. Additionally, modellers should record any assumptions and simplifications made during this step and present them to the problem owner and any relevant stakeholders to ensure the validity and credibility of the model. At this step, modellers should plan confidence-building approaches for individual modules using the existing standard approaches for single-method models.

7.2.4 Stage 4: Designing the Links between Modules

In this stage, modellers need to define the below elements to connect the modules comprising the hybrid model. Performing this stage also provides learning about stage 3. The modules' scope and content determined in stage 3 must be sufficient to provide the links between the modules and define their interfaces.

7.2.4.1 Step 4.1: Defining the Flows of Information between Modules

In this step, modellers decide what information and the directions of this information's flow between modules (e.g., see Figure 9.1). Modellers explicitly define whether information flows between two modules in one or both directions. This will inform the design of interfaces between modules in step 4.2. Modellers also need to describe the frequency of information flows that inform the detailed design of updating rules in step 4.3.

7.2.4.2 Step 4.2: Defining Interfaces

In this step, modellers need to define clear and logical interfaces for each pair of modules. An interface between the two modules defines how the information is passed from the generating module to the receiving module during the running time of the hybrid model. Figure 7.2 provides an overview of information flows between components of an SD module and an ABM module. A detailed discussion of categories of information flows follows. These categorisations emerged from a literature review of hybrid SD-ABM models across various domains and were based on reflection from the modelling process. For each category of information flow, we provide a description and one or two example models selected from the literature. The complete description of hybrid modelling studies and information flows can be found in Appendix D.

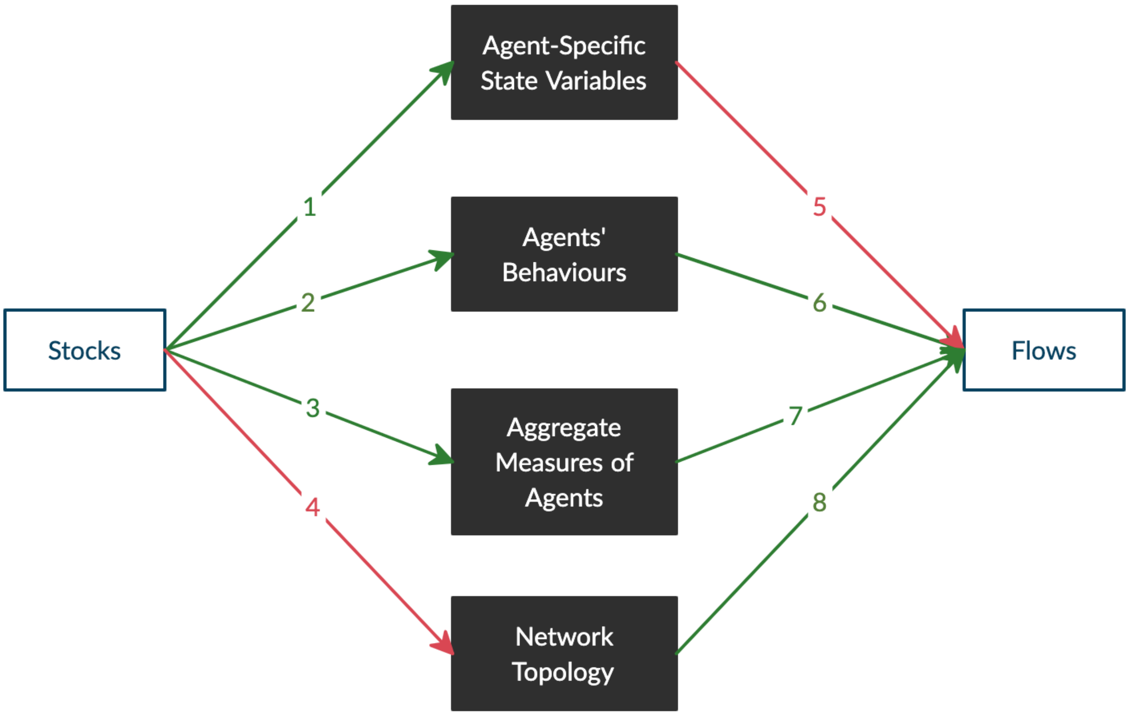

Figure 7.2: Flows of information between an SD module and an ABM module of a hybrid SD-ABM model White and black boxes denote elements of an SD and ABM module respectively. Green arrows denote the flows of information found in the literature and red arrows denote the proposed flows based on reflection from the modelling process (1) Stock levels affect agent-specific state variables or are used to generate a small crowd of agents; (2) Stock levels affect agent's behaviours; (3) Stock levels bound aggregate measures of agents; (4) Stock levels affect the network topology of agents; and (5), (6), (7), and (8): Agent-specific state variables, agents' behaviours, aggregated measures of agents, and the network topology of agents affect flows of an SD module respectively.

Information Flows from SD Module to ABM Module

(1a) Stock levels define agent-specific state variables

Description: The level of a stock in an SD module embedded in each agent of an ABM module can determine a characteristic (i.e., state variable) of that agent (Figure 7.3).

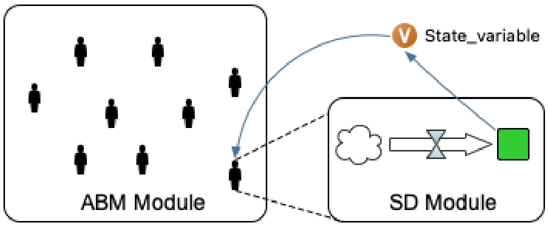

Figure 7.3: Stock levels define agent-specific state variables

Example study: The integrated hybrid model in Caudill and Lawson (2013) represents the intra-host dynamics of antibiotic-resistant bacteria and the inter-host transmission dynamics of infections caused by such bacteria occurring among patients and HCWs in a hospital using SD and ABM, respectively. SD modules embedded within patient and HCW agents simulate changes in their internal pathogen population, called the bacteria population vector, over time. The stock level for the bacteria population vector determines the infection state of an agent and influences transmission probabilities when an agent interacts with other agents.

(1b) Generating agents from stocks

Description: Small crowds of individual agents with specific characteristics can be generated from stocks representing large population numbers. Individual agents can be generated using distribution functions based on existing empirical data or theories to represent the necessary heterogeneity of these agents.

Example study: Figure 7.4 shows an example of generating small affected[14] crowds differentiated by age from a larger population in prospective Health Technology Assessment studies (Djanatliev and German, 2013b; Kolominsky-Rabas et al., 2015). In these studies, a small crowd of affected agents are generated from a stock representing a larger affected

[14] "Affected" represents a health state.

population in an SD module. The affected population stock is categorized into different age groups to parametrize agents afterwards. In essence, the different stocks and flows represent different types of agents classified by the age dimension. However, in order to simplify the presentation of the model, as these agent types have the same stock and flow structure, they are presented as one structure with a vector holding the level of the affected population for different age groups. The vector of the affected population is calculated by multiplying the age-specific incidence rates and the corresponding age distribution.

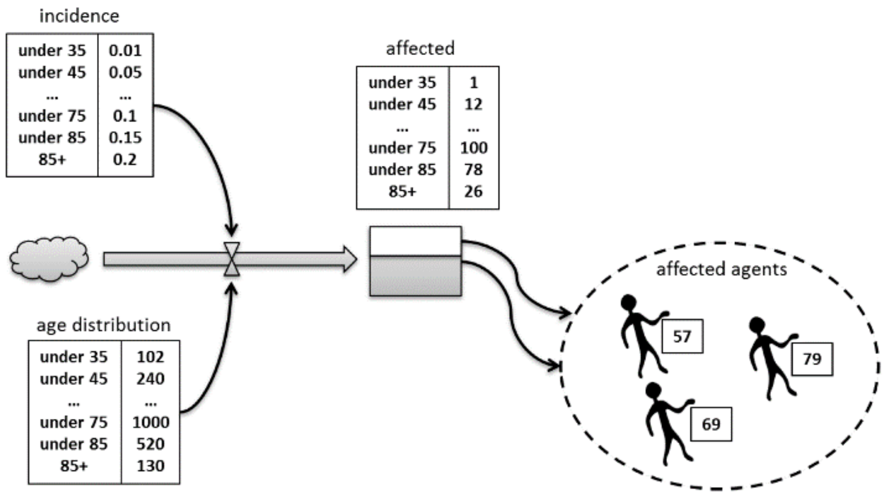

Figure 7.4: An example of generating agents from stock

Reproduced from "Prospective healthcare decision-making by combined system dynamics, discrete-event and agent-based simulation", by Djanatliev, A. and German, R., 2013, 2013 Winter Simulations Conference (WSC), 270-281. Copyright 2013 by IEEE. Reprinted with permission. A vector of affected persons can be calculated using the age specific incidence values and the corresponding age distribution which is calculated in parallel by the demographic component. The resulting stock is a vector containing a dedicated number of affected persons with different age groups.

(2) Stock levels define behaviours of individual agents

Description: Stock levels in an SD module determine the corresponding behaviours that individual agents in an ABM module will execute. As shown in Figure 7.5, if the stock level satisfies Condition 1 (e.g., the level is greater than a threshold or falls within a certain range of values), agents will execute Behaviour 1.

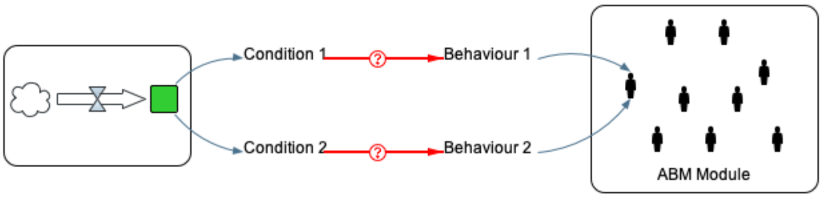

Figure 7.5: Stock levels in the SD module of a hybrid model define the behaviours of agents in its ABM module

Example studies: The SD module can act as an environment for which characteristics represented by stock levels influence the behaviours of agents living in it. In a hybrid model for project management, Jo et al. (2015) represents the benefits, cost, and feasibility of an investment project as stocks in the SD module. The stock levels affect the decision-making process of user agents which represent individuals who potentially use and participate in a public investment project.

The levels of stocks of SD modules that are embedded in each agent of an ABM module can also influence the behaviours of these agents. In the hybrid SD-ABM model for public health policy formation published in Cernohorsky and Voracek (2012a), an individual agent dies when their health capital stock level, modelled in an SD module, drops below a threshold.

(3) Stock levels bounds aggregate measures of agents

Description: A stock level in an SD module bounds an aggregated measure of agents in an ABM module. The aggregated measure of agents must not exceed the level of a particular stock. Aggregate measures of agents can be the sum of values for an agent-specific state variable or the size of the agent population with a specific characteristic (Figure 7.6). While a stock level directly affects the behaviour of individual agents in interface design (2), in this design, it indirectly affects behaviour based on the collective measure of agents, summing up their state variables.

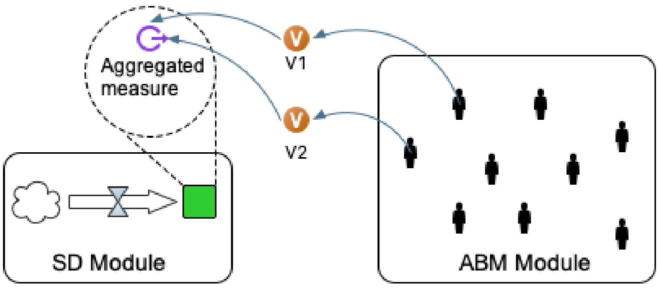

Figure 7.6: Stock levels bound aggregate measures of the ABM module

Example studies: In a hybrid model for land use, Verburg and Overmars (2009) models the spatial allocation of demand for urban and agricultural land-use types on a grid. The regional demands for different land use types are represented by stocks in the SD module. The individual cells (agents in the ABM module) on the grid are local pieces of land with different characteristics such as location suitability, neighbourhood suitability, and conversion elasticity. The regional level demands are spatially allocated to individual grid cells until the demand is satisfied by iteratively comparing the sum of the allocated area of the land use types with the demand.

(4) Stock Levels Define Agents' Network Topologies

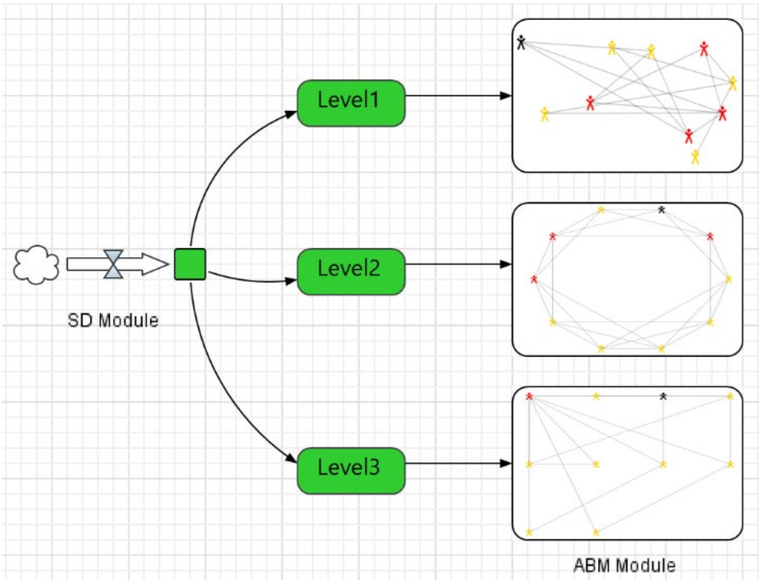

Figure 7.7: Stock levels in an SD module of a hybrid model define the spatial relationship and/or network topology of agents in an ABM module

Description: The levels of stocks in the SD module determine the corresponding spatial relationship and/or interacting network topology among agents in the ABM module (Figure 7.7).

Example study: A hybrid model for a pandemic can comprise an SD module that simulates the spread of an infectious disease in the community and an ABM module that represents a network of healthcare facilities (i.e., agents) in the same area. The network topology defines the transferring pathways between facilities. The level of a stock representing the infected population in the community that require medical care may reach a threshold that the current network topology of healthcare facilities could no longer efficiently handle. When this happens, the transferring pathways between facilities may need to reform to cope with the increasing demand, leading to a change in their network topology.

Information Flows from ABM Module to SD Module

(5) Agents' state variables affect flows

Description: Agents' state variables may evolve during a simulation as they execute a behaviour or interact with other agents and/or the environment. Changes in agents' state variables can affect flows in an SD module (Figure 7.8).

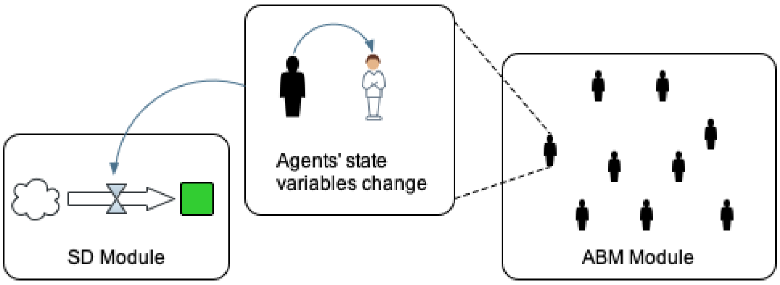

Figure 7.8: Changes in agents' properties can affect flows in an SD module

Example study: A hybrid model representing a network of healthcare facilities can include an ABM module representing a care home (i.e., the care home module), where individuals including residents and staff are agents, and an SD module representing its connected hospitals (i.e., the hospital module). Resident agents in the care home can be characterized by their infection status (susceptible or infected). Infected residents are assumed to require acute medical care, and, therefore, they are admitted to hospitals. This means that when a resident agent becomes infected, this change in its infection status will affect the admission inflow to a patient stock in a hospital SD module.

(6) Behaviours of agents affect flows

Description: Behaviours of agents in an ABM module can influence flows in an SD module (Figure 7.9).

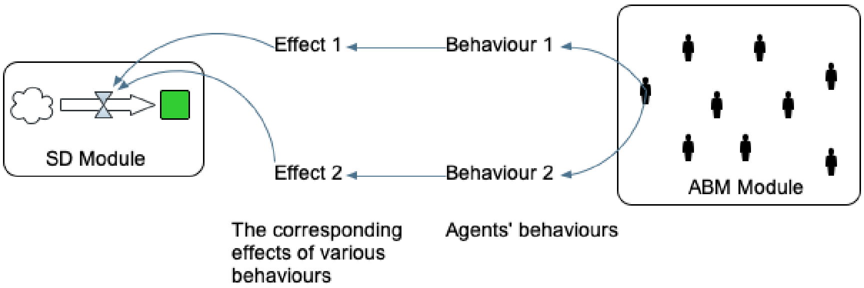

Figure 7.9: Behaviours of agents in the ABM module of a hybrid model affect flows in the SD module

Example studies: In Mazhari et al. (2009) hybrid SD-ABM model for capacity planning, the ABM component models the electricity consumption behaviours of household agents. The consumption behaviour of household agents affects the flow into the electricity demand stock in the SD component.

Chen and Desiderio (2020) develops a hybrid model to investigate a problem in labour market rigidity and its impact on unemployment. The model is the abstraction of a closed economy with markets for labour and consumption goods. Agents include households (on the supply side in the labour market and on the demand side in the goods market) and firms (on the demand side in the labour market and on the supply side in the goods market). These agents are characterized by internal SD modules representing their balance sheets (stocks), which reflect all of their market transactions undertaken (flows). The relationship between stocks and flows is regulated by rules that follow coherent accounting principles. The actions of agents result in market transactions which influence the flows to the balance sheet stocks within each agent.

(7) Aggregated measures of agents affect flows

Description: An aggregated measure of agents in an ABM can influence a flow in an SD module (Figure 7.10). When SD and ABM modules represent different parts of a system and agents physically move from the ABM module to the SD module, they are removed from the ABM module and aggregated into a stock in the SD module. This movement is represented as an inflow of the stock.

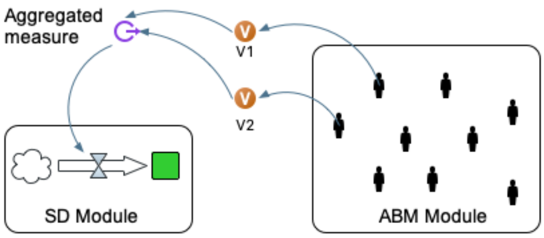

Figure 7.10: Aggregated measures of the ABM module of a hybrid model affect the flows in its SD module

Example studies: In the Swinerd and McNaught (2015) hybrid SD-ABM model for the international diffusion of technological innovations, agents describe individual nations. The nations' state of adoption, which, if set to true implies they decide to adopt the innovative technology, are aggregated into the international adoption stock in the SD module.

Jo et al. (2015) models the traffic of road stock in an SD module as the aggregation of driver agents who are potential users of the construction project.

(8) Network topologies affect flows

Description: The spatial/social relationship and/or network topologies of agents in an ABM module can affect the flows in an SD module (Figure 7.11).

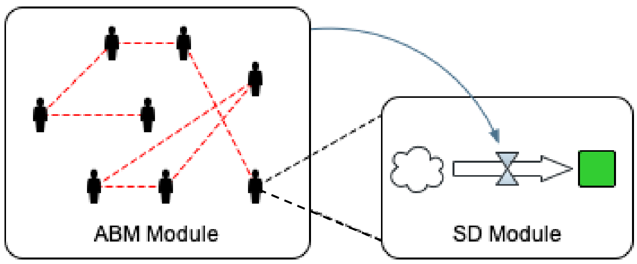

Figure 7.11: The network topology of agents in the ABM module affects flows in the SD module

Example study: The hybrid SD-ABM model developed by Vincenot and Moriya (2011) simulates the dynamics of infectious disease transmission in very large fragmented populations at both the local and global scales (Figure 7.12). It aims to investigate the influence of network topology upon the resurgence of epidemics. Each "site" agent equals one population generated based on a geographic breakdown of metapopulations and is represented by a classic SD module comprising stocks for susceptible, infected, and recovered individuals (Kermack and McKendrick, 1927; Anderson and May, 1979; Hethcote et al., 1981). As individuals within a population could emigrate to other connected populations, the network topology affects the ongoing emigration and immigration of infected individuals between site agents.

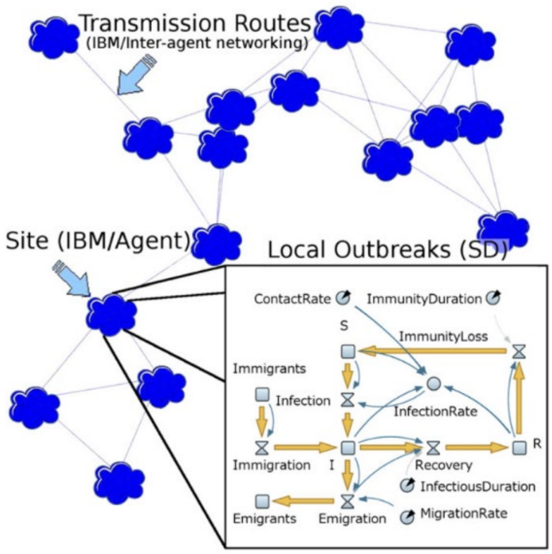

Figure 7.12: The visual structure of the hybrid SD-ABM model in Vincenot and Moriya (2011)
Reproduced from "Impact of the topology of metapopulations on the resurgence of epidemics rendered by a new multiscale hybrid modelling approach", by Vincenot, C.E. and Moriya, K., 2011, Ecological Informatics, 6(2011), 177-186. Copyright 2011 by Elsevier B.V. Reprinted with permission. Communicating ABM agents, representing sites (here, visualized as clouds), each incorporate an SD submodel (a partial view of which is inserted in the bottom-right corner of the figure) computing the evolution of the local outbreaks. These agents are in charge of the exchange of infected individuals between sites composing the network.

7.2.4.3 Step 4.3: Defining Updating Rules

Updating rules define when information is sent from one module to another and how new information is handled by the receiving module to maintain the logical consistency of the hybrid model (Onggo, 2014). Modellers specifically need to consider the following aspects when defining update rules: i) SD and ABM modules in a hybrid simulation model may use different time advancement methods. SD is compatible with both the continuous and the discrete concept of time (Sterman, 2000); the latter allows SD to advance using fixed-time increments. ABM typically advances using fixed-time increments but can adopt variable-time increments, ii) although the modules in a hybrid SD-ABM model may use the same time advancement method, they may use different time units, iii) modellers need to consider how updating rules would impact the modelling results and what implications there are for interpreting the model findings, iv) it is crucial to determine the logical order of several updates occurring at a pre-defined point in time, v) modules can be run using different simulation modelling software which has its own internal time management, and vi) modellers need to consider the run-time of a model when defining updating rules. We will discuss the first two aspects concerning the synchronisation of time advancement methods and time units of modules in the next two paragraphs. The last two paragraphs of this section will explore the third and fourth aspects. The fifth and sixth aspects are out of the scope of this framework as it focuses on building a conceptual model.

If the modules in a hybrid SD-ABM model use fixed-time increment advancements with the same unit of time, updates can be easily done when the hybrid model advances its simulation time. If the modules use fixed-time increments but different units of time, updates can occur synchronously or asynchronously. Synchronously, all modules in a hybrid model will pass their information to other recipient modules at predefined simulation points, which can be, for example, the time step of one of the modules (Figure 7.13A). Asynchronously, every time a module advances its simulation time, the module's status may alter and it will send new information to recipient modules which the interfaces define (Figure 7.13B).

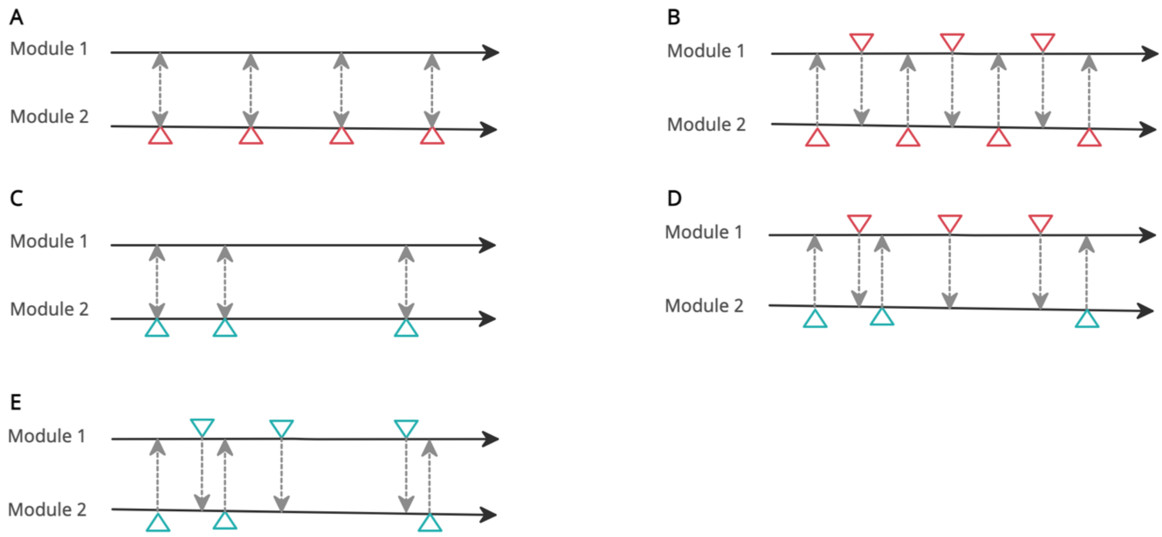

Figure 7.13: Synchronization between modules in a hybrid SD-ABM model

Red triangle: Fixed-time increments advancement; Cyan triangle: Variable-time increment advancement

Additionally, information exchanges and updates can occur at variable-time increments in one module or both modules. The updating points can be triggered by stock levels or rates of an SD module reaching particular thresholds, agents of an ABM module executing specific behaviours, or specific properties of an ABM module emerging. Updates can occur synchronously when all modules in a hybrid model pass their information to other recipient modules at triggered variable-time increments in one module (Figure 7.13C). Asynchronously, one module can send its information to the recipient module at its predefined simulation points (e.g., end of its time step) whilst the other module passes its information at triggered variable-time increments (Figure 7.13D). All modules can also send their information to other recipient modules at their own triggered variable-time increments (Figure 7.13E).

As a model is an abstraction of reality used for a specific objective, updating is unlikely to occur at the same frequency as in a real system. Therefore, modellers need to assess how the timing of updating rules would affect the modelling results and their interpretations. For example, components of a system may exchange information and update their status every second in reality; however, the modules of a hybrid model representing these components may be defined to update every hour or every day. Less frequent updates, in this case, are chosen as they are sufficient to meet the modelling objective and reduce the runtime.

At a pre-defined point of time, several modules of the hybrid model may need to exchange information and update their status. Determining the order of these updates is important to ensure the logic underlying the model and, thus, has implications on the modelling results. A tabular summary of updating rules is helpful for communicating the hybrid model design and facilitates face validation and computerized model building. Such a table can include when updates occur, the order of the updates at each updating point of time, the modules that send and receive information, and what information is exchanged between the modules (e.g., Table 9.2).

7.3 Chapter Summary

This chapter aims to propose a stepwise applicable, relevant, and helpful framework that modellers can adopt to inform the selection of hybrid SD-ABM methods and design a conceptual hybrid model. This work seeks to address the gap identified in Chapter 5 concerning a lack of methodology clarity when developing and presenting hybrid models with a focus on combining SD and ABM. The framework builds on the analysis of the existing guidance on mixing SD and ABM and the researcher's reflection on building a hybrid model introduced in Chapter 9. The modules constituting a hybrid model, justification for the selected simulation method for each module, interfaces, and updating rules are characteristics of the hybrid model. Reporting these characteristics provides a comprehensive overarching presentation of a conceptual hybrid model that facilitates communications of the model design and enables other modellers to take forward general lessons. The framework is intended to guide modellers think through different aspects and issues critical for developing a hybrid model. Whilst it presents a number of possible ways in which modules can be linked, it is not suggested that the framework provides an exhaustive list. This is particularly due to the 'art' of modelling where different modellers may choose to represent a situation in different ways. However, the framework provides a guiding structure which future research can add to. At this point, the current framework should be considered as a proposal that needs to be assessed in practice beyond the application in this thesis to build confidence in its validity and practicality.

Chapter 9 discusses the application of the framework to the context area of the spread of COVID-19 across care homes in Lanarkshire, as discussed in section 9.4. The current chapter and Chapter 9 address the fourth objective of this research with respect to providing methodological clarity on combining SD and ABM. Before presenting Chapter 9, Chapter 8 showcases an ABM model that simulates the spread of COVID-19 within a care home and evaluates various interventions to mitigate the impact of COVID-19 in this setting. The ABM model also helps inform the structural and experiment design and white-box validation of the hybrid model, as presented in Chapter 9. Both Chapter 8 and Chapter 9 address the third objective of this research with respect to preventing and controlling the spread of COVID-19 within and across care homes.

Chapter 8. Lanarkshire Project: Modelling Transmission of COVID-19 within a Care Home

8.1 Introduction

Care homes are vulnerable to the widespread transmission of SARS-CoV-2 with poor outcomes for staff and residents. Infection control interventions in care homes need to not only be effective in containing the spread of coronavirus disease 2019 (COVID-19) but also feasible to implement in this special setting which is both a healthcare institution and a home. This chapter presents an ABM that simulates the transmission dynamics of COVID-19 via contacts between individuals, including residents, staff members, and visitors in a care home setting. We explored a representative care home in Lanarkshire in our base case and other care home setups in an uncertainty analysis. We evaluated the effectiveness of a range of intervention strategies in controlling the spread of COVID-19.

This chapter combines content taken from the below two publications

Nguyen, L. K. N.[a], Howick, S.[a], McLafferty, D.[b], Anderson, G. H.[a], Pravinkumar, J.[c], Van Der Meer, R.[a], & Megiddo, I.[a] (2020). Evaluating intervention strategies in controlling COVID-19 spread in care homes: an agent-based model. *Infection Control and Hospital Epidemiology*. https://doi.org/10.1017/ice.2020.1369

Nguyen, L. K. N., Howick, S., McLafferty, D., Anderson, G. H., Pravinkumar, S. J., Van Der Meer, R., & Megiddo, I. (2021). Impact of visitation and cohorting policies to shield residents from COVID-19 spread in care homes: an agent-based model. *American Journal of Infection Control*, *49*(9), 1105-1112. https://doi.org/10.1016/j.ajic.2021.07.001

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As the model informing the analysis in the second paper was adapted from the model presented in the first paper, the two papers have been combined section by section to reduce the redundancy and ensure the flow of the thesis (see the footnotes of section headings for detail).

8.2 Research in Context[15]

Many studies have investigated the spread of COVID-19 in the general population, but research on the unique transmission dynamics and interventions for COVID-19 in healthcare settings, and care homes, in particular, is scarce. We carried out searches on PubMed, MedRxiv, and BioRxiv for papers published between 1 January 2020 to 15 July 2020 and containing the terms (COVID OR coronavirus OR nCoV OR SARS-CoV-2) AND (care home* OR nursing home* OR skilled nursing facilit* OR long-term care OR LTCF* OR residential care). We identified 152 preprints and articles published in academic journals, mostly outbreak reports, point prevalence surveys, commentary, and editorial papers that discuss the importance and challenges of controlling COVID-19 spread in this setting. They describe experiences of containing spread in some specific care homes, a need for improved control interventions, and a call for more attention and a plan from governments. We found one preprint modelling study (Smith et al., 2020) that evaluates the capability of surveillance strategies to detect simulated outbreaks under limited testing capacity in a long-term care hospital. This paucity suggests a lack of research on the transmission dynamics of COVID-19 and the effectiveness of infection control interventions in this setting. Implementing interventions to prevent and control COVID-19 in care homes without understanding their potential outcomes can have adverse effects on residents and be costly.

Many care homes across the globe implemented strict "no visitor" and/or cohorting policies and curtailed group activities as part of their infection prevention and control strategies. Although there have been several modelling studies of the impacts of non-

[15] This section includes the last paragraph in the Introduction section in Nguyen et al. (2020a) and the Introduction section in Nguyen et al. (2021a) with the addition of a connecting sentence.

pharmaceutical interventions on COVID-19 epidemics, few have examined shielding (van Bunnik et al., 2020; Van Zandvoort et al., 2020; McKeigue and Colhoun, 2020; Neufeld et al., 2020; Weitz et al., 2020). These studies have modelled shielding strategies targeting vulnerable groups in the general population and provided different views on how such strategies could be ended. None of them have explicitly considered shielding care home residents to our knowledge.

Although visitation restrictions to shield residents have been suggested as an intervention to partially prevent the introduction of COVID-19 into care homes, experts and advocates are increasingly concerned that such practice may cause substantial unintended harm to the health and well-being of residents (Stall et al., 2020). A recent survey conducted in English care homes reported that the deprivation of visitation from and physical contact with loved ones have predominantly contributed to lowering residents' mood, exacerbating irritability, agitation, and anxiety among residents and the symptoms of their dementia, and reducing oral intake (Rajan and Mckee, 2020). A more sustainable and balanced approach that both allows needed contact with family visitors but also prevents the introduction and spread of COVID-19 in care homes may be needed. Understanding to what extent these visiting policy interventions protect residents is important to inform decisions about how to balance the risk of COVID-19 and care home residents' well-being.

Cohorting is considered a common and effective infection control measure in acute care settings such as hospitals (Lee et al., 2005), and some studies showed the association between the presence of an outbreak and the care home resident population (Burton et al., 2020a; Abrams et al., 2020). However, the impact of this intervention in care homes has not been well studied. As healthcare systems are likely to bear additional costs for staffing, equipment, and support to implement cohorting in care homes, evaluating the effectiveness of this intervention is important.

To address these issues, we developed an ABM to investigate the transmission dynamics of COVID-19 in a care home and the effectiveness of a range of infection control intervention strategies using ABM. The model simulated the transmission dynamics of COVID-19 via contact between individuals, including residents, staff members, and visitors.

8.3 Choosing Appropriate Simulation Modelling Method: ABM

We present an ABM that captures heterogeneity and stochasticity of individuals' disease progression and interaction patterns and their effect on transmission dynamics of COVID-19 and the effectiveness of control interventions in a care home setting. Care homes are diverse in terms of their resident population, structure, and management, and ABMs have more flexibility compared to simpler epidemiological compartment models to reflect this variation and examine how it impacts findings. The stochastic feature of ABM is well-suited for simulating a small population in an intricate setting like a care home, where chance events can lead to major effects. Further, while deterministic compartment models yield a single output for each parameter set, an ABM produces a distribution of outputs accounting for stochastic uncertainty of interactions within the care home and disease progression.

8.4 Agent-Based Model: Overview, Design Concepts, and Details[16]

A complete, detailed model description following the ODD protocol (Grimm et al., 2006; Grimm et al., 2010; Grimm et al., 2020) is provided in Appendix E. In this section, the model assumptions are described in the Overview sections (Entities, state variables, and scales – section 8.4.2 and summary Process overview and scheduling – section 8.4.3) and the design choices in the Design concepts section (section 8.4.4).

8.4.1 Purpose and Patterns

The purpose of the model is to understand the spread of COVID-19 and anticipate the prevalence and the cumulative number of infected residents over time in a care home. It also aims to examine the effectiveness of various infection control strategies in controlling COVID-19 in this setting. We evaluate our model by its ability to reproduce the patterns of the dynamics of outbreaks reflecting what has happened in Scottish care homes that have experienced outbreaks and the proportion of asymptomatic infections reflecting what has been reported in long-term aged care settings in the literature.

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[16] Sections 8.4.1, 8.4.2, and 8.4.4 have been taken from sections 1, 2, and 4 respectively in the ODD protocol included as an appendix in Nguyen et al. (2020a) and Nguyen et al. (2021a).

8.4.2 Entities, State Variables, and Scales

The following entities are included in the model: two types of agents, namely resident and staff agents, representing residents and staff in the care home. Each agent entity is characterized by a unique set of state variables which is described in greater detail in Table 8.1.

The resident agents are split into two units, each with their own group of staff agents representing care staff members including nurses and nursing/care assistants. There is a separate group of staff agents which are shared between the two units and represent staff in other roles including housekeepers and wellbeing coordinators.

The model runs at a daily time step as epidemiological data are collected on a daily basis, and the unit of time commonly used to describe clinical characteristics of COVID-19 in the literature is a day. Simulations are 180-day time steps long as this covers the period from the beginning of the pandemic until the time when the model is developed and the upcoming period for which the clients are planning.

Table 8.1: The state variables of resident and staff agents and the global environment

Variable name	Variable type, units and range	Meaning and rationale
Resident-agent-specific state variables		
unitID	Integer, static; no unit; [1,2,3]	The ID of the unit where a resident stays. It affects with whom a resident can come into contact. E.g. A resident only comes into contacts with other residents living in the same unit.
Age	Integer, static; years old; [18 – 110]	The age of a resident which affects the infection fatality rate
ResidentInState	String, dynamic; no unit; “susceptible”, “exposed”, “asymptomatic”, “presymptomatic”, “symptomatic”, or “recovered”	The state of infection of a resident. Asymptomatic, presymptomatic and symptomatic residents are infectious.
Severity	Integer, dynamic; no unit; 0 = no symptom, 1 = mild, 2 =severe	The severity of symptoms in symptomatic cases that affect the duration of infectiousness

Variable name	Variable type, units and range	Meaning and rationale
AdmissionScheduled	Boolean, dynamic; no unit; true/false	This variable denotes a resident agent leaving the care home or dying, and waiting for admission as a new agent
Isolation	Boolean, dynamic; no unit; true/false	This variable indicates whether a resident is isolated
Tested	Boolean, dynamic; no unit; true/false	This variable indicates whether a resident receives a RT-PCR test for COVID-19
Staff-agent-specific state variables		
unitID	Integer, static; no unit; [1, 2, 3]	The ID of the unit where a member of staff works. It affects with whom a staff can come into contact.
Employment	String, static; no unit; “casual” (Bank or Agency staff) or “permanent”	The employment status of a staff
StaffInState	String; dynamic; no unit; “susceptible”, “exposed”, “asymptomatic”, “presymptomatic”, “symptomatic” or “recovered”	The state of infection of a member of staff
Severity_Staff	Integer, dynamic; no unit; 0 = no symptom, 1 = mild, 2 =severe	The severity of symptoms in symptomatic cases that affect the duration of infectiousness
AtWork	Boolean; dynamic; no unit; true/false	The variable indicates whether a staff member is on duty
SelfIsolation	Boolean; dynamic; no unit; true/false	The variable indicates whether a staff member is self-isolating at home
Replaced	Boolean; dynamic; no unit; true/false	The variable indicates whether a staff member is replaced by or replaces another staff member in the next time step
Tested	Boolean, dynamic; no unit; true/false	This variable indicates whether a resident receives a RT-PCR test for COVID-19

8.4.3 Process Overview and Scheduling

This section summarizes the processes of the model, which are repeated every time step (see Appendix E for detail): (1) Residents, admitted from either hospitals or the community at equal probabilities, and staff can introduce the virus into the care home. The model assumes that the care home operates with a constant daily number of staff members on duty. Staff, who are absent due to contracting COVID-19, are replaced by casual bank/agency staff; (2) Residents, staff on duty, and visitors interact with one another following specific contact patterns. Transmission occurs in a susceptible-infectious contact at a pre-defined probability. (3) Infected residents and staff progress through different stages of infection. (4) Residents, who decease (COVID and non-COVID causes) or leave the care home, are replaced with newly admitted residents in the next time step as the model assumes that the care home operates at its capacity. Staff members, who decease due to COVID-19 or resign, are replaced with new susceptible staff members.

8.4.4 Design Concepts

Basic principles:

The model simulates the transmission dynamics of COVID-19 via contacts between individuals, including residents, staff, and visitors within a hypothetical care home that represents a Scottish care home (Figure 8.1). The progression of COVID-19 infection after transmission occurs is described in Figure 8.2 based on the current understanding and evidence of clinical characteristics of COVID-19 (Ferguson et al., 2020; Verity et al., 2020; He et al., 2020). It is assumed that recovered people are immune to re-infection in the short term, and pre-/asymptomatic individuals are just as likely to transmit infection as symptomatic individuals (CDC, 2020). Individuals' characteristics, behaviours, and contact networks and patterns, along with the operational and managerial features of the care home, can influence how the virus is disseminated. Such information is based on discussions, surveys, and interviews with stakeholders, including HSCP, Public Health, and care homes in Lanarkshire. Infections can be imported into the care home by asymptomatic residents upon admission, staff, and visitors who acquired the infection somewhere else. Infection control measures are implemented to reduce the imported infections (e.g., testing upon admission, visit restriction) and contain intra-facility transmission by reducing contact rates (e.g., social distancing, isolation) and the risk of transmission per contact (e.g., hand hygiene and use of PPE).

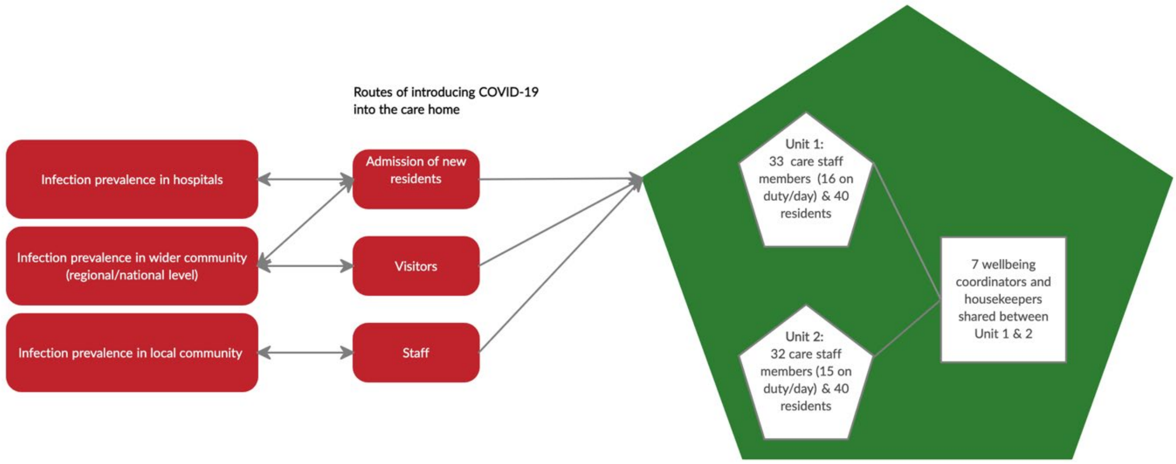

Figure 8.1: The structure of the care home and routes of introducing SARS-CoV-2 into the home
The base case care home, representative of a care home in North Lanarkshire, Scotland, has 80 residents and a team of 72 staff members. It is split into 2 units containing 40 residents and 16 and 15 care staff members on duty per unit per day. The staff pools for the 2 units contain 33 and 32 care staff members respectively. A group of 7

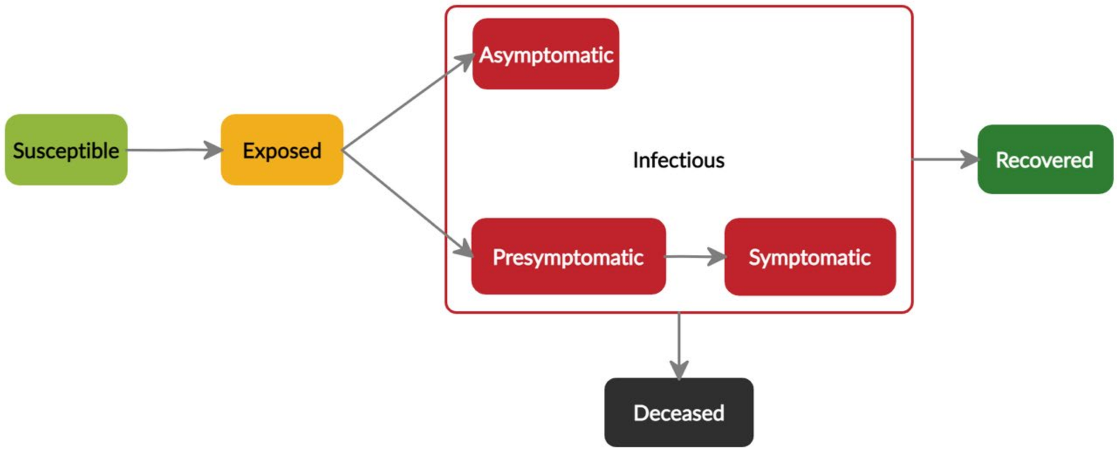

Figure 8.2: The progression of COVID-19 infections
Susceptible people may acquire the infection when exposed to infectious sources. They are infected but not yet infectious (exposed state). Once exposed people become infectious, they can either remain asymptomatic for the entire infectious period or develop symptoms after a pre-symptomatic period. Symptoms could be mild or severe and require hospitalizations. Infectious people will eventually recover or die.

Emergence:

The key outcomes of the model are patterns for the occurrence and recurrence of outbreaks, surges of COVID-19 related deaths, and staff acquiring infections in the care home. These outcomes emerge from the contact network and pattern among residents and staff, how infections are imported into the facility, infection control measures implemented, and staff's compliance with such measures.

Adaptation:

Staff agents that exhibit symptoms or are tested positive leave the care home. In isolation scenarios, residents who exhibit symptoms or are tested positive are isolated. When social distancing is implemented, staff and residents adapt to the situation by decreasing their contact rate with other staff members and residents, respectively. Residents do not come into contact with other residents in the other unit either.

Objectives:

The objective measure used by staff agents to decide whether to comply with infection control measures such as hand hygiene, using PPE, and practicing social distancing is the existence of an outbreak in the care home. Their adaptive behaviours aim to reduce transmission rates and help contain the outbreak.

Prediction:

The staff's adaptive behaviour is based on implicit predictions that i) they will stay home the next day after exhibiting symptoms, ii) social distancing will reduce the number of contacts which, in turn, limits the spread of infections, and iii) increasing compliance to hand hygiene and using PPE will reduce the risk of transmission per contact.

Sensing:

Agents can sense with whom they are in contact. Staff agents can sense the infection status of residents who display symptoms and exposed or asymptomatic residents who are tested positive. Staff who develop symptoms can also sense their own state of health and do not return to work the next day.

Interaction:

Agents have direct interactions, as shown in Figure 8.3. Residents can interact with other residents, staff, and visitors. Staff can interact with other staff and visitors. The network and rates of interactions between residents and staff are defined based on the management policy of a care home and the implemented infection control interventions such as social distancing.

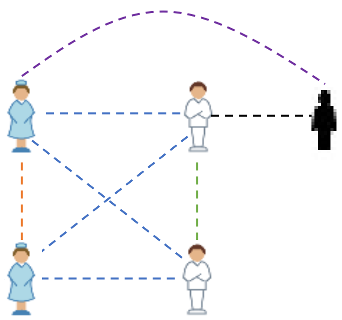

Figure 8.3: Interactions between residents, staff and visitors in a care home
The dashed lines linking individuals denote their possible ways of interaction. Different colours are used for these lines to distinguish different types of interaction: blue – staff-resident interaction; green: resident-resident interaction; red: staff-staff interaction; black: resident-visitor interaction; purple: staff – visitor interactions.

Stochasticity:

Residents' age is initialized stochastically as this characteristic affects residents' risk of death as an outcome of the infection. Stochasticity is used to describe variability in the parameters that determine the transitions of individuals between different states of infection, including the incubation time and the transmission probability. This represents variations in the risk of acquiring the infection and the progression and outcome of the infection among people, influenced by factors such as their health status, underlying conditions, and immune system. Additionally, the interaction between individuals is a stochastic process as randomness exists in contact rates, with whom they come into contact, and the order in which contacts between individuals occur. Another stochastic element is individuals' compliance with an infection control intervention. Such stochasticity is added to demonstrate how individuals' heterogenous behaviours and contact networks and patterns can affect the spread of the infection. The time at which individuals (staff members, new residents, and visitors) introduce the infection into the care home is also stochastic.

Collectives:

The model has three collectives: the two units and the shared ancillary staff group. The collective to which agents belong affects with whom they can interact.

8.5 Data Collection and Parameters[17]

We interviewed care-home stakeholders, including managers and staff in different roles, and we had regular discussions with representatives from the HSCP and Public Health in Lanarkshire to analyse the problem, build the model, and design the intervention strategies as described in section 6.5.2. We also conducted literature reviews to obtain the values for parameters characterizing the transmission of SARS-CoV-2 and the disease progression. Other parameters are based on national data for Scotland and regional data for North Lanarkshire where available.

Base-case model: The model is initialized with 80 resident agents and 72 staff agents in the base case. The first unit (UnitID = 1) has 40 resident agents and 33 staff agents. The second unit (UnitID = 2) has 40 resident agents and 32 staff agents. A group of seven staff agents are shared between the two units (UnitID = 3). The number of staff agents present in the care home is 16 and 15 for Unit 1 and 2 respectively. All shared staff are on duty. There are two bank/agency staff members in Unit 1 and one in Unit 2. The number of residents and staff and the operational structure were provided by the manager of a representative care home for older people. The variable Age of residents is drawn from an empirical distribution based on the demographic data of older people adult care homes in North Lanarkshire. Model input parameters used for the base case simulation are presented in Table 8.2.

[17] This section includes the Data Collection and Parameters sections in Nguyen et al. (2020a) and the Initialization section in the ODD protocol appendix in Nguyen et al. (2021a).

Table 8.2: Parameters used in the model

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
InfectionPrevalence Hospital	Infection prevalence in the hospital	0.02	Triangular distribution (min = 0, max = 0.5, mode = 0.2)	(NRS, 2021; PHS, 2020; Scottish-Government, 2020a)(estimated)
InfectionPrevalence Community	Infection prevalence in the community	Time-series of data from Scotland adjusted for undetected cases	Triangular distribution (min = 0, max = 0.2, mode = 0.05)	(Perez-Reche and Strachan, 2021; PHS, 2020) (The undetected cases represent 50 – 80% of the total cases in the community. We adopted the worse situation (80% cases undetected) for the base case scenario)
DeathProbability	The probability that an infected resident dies (age-specific)	Drawn for each individual resident from empirical distribution: 80+ years old: 11% 70-79 years old: 6.0% 60-69 years old: 2.6% 50-59 years old: 0.71% 40-49 years old: 0.18% 30-49 years old: 0.09% 20-29 years old: 0.04% 18-20: 0.007%	No (This parameter does not impact our main model output, the number of infected residents, significantly. It will likely be the most important parameter when we consider deaths as an outcome of the model)	(Ferguson et al., 2020; Kulu and Dorey, 2020) (The Infection Fatality Rate (IFR) for Scotland is adjusted based on the overall aged-adjusted IFR value for the UK and the relative IFR value (= 1.18) for other urban areas in Scotland. The majority of population (>80%) in North Lanarkshire live in areas classified as other urban areas.)
StaffDeath Probability	The probability that an infected staff member dies	Drawn for each individual staff member from a uniform distribution (0.0003 – 0.022)	No	(Ferguson et al., 2020; Kulu and Dorey, 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
ClosedTo Admission	The state variable determines whether the care home is opened to admissions	False	No	
ContactRateRR	The number of contacts that a resident has with other residents per day	Drawn for each individual resident from a Poisson distribution with a mean of 3.9 contacts per resident per day	Mean of the Poisson distribution is drawn from a triangular distribution (min = 1, max = 5, mode = 3.9)	(van den Dool et al., 2008; Chamchod and Ruan, 2012)
ContactRateSS	The number of contacts that a staff has with other staff per day	Drawn for each individual staff member from a Poisson distribution with a mean of 7.3 contacts per staff member per day	Mean of the Poisson distribution is drawn from a triangular distribution (min = 1, max = 10, mode = 7.3)	(van den Dool et al., 2008)
ContactRateSR	The number of contacts that a staff has with residents per day	Drawn for each individual staff member from a Poisson distribution with a mean of 16.2 contacts per staff per day	Mean of the Poisson distribution is drawn from a triangular distribution (min = 10, max = 20, mode = 16.2)	(van den Dool et al., 2008; Chamchod and Ruan, 2012)
ContactRateSV	The number of contacts that a staff has with visitors per day	5.0 contacts per staff member per day	Triangular distribution (min = 0, max = 10, mode = 5.0)	Discussions with the manager and staff of a Scottish care home for older people
ContactAcross Units	The probability that a resident comes into contact with another	20%	Triangular distribution (min=0, max = 0.5, mode =0.2)	Discussions with the manager and staff of a Scottish care home for older people

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
	resident in the other unit			
VisitorsPerDay	The average number of people visiting a resident per day	1.0 visitor per resident per day	Triangular distribution (min = 0, max = 2.0, mode = 1.0	(Port et al., 2003; van den Dool et al., 2008)
LeavingRate	The rate at which residents leave the care home because of deaths caused by other reasons, moving to another facility, admitted to hospitals, or returning to their own home (rare)	0.005 deaths or discharges per resident per day	Triangular distribution (min = 0.001, max = 0.005, mode = 0.004)	(ISD, 2018) (Calculated from data for care homes in North Lanarkshire)
StaffTurnover	Staff turnover rate	24% per year	Triangular distribution (min = 0.1, max = 0.5, mod = 0.24)	(Scottish-Care, 2018)
pSymptomatic	The probability that an infected resident will develop symptoms	Drawn for each individual resident from empirical distribution: 80+ years old: 0.9 70-79 years old: 0.85 60-69 years old: 0.8	Triangular distribution (min = 0.5, max = 0.9, mode = 0.8)	(Ferguson et al., 2020; Verity et al., 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
		50-59 years old: 0.75 40-49 years old: 0.7 30-49 years old: 0.65 20-29 years old: 0.6 18-20: 0.55		
pStaff Symptomatic	The probability that an infected staff member will develop symptoms	0.7	Triangular distribution (min=0.5, max=0.9, mode=0.7)	(Ferguson et al., 2020; Verity et al., 2020) (For a population like the UK or US)
pSevere	The probability that a symptomatic resident has severe symptoms	Drawn for each individual resident from empirical distribution: 80+ years old: 0.28 70-79 years old: 0.25 60-69 years old: 0.17 50-59 years old: 0.11 40-49 years old: 0.05 30-49 years old: 0.03 20-29 years old: 0.01 18-20: 0.001	No (This parameter does not affect number of infections significantly given the assumptions that symptomatic individuals are isolated with perfect effectiveness)	(Ferguson et al., 2020; Kulu and Dorey, 2020) The proportion of symptomatic cases requiring hospitalizations for Scotland is adjusted based on the overall aged-adjusted value for the UK
pSatffSevere	The probability that a symptomatic staff member has severe symptoms	Drawn for each individual staff member from a uniform distribution (0.01-0.17)	No	(Ferguson et al., 2020; Kulu and Dorey, 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
InfectionProbability	The probability that an individual (resident or staff) is infected after coming into contact with another infectious individual (resident, staff or visitor)	0.02	Triangular distribution (min = 0.001, max = 0.1, mode = 0.02)	(Wang et al., 2020c; Tang et al., 2020a; Ferguson et al., 2020)
ExposedTime	The time elapsed between first exposure and becoming infectious	Lognormal ($\mu = 1.16$, $\sigma = 0.85$)	No (This parameter does not significantly affect number of infections as exposed individuals are not infectious. Also, values for this parameter are relatively consistent across studies.)	(Lauer et al., 2020; McAloon et al., 2020; Nishiura et al., 2020) (Lognormal (mean = 4.6, std = 4.8)
Presymptomatic Time	The time elapsed between becoming infectious and onset of symptoms	Discrete uniform distribution (1,3)	No (Values for this parameter are consistent across studies)	(He et al., 2020; Gatto et al., 2020; Byrne et al., 2020)
Infectiousness	The time elapsed between onset of symptoms and recovery (or recovery	Asymptomatic: Lognormal ($\mu = 2.049$, $\sigma = 0.246$) Symptomatic:	No (There is a strong consensus about the distribution of this parameter in literature.)	(Wölfel et al., 2020; Kerr et al., 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
	time for those who remain asymptomatic)	-Mild: Lognormal (μ = 2.049, σ = 0.246) -Severe: Lognormal (μ = 2.624, σ = 0.170)		
SDCompliance	The reduction of resident-resident and staff-staff interactions when social distancing is implemented	0.75	Triangular distribution (min = 0.2, max = 0.9, mode = 0.75)	Assumed (based on other models' assumption (Ferguson et al., 2020; Matrajt and Leung, 2020) and discussions with care home staff and managers)
TestSensitivity	The sensitivity of RT-PCR test	0.7	Triangular distribution (min = 0.6, max = 0.98, mode = 0.7)	(Watson et al., 2020; Arevalo-Rodriguez et al., 2020)
TestDelay	The lag between testing and test result	1 days	No (Implemented in scenario-based uncertainty analysis)	Discussion with representatives from Public Health Medicine (NHS Lanarkshire) and Lanarkshire Health and Social Care Partnership
Isolation Effectiveness	Effectiveness of isolation of infected residents	100%	50%, 75%, and 100%	Assumed (based on other models' assumption(Ferguson et al., 2020; Matrajt and Leung, 2020))

8.6 Experimentation

8.6.1 Intervention Scenarios Explored in Early Pandemic[18]

We considered the impact of nine different intervention strategies summarised in Table 8.3. The reference intervention strategy (Inter1) is based on discussions with local care home stakeholders in Lanarkshire and aligned with the guidance for controlling COVID-19 by the Scottish government. One random resident is exposed to the virus at the beginning of the simulation. The remaining agents are susceptible. Interventions such as hand hygiene and using PPE change the infection probability per contact, representing the reduction in transmission risk and compliance. Residents and staff members who are symptomatic or tested positive are isolated and excluded from work respectively the day after being tested since it was assumed to take one day for results to be returned in base case simulations. As standard RT-PCR testing is highly specific (Corman et al., 2020), we assumed perfect specificity. Finally, the examined intervention strategies were in force during this period.

Table 8.3: Summary of intervention strategies considered

Intervention strategy	Description
Inter0	No intervention
Inter1	Isolation of symptomatic cases & testing of new admissions (two tests) & social distancing & restricted visiting (referred to as the reference intervention).
Inter2	Inter1 & 14-days compulsory isolation for new admissions regardless of the result of their tests
Inter3	Inter1 & adaptive testing (i.e. testing staff and residents and the care home is closed to new admissions when there is a symptomatic case, reopening when all symptomatic and confirmed residents recover)
Inter4	Inter3 & 14-days compulsory isolation for new admissions
Inter5	Inter1 & weekly testing of residents
Inter6	Inter1 & weekly testing of staff
Inter7	Inter1 & weekly testing of staff and residents
Inter8	Inter6 & 14-days compulsory isolation for new admissions
Inter9	Inter7 & 14-days compulsory isolation for new admissions

[18] Taken from the Intervention Scenarios section in Nguyen et al. (2020a)

8.6.2 Exploring the Effect of Visiting Policy[19]

We investigated the impact of the number of visitors per resident per day for different infection probabilities per contact, which reflect the adherence to measures such as hand hygiene and using PPE in the care home. All agents are susceptible at the start of the simulation. We also examined a scenario in which the transmission risk between visitors and residents is different from the risk between other types of contacts in the facility. We varied the infection probability of visitor-resident contacts and used a fixed infection probability for other types of contacts.

Additionally, we investigated the effect of visiting policy when the prevalence of COVID-19 in the communities where staff and visitors come from are different. We used the base case value of community infection prevalence to determine the probability at which visitors can introduce COVID-19 into the care home and then applied the relative prevalence to determine the probability at which a staff member can introduce the infection into the facility.

8.6.3 Exploring the Effect of Care Home Population Size and Structure

When examining the effect of care home population size, we scaled the staffing levels based on the resident:staff ratio used in the base case simulation. All agents are susceptible at the start of the simulation. In cohorting interventions, we assumed that residents and staff are split evenly into smaller, self-contained units within a care home and examined two scenarios: individuals, including staff and residents across units, do not interact, and interactions across units occur at the probability of 20%.

8.6.4 Outcomes[20]

While deterministic models yield a single outcome for each set of parameters, due to stochasticity, the ABM produces a distribution of possible outcomes and, therefore, requires a large number of simulations to gain an understanding of the system behaviour. We reported outcomes in our base case for a care home with a capacity of 80 residents. When simulations were seeded with one infection in residents, we ran 300 simulations for each scenario. When

[19] Sections 8.6.2 and 8.6.3 are the same as Experiment Designs in Nguyen et al. (2021a).

[20] The Outcomes sections in Nguyen et al. (2020a) and Nguyen et al. (2021a) are combined.

simulations started without a seeded infection, we ran 1,000 simulations for each scenario as the mean for all outcomes we reported converged after this number of simulations. We defined that outcomes converged for our purpose when 95% confidence intervals of the mean outcomes were within ± one infection or one day. The probability of outbreak occurrence was also stable (±0·5%) for more than 500 simulations.

The outcomes we collected include the prevalence of infected residents over time (means and distribution of prevalence at peak), the cumulative number of infected residents (means, medians, interquartile ranges (IQRs), and 1.5IQRs), the time elapsed until the first resident is infected (distributions, means, and confidence intervals (CIs)), and the probability of outbreak occurrence (i.e., the presence of at least two infected residents). We reported the cumulative number of infected residents and the risk of outbreak occurrence after 90 days as discussions with representatives from the HSCP and Public Health Lanarkshire suggested the importance of identifying the risk of outbreaks within this period for decision-making. Our estimate of this risk is represented by the percent of simulations in which an outbreak occurred over this period.

8.6.5 Statistical Analysis[21]

We used Welch's *t*-test at a significant level of α = 0.05 to perform hypothesis testing for differences in the mean cumulative numbers of infections after 90 and 180 days between scenarios (Table E.3 and Table E.4 in Appendix E). We also adopted the Bonferroni correction method in which the p-values were multiplied by the number of tests to counteract the potential type one error in multiple comparisons.

8.7 Confidence Building

8.7.1 Verification and Validation Approaches[22]

Our simulation model was built in Anylogic PLE 8.7.2. For verification, we performed tracing of randomly chosen agents of each type via simulation output and using the debugger, bottom-

[21] Taken from the Statistical Analysis section in Nguyen et al. (2020a)

[22] The Uncertainty and Sensitivity Analyses section (under Methods) in Nguyen et al. (2020a) and the Verification and Validation section (under Methods) in Nguyen et al. (2021a) are combined.

up testing, stress testing, and regression testing. We validated our model using three approaches: face validation, cross-validation to observed data in care homes in Lanarkshire and published literature, and sensitivity and uncertainty analyses. In face validation, the model was developed in conjunction with care home stakeholders, including representatives from HSCP and Public Health Lanarkshire, care home managers, the Scottish Government Data Analysis Research Group, and SCWG. This helped ensure that the model sufficiently represents the investigated system while making the appropriate assumptions to develop such a model. In cross-validation, we ran the scenario in one of the care homes in Lanarkshire and compared the time series prevalence of COVID-19 in residents to observed data provided by that care home. We also compared the risk of outbreak occurrence in care homes with different population sizes to Scottish data and the analysis of care homes in Lothian.

Sensitivity and Uncertainty Analyses: We carried out global probabilistic sensitivity analyses for parameter uncertainty. Table 8.2 summarizes the probability distributions of the model parameters. We simulated the model for 100,000 sets of samples generated using the Latin Hypercube Sampling (LHS) method. The calculated Partial Rank Correlation Coefficient (PRCC) determined the strength of the relationship between each LHS parameter and each outcome measure. We also examined how robust the relative effectiveness of interventions (Inter1 – Inter 9) was with respect to the most impactful uncertain parameters determined in the PRCC analysis. Furthermore, we assessed the impact of the testing interval between 1 and 30 days on the effectiveness of routine testing interventions (Inter6, Inter7, Inter8, and Inter9). We also examined the robustness of the findings to the care home's population size, structure, and staff pooling system (Table E.6 in Appendix E).

8.7.2 Validation Results[23]

Cross-Validation:

The model-generated time series prevalence of COVID-19 among residents matched closely to the observed data in a care home in Lanarkshire (Figure E.6 in Appendix E). The

[23] The Uncertainty and Sensitivity Analyses section (under Results) in Nguyen et al. (2020a) and the Validation Results section (under Results) in Nguyen et al. (2021a) are combined.

risk of outbreak occurrence in care homes, which varied in population size, agreed with Scottish data and the analysis of care homes in Lothian as we described in the results.

Sensitivity and Uncertainty Analyses:

Outputs from the PRCC analyses are summarized in Table E.7 and Table E.8 in Appendix E. The PRCC values measure the associations between each of the parameters and the modelling outcomes. The infection probability per contact, the infection prevalence in the community, and the average staff–resident contact rate were the highest contributors to uncertainty in the cumulative prevalence of COVID-19 in care homes. Additionally, the outcomes in testing scenarios were sensitive to test sensitivity. Increasing these parameters led to an increase in cumulative COVID-19 prevalence in care homes. Due to the large correlation between the infection probability and the outcomes, measures including individuals' hand hygiene and PPE that reduce the risk of transmission are highlighted as extremely important for COVID-19 prevalence.

The examined outcomes were also sensitive to the infection prevalence in the community and staff–resident contact rate but to a significantly lesser extent. The model outcomes were sensitive to the staff–resident contact rate but not to staff–staff and resident–resident contact rates in both scenarios. The difference in sensitivity to different types of contacts occurred because a social distancing measure was implemented in the reference intervention, and we assumed that the intervention reduced staff–staff and resident–resident contact while staff–resident contact rates remained unchanged. Test sensitivity affected the effectiveness of routine testing of staff strategy. Across values of the most impactful parameters, the relative effectiveness of intervention strategies remained unchanged (Figure E.7 in Appendix E).

The findings regarding the relative effectiveness of interventions were robust when modifying the structures (unit size and residents-per-staff ratio) and capacity of the care home. Unit size or residents-per-staff ratio did not significantly impact the cumulative number of infected residents. Neither did care-home capacity affect the proportion of infections among residents. Furthermore, the findings of the scenarios in which the impact of relaxing visitation was statistically insignificant, small, or significant were robust to modifying the population size and structures (unit sizes, residents-per-staff ratios) of the care home.

8.8 Results[24]

8.8.1 Spread of COVID-19

In all scenarios, the mean prevalence of infected residents peaked approximately 30 days after the first infection in the care home, decreased, and then stabilized after around 90 days (Figure 8.4A). The distribution of prevalence at peak (mean = 34, std = 4.9, range [19 – 47]) in the no intervention scenario is illustrated in Figure 8.4B. Relatively large variations in prevalence values are due to stochastic uncertainty of interactions within the care home and disease progression.

In the absence of any control measures and spontaneous changes in the behaviours of individuals, the introduction of a single infected resident resulted in an outbreak (i.e., at least two residents are infected) in 99.7% of simulations; in one simulation, the transmission died out quickly. By the time that any infected residents manifest COVID-19 symptoms, an average of six residents (std = 4.2, range [1 – 23]) have acquired the infection but may not (yet) show symptoms. Infected cases that do not (yet) display symptoms make up approximately half of all infections among residents (Figure 8.5 and Figure E.2), which aligns with reported data (Kimball et al., 2020). Additionally, the proportion of asymptomatic cases among infected residents in our study (7% [4-10%]) shows a good approximation of observed data for long-term aged care (8% [3-18%]) (Byambasuren et al., 2020; Arons et al., 2020; Freitas, 2020).

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[24] The Results sections excluding the validation results in Nguyen et al. (2020a) and Nguyen et al. (2021a) are combined.

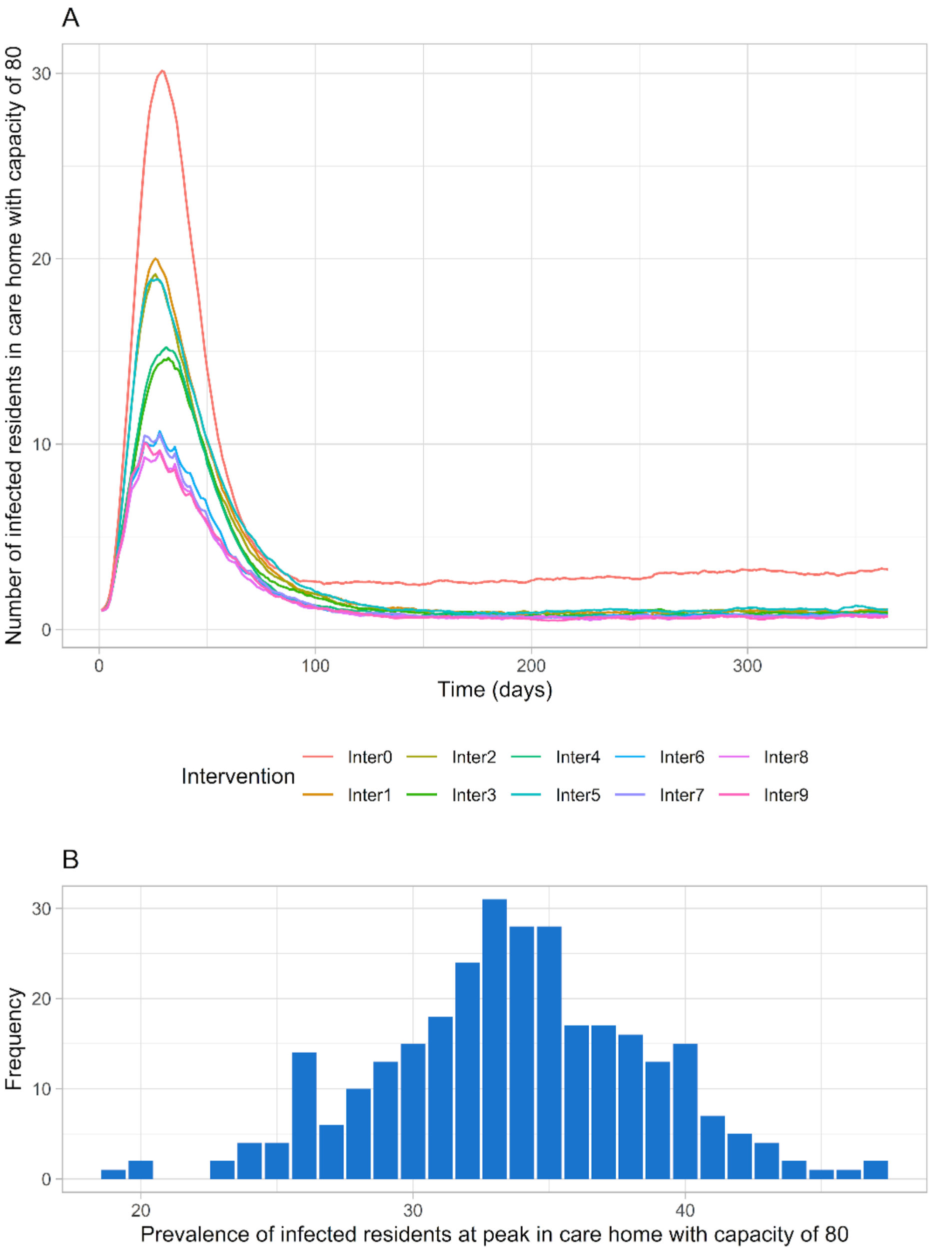

Figure 8.4: Time series of COVID-19 prevalence among residents in care home with capacity of 80 residents across all scenarios

*(A) using the base-case parameters (means of 300 simulations for each scenario) and (B) using distribution of the prevalence at peak for no intervention scenario (Inter0) using the base-case parameters for 300 simulations (**Inter0:** No intervention; **Inter1:** Reference intervention (isolation of symptomatic/confirmed residents, testing of new admissions, closed to visitors, social distancing); **Inter2:** Inter 1 + isolation upon admission; **Inter3:** Inter1 + adaptive testing strategy; **Inter4:** Inter3 + isolation upon admission; **Inter5:** Inter1 + Weekly testing for residents; **Inter6:** Inter1 + weekly testing for staff; **Inter7:** Inter1 + weekly testing for staff and residents; **Inter8:** Inter6 + isolation upon admission; **Inter9:** Inter7 + isolation upon admission)*

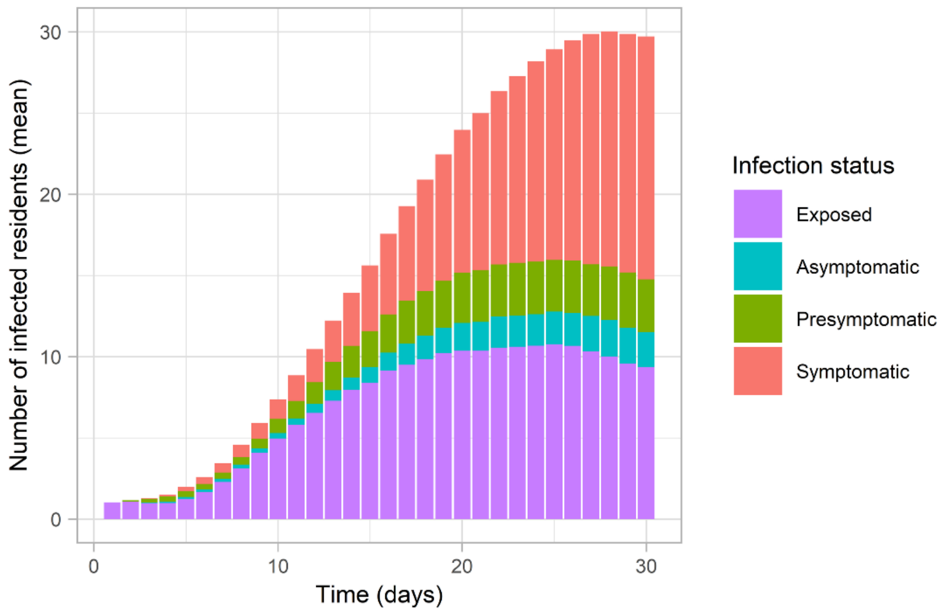

Figure 8.5: Time series of prevalence of infected residents (mean) in different infection status (across 300 simulations when no intervention is implemented (Inter0) using the base-case parameters)

8.8.2 Effectiveness of the Examined Intervention Strategies

Implementing the reference intervention, which combines isolation of symptomatic residents, testing of new admissions, social distancing, and restricted visiting (Inter1), clearly lowered the peak and reduced the cumulative number of infections after 90 days compared to the no intervention scenario (Inter0) (Figure 8.4A and Figure 8.6). There was very strong evidence ($p<0.001$) for rejecting the null hypothesis in favour of the alternative hypothesis that the mean cumulative number of infected residents for the reference intervention scenario was lower than the mean when doing nothing (95% CI of the difference: 20 – 22 (90 days)).

Adding the 14-days compulsory isolation of new admissions (Inter2) slightly decreased the number of infections compared to the reference intervention strategy ($p<0.001$, 95% CI of the difference: 2 – 4 (90 days)). Replacing the isolation of new admissions in strategy Inter3 with or adding the adaptive testing intervention (Inter4) further improved the outcomes. However, as the care home was closed to new admissions for part of the time in these scenarios, the total number of residents was smaller than those in other scenarios, contributing to the lower infections shown in Figure 8.6 for interventions Inter3 and Inter4. Furthermore, weekly resident testing (Inter5) did not lead to lower infections when compared with the reference intervention (Inter1) (p ~ 1.0).

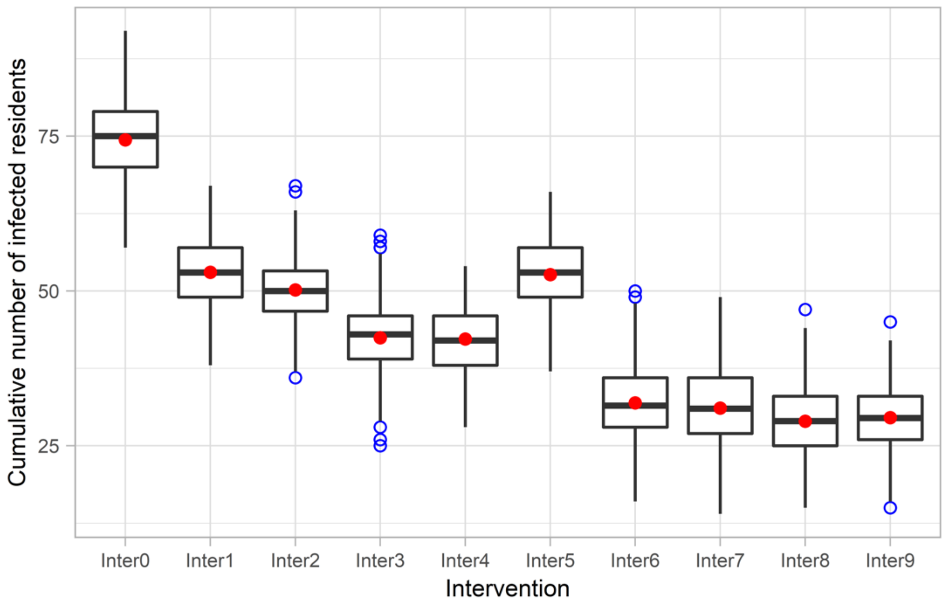

Figure 8.6: Cumulative numbers of infected residents in nine intervention scenarios

Box plot of the outcomes 90 days after a resident is infected at the start of the simulation using the base case parameters. (Lower hinge: 25% quantile; lower whisker: smallest observation greater than or equal to lower hinge − 1.5×IQR; middle: median; upper hinge: 75% quantile; upper whisker: largest observation less than or equal to upper hinge + 1.5×IQR; red dot: mean; blue dot: outlier).

Weekly testing of staff in the presence of the reference intervention strategy (Inter6) was more effective than Inter2 – Inter5, significantly reducing the peak and the cumulative number of infected residents. This intervention strategy reduced the cumulative infections among residents by approximately 20 cases after 90 days compared to the reference intervention (Inter1) and by approximately ten cases compared to adaptive testing (Inter4) ($p<0.001$). A more stringent strategy that involves routine testing for both residents and staff (Inter7) showed little evidence of improving the outcomes (p ~ 1.0). Supplementing these routine testing interventions with isolation of new admissions (Inter8 and Inter9) only slightly reduced the peak and cumulative outcomes. Additional plots of modelling results for different time intervals are included in Appendix E.

8.8.3 Effectiveness of Various Routine Testing Strategies and Compliance

Routine testing of residents (Inter5) was predicted to be no more effective than the reference intervention strategy (Inter1) regardless of testing frequency (p ~ 1.0). The effectiveness of routine testing of staff (Inter6) and of staff and residents (Inter7) decreased non-linearly with increased testing intervals (Figure 8.7A). The difference between the two interventions (Inter6 and Inter7) reduced as the infection probability reduced (Figure E.7). Increasing compliance to routine testing of staff linearly reduced the cumulative number of infected residents (Figure 8.7B). Moreover, compliance with routine testing of staff had a significant effect on the model outcome when a testing interval was less than ten days (Figure 8.7C).

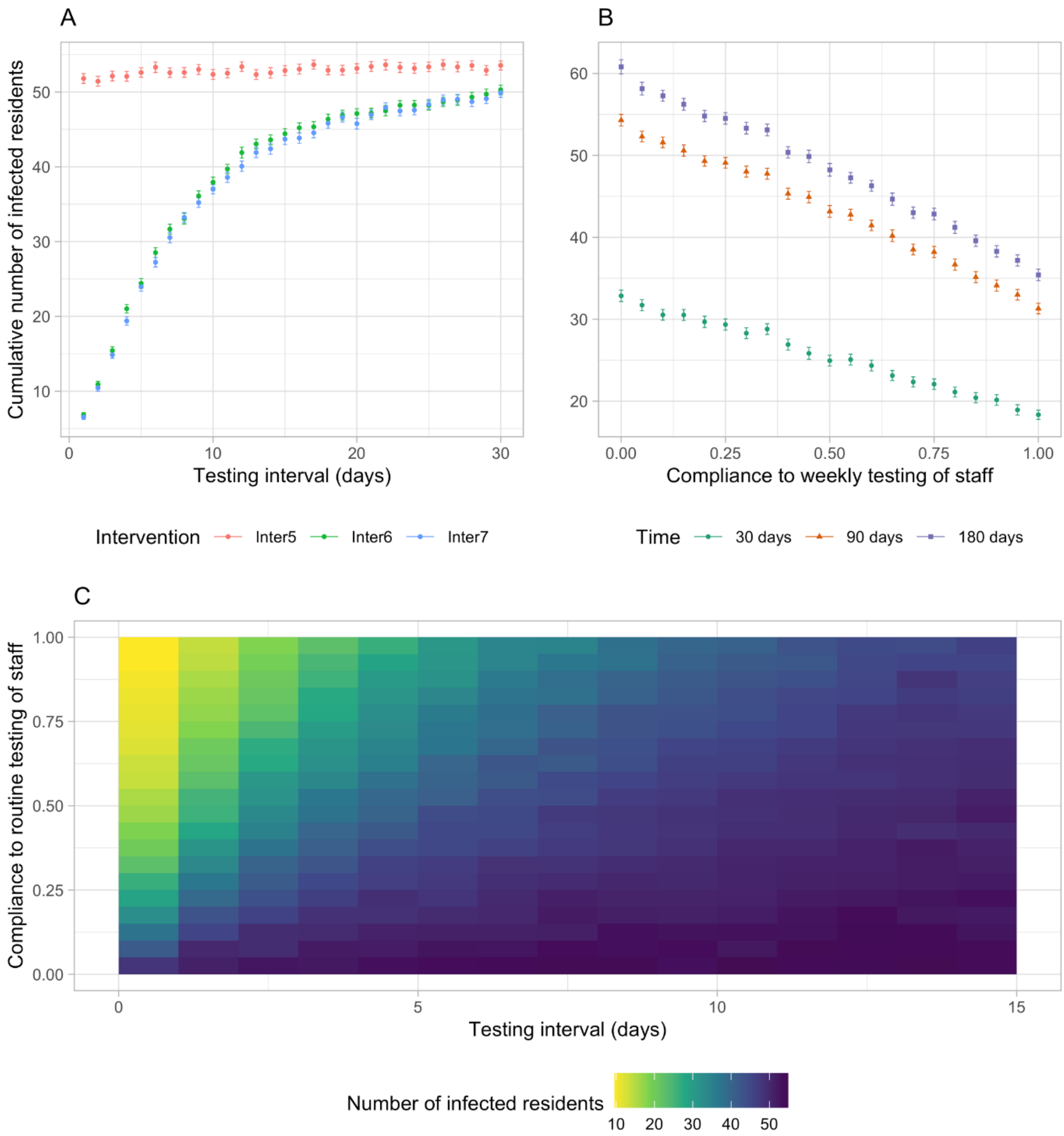

Figure 8.7: Effectiveness of different routine testing strategies and compliance

(A) The impact of different testing intervals in routine testing scenarios on the cumulative number of infections after 90 days. (B) The impact of compliance to weekly testing of staff (Inter6) on the cumulative number of infections after 30, 90, and 180 days. Other parameters take the values at base case. (Dots denote the mean values of 300 simulations and error bars represent 95% confidence interval of the mean.) (C) Heatmap plot for the impact of testing interval and compliance to routine testing of staff (Inter6) on the cumulative number of infections after 90 days.

8.8.4 Impact of Visiting Policy

Different Risks of Transmission per Contact

In the first experiment, we assumed that all infectious-susceptible contacts between individuals in the care home, including residents, staff, and visitors, have the same infection probability and that the community prevalence of COVID-19 where staff live and where residents live is equal.

Relaxing the visiting policy did not significantly impact the cumulative number of infected residents (Figure 8.8). The difference in the mean cumulative number of infected residents between no visiting and normal visiting policy (one visitor/resident/day) after 90 days was 1 – 2 (95% CI) infections among residents for the infection probability per contact of 0.02 in the base case scenario. There was no difference in this outcome when the infection probability was below 0.02, while the mean difference was 2 – 5 (95%CI) for the value of 0.1. The mean difference in the cumulative number of COVID-19 deaths among residents after 90 days were 0 – 2 (95%CI) across the values of infection probability per contact. The mean elapsed time until the first resident is infected was prolonged by 1 – 6 days (95%CI) when visiting was banned across the values of infection probability per contact (Figure 8.8B). The distributions of outputs for each of these outcomes in both visitation scenarios were almost identical when the transmission risk per contact was very low. When this parameter was higher, they still had similar unimodal, relatively symmetrical shapes and spread but slightly shifted. The impact of the size of infection probability per contact was much more significant than the visiting policy. In addition, the visiting policy had little impact on the probability of an outbreak in the care home within the first 90 days of the epidemic. Unless the risk of transmission per contact was very low (<0.02) and weekly testing of staff was implemented, an outbreak occurred in 97%-100% of simulations after 90 days.

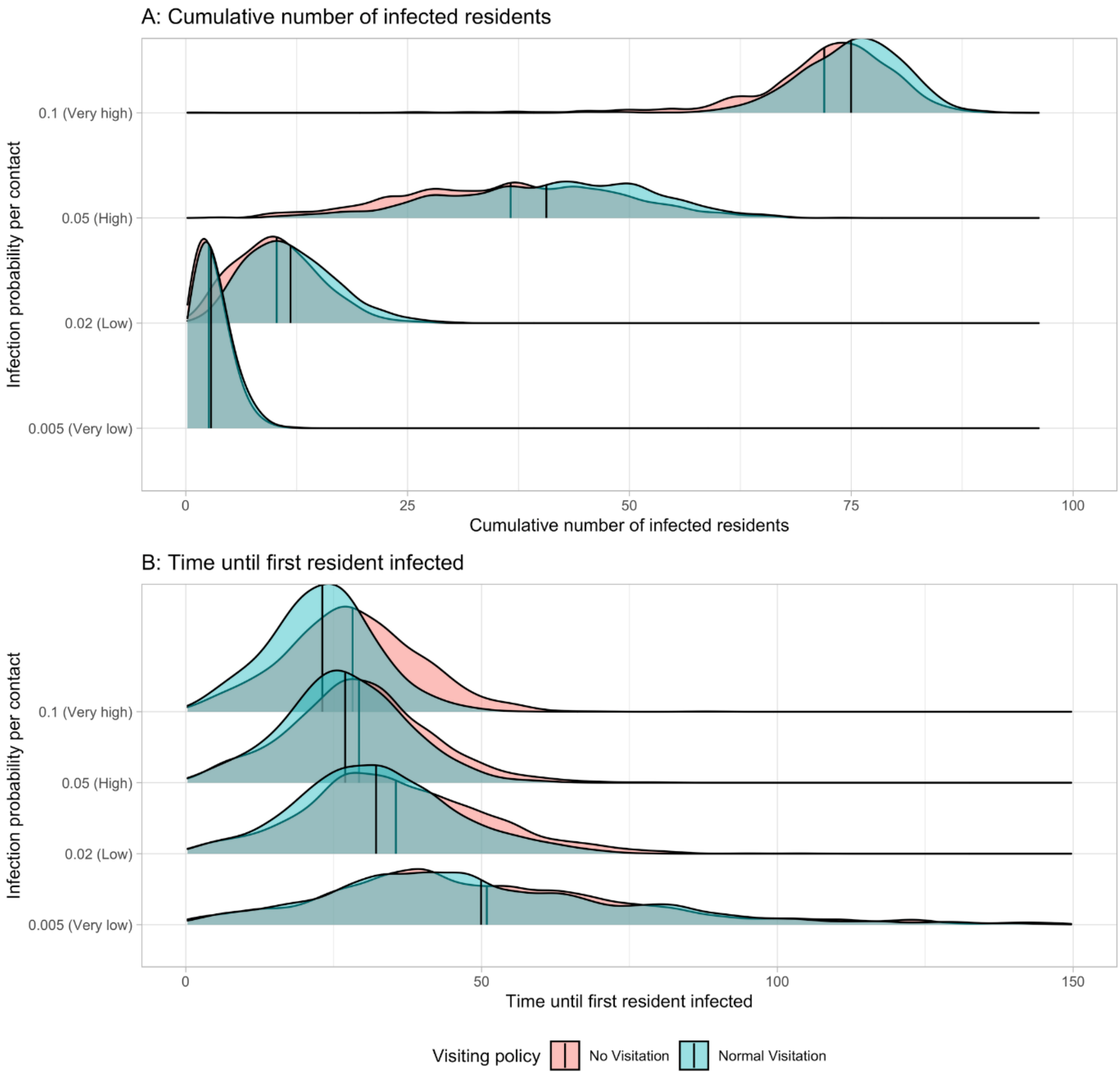

Figure 8.8: Impact of visiting policy and transmission risk per contact on the spread of COVID-19

(A) Distributions of the cumulative number of infected residents 90 days after the simulation starts

(B) Distribution of the elapsed time until the first resident is infected in the care home

Under no visitation and normal visitation policy across different values of infection probability per contact for the base case care home with population size of 80 residents. Vertical lines denote the means of distributions. The weekly testing of staff is implemented. The care home operates at full capacity; residents who decease or leave are replaced by admissions of new residents. Other parameters take the base case values. All infectious-susceptible contacts have the same infection probability. The community prevalence of COVID-19 where staff live and where residents live are equal.

Lower Community Infection Prevalence where Staff Live Compared to Prevalence where Visitors Come from

In this section, we report the modelling results when relaxing the assumption about equal community infection prevalence where staff and visitors live. As the relative infection prevalence in communities where staff live reduces compared to the infection prevalence in communities where visitors live, the number of infected residents also reduces (Figure 8.9A).

Restricting visiting was more effective when the infection prevalence in the staff community was comparatively low. When the staff community infection prevalence was significantly lower than the prevalence among visitors' community (i.e., the former equalled 0% – 30% of the latter), relaxing the visiting policy increased the cumulative number of infected residents and the risk of outbreak occurrence in the care home. In particular, the mean difference in the cumulative numbers of infected residents after 90 days between no visiting and normal visiting policy was two to three (95%CI, the same relative infection prevalence of less than 30%) in the weekly staff testing intervention. Halting visitation delayed the time until the first infection occurred among residents by 9 – 16 days (95%CI) (Figure 8.9B). Additionally, when the community infection prevalence where staff live was extremely low (i.e., between zero and 10% of the infection prevalence where visitors come from), resuming the normal visitation policy doubled the risk of an outbreak within the first 90 days of the epidemic (Figure 8.9C). The impact of modifying the visiting policy on the model outcomes was much smaller when the infection prevalence in communities where staff live was above 30% of the prevalence in communities where visitors live.

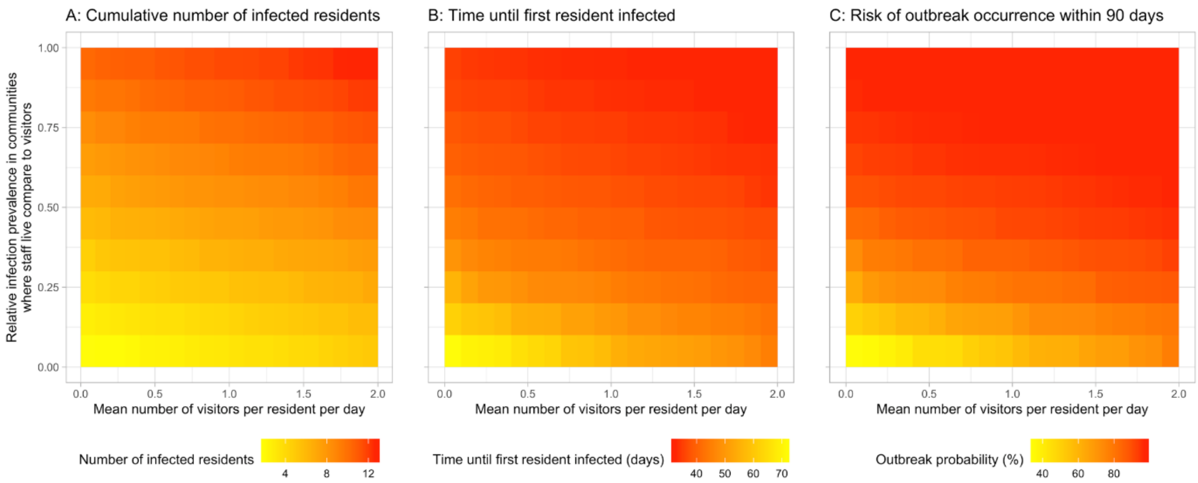

Figure 8.9: The impact of visiting policy and relative community infection prevalence on the spread of COVID-19

Heatmap plot for the impact of different number of visitors allowed in the weekly testing of staff strategy upon

(A) The cumulative number of infected residents 90 days after the simulation starts

(B) The elapsed time until the first resident is infected

(C) The probability of an outbreak occurrence within the first 90 days

Other parameters take the base case values. All infectious-susceptible contacts have the same infection probability of 0.02.

8.8.5 Impact of Care Home Population Size

Figure 8.10 shows that the larger the care home's size, the more quickly a resident acquires COVID-19 on average. As a result, the risk of an outbreak in a large care home was higher than in a smaller one (Table E.5 in Appendix E). There was a statistically significant association between the presence of an outbreak and the size of a care home (mean OR per 20-bed increase 2.57, range: 1.15 – 5.74 for different infection probabilities in both the reference and weekly staff testing scenarios). The modelling results on the risk of outbreak occurrence in care homes with different sizes were in line with the reported data in Scottish care homes (Scottish-Government, 2020a). The prediction on the association between the care home size and the risk of experiencing an outbreak showed a good approximation of observed data in Lothian Health Board (OR per 20-bed increase 3.5, 95%CI: 2.06 – 5.94) (Burton et al., 2020a). Additionally, both intervention strategies were more impactful for the smallest care homes (i.e., size of 10 residents).

Although smaller care homes were less likely to have an outbreak, the size of care homes did not affect the attack rate. There was no statistically significant association between the proportion of infections among residents and care home population size under the same intervention strategy once the infection was already in the care homes. The addition of weekly staff testing and/or a decline in the infection probability per contact significantly improved the outcomes irrespective of size.

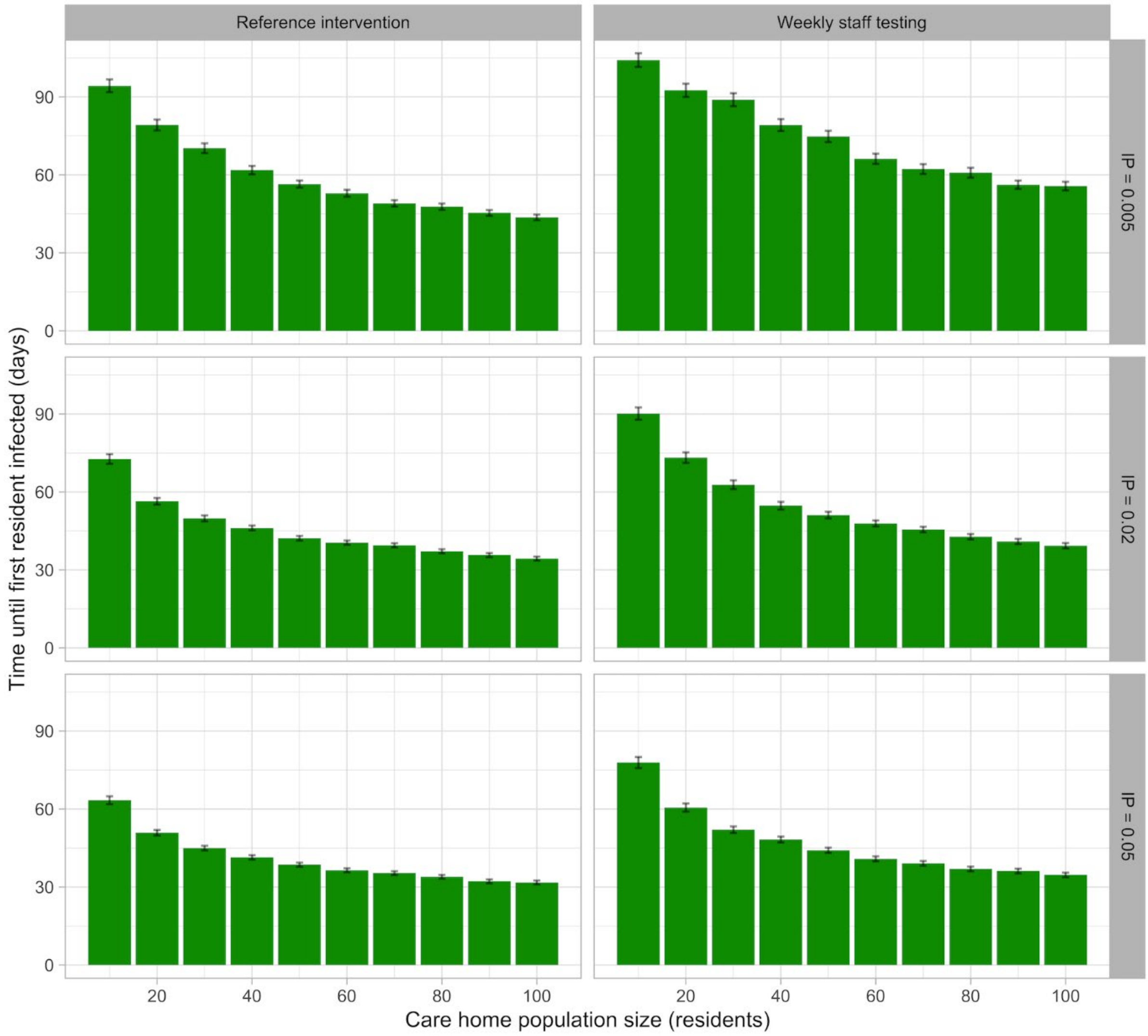

Figure 8.10: Impact of care home population size on the elapsed time until the first resident becomes infected
The results are presented for the weekly staff testing scenario at across low-high values of infection probability (i.e., IP = 0.005, 0.02, and 0.05) in the reference and weekly staff testing scenarios. The simulations in which no resident is infected are excluded. Base case values are used for other parameters. Columns denote the mean values of 1,000 simulations and error bars denote 95% CI of the means.

8.8.6 Impact of Cohorting

When the infection probability per contact was set to a very low value (< 0.02), dividing the care home into smaller units had little effect on the cumulative number of infected residents after 90 days (Figure 8.11A). However, when the risk of transmission per contact was increased, the effectiveness of cohorting was noticeable. The impact of cohorting was most significant when the size of a unit was reduced from 20 to 10 residents. Our model predictions remained robust when we relaxed the assumption of no interactions across units. By contrast, splitting a care home into smaller units did not show any impact upon the elapsed time until the first resident acquired the infection or the probability of outbreak occurrence (Figure E.4 and Figure E.5 in Appendix E). Regardless of the cohort size, the weekly staff testing strategy was more effective in controlling the spread of COVID-19 than the reference intervention alone (Figure 8.11B).

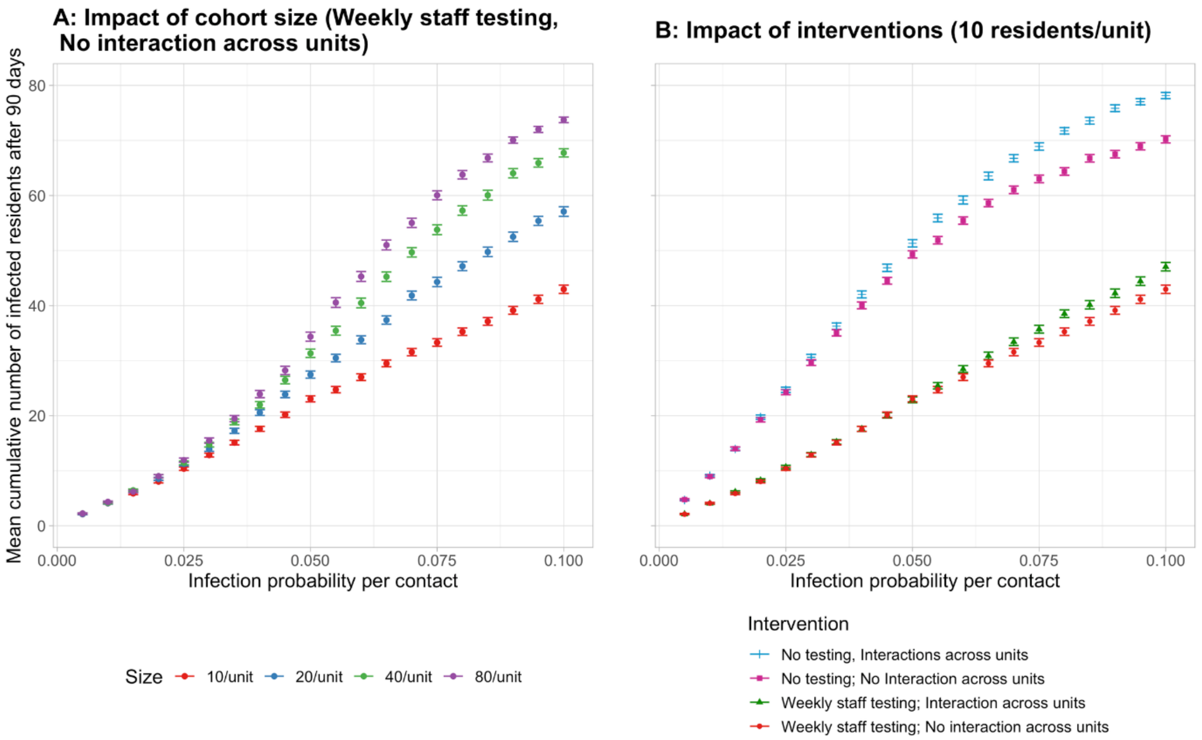

Figure 8.11: Impact of cohort size and interventions in the smallest examined cohort on the spread of COVID-19 The care home with capacity of 80 residents are split into one, two, four, and eight units with 80, 40, 20, and 10 residents per unit Interactions of residents and staff across units of the care home occur at zero and 20% of total contacts for the "no interaction across units" and "interaction across units" scenarios respectively. The reference intervention is implemented across all plotted scenarios. Points represent the mean values of 1,000 simulations; error bars represent 95% CIs of the means.

8.9 Discussion[25]

8.9.1 Spread of COVID-19

Our simulations show that once COVID-19 is introduced into care homes, it spreads very quickly, and stopping the spread is very difficult. As the risk of transmission per contact

[25] The Discussion sections in Nguyen et al. (2020a) and Nguyen et al. (2021a), excluding the discussion with respect to the limitations of the studies, are combined.

appears to be the most impactful factor on the prevalence and cumulative prevalence of infections among residents, interventions such as hand hygiene and PPE that reduce this risk are crucial for controlling the spread of COVID-19. The importance of these measures in controlling COVID-19 should be emphasized and reinforced among staff in care homes as they may become less compliant when community transmission improves and interventions are relaxed.

8.9.2 Impact of Various Testing Strategies

Among the examined COVID-19 testing strategies, routine testing of staff appears to be the most effective and practical approach in the presence of the reference intervention strategy. When the risk of transmission per contact is reduced by enhancing compliance to hand hygiene and PPE use, the strategy of routine testing of staff is as effective as more stringent interventions strategies. This includes the combination of this strategy and 14-days compulsory isolation of new admissions, routine testing of both staff and residents with/without isolation of new admissions. Routine testing of residents does not show additional effect compared to the reference intervention strategy. Therefore, our model predictions suggest that routine testing should target staff in care homes in conjunction with encouragement and support to enhance compliance to hand hygiene and using PPE.

Our modelling results on the effectiveness of routine testing of staff and residents are supported by a number of published studies at the time. Weekly universal testing of all staff and residents irrespective of symptoms conducted in 123 West Virginia nursing homes showed that this intervention was more effective in lowering the prevalence of COVID-19 than daily symptom-based resident and staff screening (McBee et al., 2020). Other empirical studies in nursing homes in the US and France also reported that routine universal testing helped identify cases among staff and residents more quickly and interrupted transmission in the facility (Dora et al., 2020; Sacco et al., 2020; Hatfield et al., 2020). These studies, however, did not examine the impact of routine testing targeting staff only and compared it to resident testing, which is easier to study in a simulation model such as ours than designing a controlled experiment.

Regarding testing intervals, our model predictions, along with discussions with local experts and management regarding feasibility, suggest that routine testing of staff should be carried out every 7–10 days. Although more frequent intervals of testing of staff result in better outcomes, this may not be feasible and is costly. The adverse effects of more frequent testing of staff include increased workload, time pressure, worsened staff shortages, and decreasing tolerance, and therefore, may lead to reduced compliance to testing among staff members. Increasing workload and time pressure may, in turn, affect other care activities provided to residents and staffs' compliance with testing and hand hygiene, which has the greatest impact on the transmission of COVID-19. A more frequent testing policy could be tailored to care homes with outbreaks to achieve the best outcomes at an acceptable cost. We did not at this stage explicitly consider the implications of these additional costs in our model.

8.9.3 Impact of Visiting Policy and Cohorting

Interventions, including halting or restricting visitation and cohorting in care homes in response to COVID-19, have been included in the UK national guidance and implemented in numerous care homes across the world. These intensive interventions have led to growing concerns about their negative impacts upon the well-being of residents and burdens on healthcare systems. However, the effectiveness of these intervention strategies has not been well investigated. Our modelling study helped address this gap in understanding the effectiveness of visitation and cohorting policies in controlling the ingress of COVID-19 and its spread in this setting.

We found that the spread of COVID-19 is relatively resistant to changes in visiting policy. Despite being restricted to no visitation, residents can still acquire the infection from staff members who interact with several other individuals in the care home and are likely to spread the virus, which affects the likelihood and size of an outbreak more than the effect of the visiting policy. Current evidence from care homes in England has highlighted that staff, particularly bank and agency staff, have been an unwitting source of infection (Hodgson et al., 2020; Ladhani et al., 2020). If indeed staff live near the care home and provided local transmission is not very low compared to the rest of the population, the finding suggests that care homes can relax their visitation policy to a level for which they are able to ensure that all visitors strictly adhere to infection control measures. An early warning system that estimates the relative community prevalence of COVID-19 in a local area and the whole region/country could help care homes decide when they should halt visitation to protect their residents and staff.

Our findings suggest that shielding residents in care homes will not be as effective as reported in a number of studies that have considered shielding vulnerable populations more broadly (van Bunnik et al., 2020; McKeigue and Colhoun, 2020; Van Zandvoort et al., 2020;

Weitz et al., 2020; Neufeld et al., 2020). These studies used age-stratified compartmental metapopulation models that assume homogeneous mixing within a compartment. Although such models incorporated different transmission rates between compartments representing age-specific populations or shielders/non-shielders, they did not account for contact patterns at an individual level that we accounted for in our model. In particular, if staff and visitors could introduce COVID-19 into a care home with equal probabilities (i.e., the equal prevalence in the communities where staff and visitors live and the same probability of infection per contact), staff are more likely to spread the virus than visitors. Staff come into contact with several residents and other staff members. Therefore, they can acquire the infection from an individual in the care home and transmit it to another, further spreading the virus. By contrast, visitors are less likely to mediate transmissions between residents as they only interact with a very limited number of staff and residents (e.g., a resident whom they come to visit and staff members looking after this resident). Thus, shielding by stopping visiting is not very effective in most circumstances as long as staff and their close contacts outside the care home are not also shielded from the community, which seems unlikely. We did not investigate the effect of shielding care home residents from visitors on the spread of COVID-19 in the community, while other models examined the effects of shielding interventions on the overall population. There may be a risk that visitors can acquire COVID-19 from staff and residents in care homes and spread it to others in the community. Furthermore, while vulnerable groups in other models were shielded from the rest of the population, our model only considered shielding residents from visitors.

Although care home size cannot be altered without losing places for existing and potential residents, cohorting residents and staff into smaller, discrete units could potentially alleviate the extent of an outbreak once it occurs. The cohorting intervention is more impactful in circumstances when the risk of transmission per contact is high, such as when PPE provision is inadequate, compliance to hand hygiene and wearing PPE is low, and/or maintaining social distancing is difficult. Reshaping the structure of care homes, however, requires the care home’s efforts to recruit and train additional staff as well as outside support to accommodate sufficient levels of staff within each unit to maintain safe care. Staff illness and absence during COVID-19 outbreaks could further complicate the cohorting situation.

8.10 Limitations[26]

This work has a number of limitations. Firstly, the model presents the historical situation in the spring/summer of 2020 and does not consider scenarios for vaccination and lateral flow tests. It does not model the effect of different variants of SARS-CoV-2 explicitly but implicitly by considering a range of infectivity values in sensitivity analyses. Secondly, although we carried out uncertainty and sensitivity analyses on a care home's size and structure, the diversity of this setting in terms of characteristics of resident populations, health and care services provided, and management would limit the generalisation of our findings. Thirdly, we have not incorporated changes in individuals' behaviours as a result of implementing the shielding and/or cohorting interventions into the model. Therefore, we have not captured how such changes would affect the outcomes. As the changes in behaviour in the presence of interventions and the relationships between behavioural changes and risks of transmission are difficult to predict (Jarvis et al., 2020), it is essential to continue to closely monitor outbreaks in care homes. Finally, as our model has assumed that visitors only come into contact with the resident whom they visit and do not interact with other residents, the effect of loosening visiting policy may be underestimated. However, relaxing this assumption will lead to the same impact as increasing the number of visitors allowed. Also, interactions between visitors and residents other than the one whom they visit are unlikely to happen amidst the ongoing pandemic.

8.11 Chapter Summary

This chapter presents an ABM study that sheds light on the transmission dynamics of COVID-19 under different intervention scenarios within a care home. The ABM study addresses the prevention and control of intra-facility COVID-19 transmission, which is one component of the third research objective. The effectiveness evaluation of different infection control intervention strategies has potentially significant implications for public health policymaking. Infection control interventions in care homes need to be both effective in containing the spread of COVID-19 and also feasible to implement in this setting which has a dual nature: a healthcare institution and a home. Routine testing that targets staff is most effective and practical, while more rigorous testing strategies may not induce additional impact. Findings

[26] The discussions with respect to the limitations of the studies under the Discussion sections in Nguyen et al. (2020a) and Nguyen et al. (2021a) are combined.

also emphasize the importance of interventions such as hand hygiene and using PPE that reduce the risk of transmission in inter-individual contacts on the spread of COVID-19.

Cohorting residents and staff into smaller, discrete units could help reduce the spread of COVID-19 in a care home. This intervention is especially effective when the risk of transmission per contact is high due to factors such as low compliance to hand hygiene, insufficient supplies of PPE, and difficulty in practicing social distancing. By contrast, the model predictions suggest that shielding residents in care homes will not be as effective as reported in a number of studies that have investigated the shielding of vulnerable populations in wider communities. Therefore, in specific circumstances, care homes could consider relaxing visitation to the extent that they can ensure that visitors strictly comply with their infection control interventions to balance the risk of COVID-19 spread and residents' non-COVID-19 well-being.

The ABM study of transmission within a care home facilitates the development of the hybrid model for transmission across a network of multiple heterogeneous care homes that will be discussed in Chapter 9 in two ways. First, the ABM analysis contributes to informing the hybrid model's structure and experiment designs. Understanding what characteristics of care homes affect their risk of having outbreaks helps identify the state variables of care home agents in the hybrid model and design the experiments with different network configurations of care homes. Second, the ABM model contributes to the white-box validation of the hybrid model by comparing the parallel stochastic SD module with this ABM model.

Chapter 9. Hybrid SD-ABM Model: Transmission across Care Homes by Sharing Bank/Agency Staff

9.1 Introduction

This chapter presents a hybrid SD-ABM simulation model to investigate the impacts of bank/agency staff working across different care homes as well as interventions to mitigate these impacts. This contributes to addressing the third research objective. We explain why this research focused on the inter-facility transmission by sharing bank/agency staff in section 9.2. With respect to interventions, we considered the impact of reducing or stopping the use of bank/agency staff, weekly PCR testing, and creating bubbles of care homes on the spread of COVID-19. Care home bubbles restrict bank/agency staff to work only within a specific group of care homes that are designated as one bubble. Our model provided a tool for exploring the interaction between interventions as they can undermine or enhance each other when implemented simultaneously. It also helped study the variations in the impact of using bank/agency staff on individual care homes in different network compositions. We adapted methodology from SD and ABM practice and theory to build confidence for validating our hybrid model.

This chapter was published as

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Section 9.2 includes the first three paragraphs of the Introduction section in the published paper. Sections 9.3, 9.4, and 9.5 have been extended from the Materials and Methods section of the paper to provide a detailed description of the model and experiments and demonstrate how the framework for combining SD and ABM (Chapter 7) informs the design of this model. The Confidence Building section (under Materials and Methods) and the Validation Results section (under Results) have been combined into section 9.6 – Confidence building.

9.2 Research in Context[27]

According to evidence at the time, staff working across different care homes are at a greater risk of COVID-19 infection than those working in a single care home, and using these staff significantly increases the risk of outbreaks among residents (Ladhani et al., 2020; Shallcross et al., 2021). Studies in English care homes showed that staff working across different care homes had a three-fold (95% confidence interval [CI], 1.9 – 4.8) higher risk of infection than those working in single care homes. Further, frequent employment of agency staff increased the odds of infection for residents by 1.65 (95%CI, 1.56 – 1.74) (Ladhani et al., 2020; Shallcross et al., 2021). New legislation may ban staff from working in more than one care home in an attempt to halt the spread of COVID-19 (GOV.UK, 2020). These types of interventions need to be thought through as they may lead to unintended consequences such as difficulties in recruiting staff. They also need to be balanced against outcomes that are not related to COVID-19.

Working across different care homes and other healthcare facilities has been a common practice among care home staff for reasons of flexibility, work-life balance, and extra income. A survey in the US showed that 17% of long-term care workers had a second job and 60% held double- or triple-duty caregiving roles (Van Houtven et al., 2020). Furthermore, care homes in many countries, including the UK and the US, are heavily dependent on the use of temporary bank or agency staff due to the long-standing problem of staff shortages in the health and social

[27] The first three paragraphs of this section are the first three paragraphs of the Introduction section in Nguyen et al. (2022)

care sector, which has been worse amid the pandemic (SSSC, 2020; Shembavnekar, 2020; Nguyen et al., 2020b).

Knowledge is limited on the extent to which staff work in multiple care homes and contribute to spreading infection as well as which interventions effectively target this group. While interventions that limit staff movement across care homes may reduce infection, they can also reduce the number of staff available in a given care home. Understaffed care homes could lead to lower quality of care for residents, and a lower staff-to-patient ratio can also increase transmission within care homes as each staff member needs to interact with more residents (Allan and Vadean, 2021; Li et al., 2020b). Care home workers hired from agencies typically have zero-hour contracts and a low income, and thus, they have little power to influence policy proposals to ban their movement. Such a proposal could lead them to leave their positions or the sector due to financial instability and job insecurity, threatening the closure of care homes (CWC, 2020).

Although we have mentioned in Chapter 4 that the spread of HAIs between care homes and hospitals due to frequent hospital admissions and readmissions of care home residents is little understood, this research will not explore this gap. Discussions with care home stakeholders revealed that hospitalization of residents had been minimized during the COVID-19 pandemic. Residents will also need to have two negative PCR tests before being transferred/readmitted to care homes from hospitals, and isolation upon admission to care homes will be required. Although the compliance to such guidance is likely to vary across care homes, it still significantly reduces the ingress of COVID-19 into care homes via this route. The ABM model's sensitivity analysis also shows that the model outcomes are not sensitive to the prevalence of COVID-19 in hospitals. An exception is a rush of discharging patients into care homes without having to be tested for COVID-19 at the beginning of the pandemic to free up hospital beds (Oliver, 2020). Therefore, this issue is not considered as urgent as the issue of using bank/agency staff at the time of conducting this study. We will discuss this matter as an opportunity for future research in Chapter 10.

9.3 Justification for Combining SD and ABM[28]

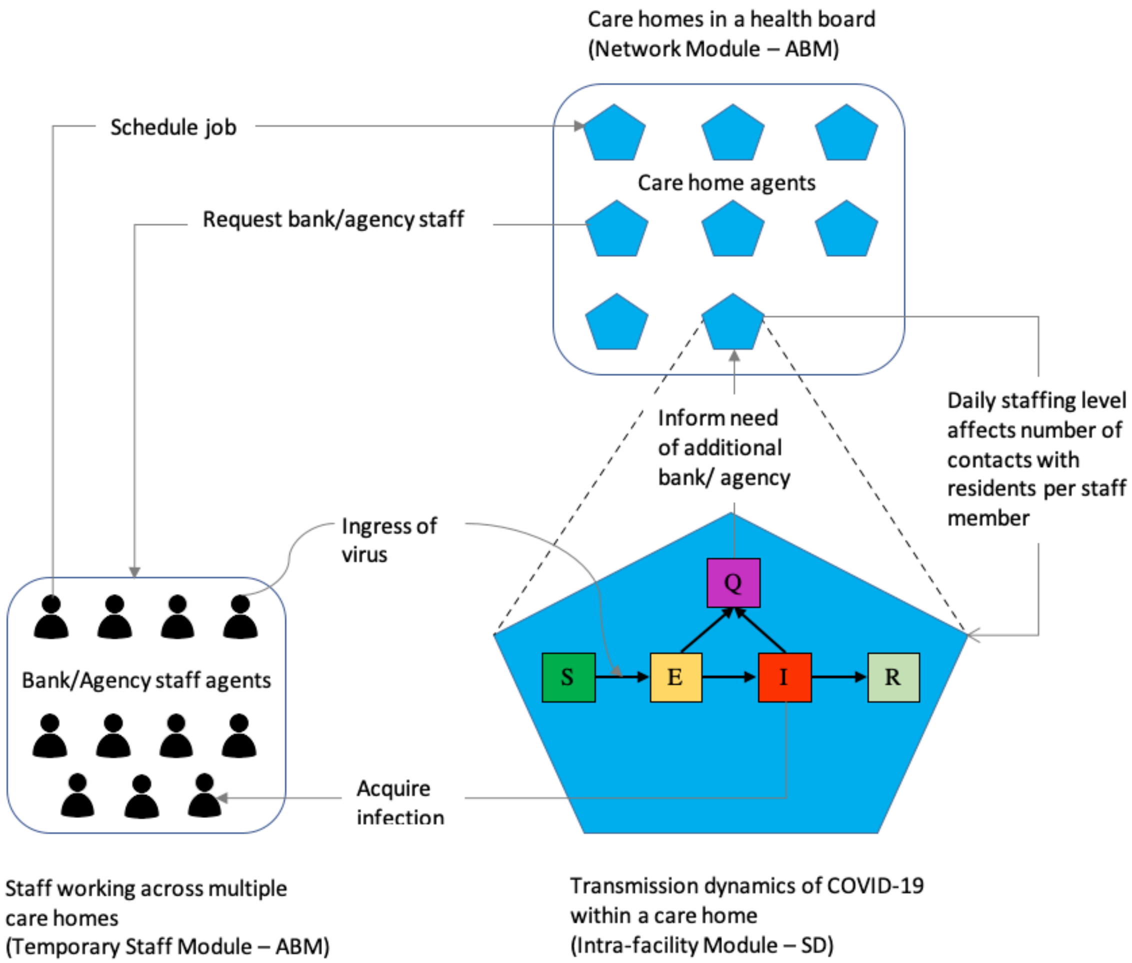

Figure 9.1: Architectural design of the integrated hybrid SD-AB model comprising three modules

We developed an integrated hybrid simulation model that combined SD and ABM as it is difficult to achieve a comprehensive appreciation of the complexity and multi-scale characteristics of the problem with a single modelling method. The hybrid model contained three modules built using either SD or ABM: Network (ABM), Temporary Staff (ABM), and Intra-facility (stochastic SD) (Figure 9.1). The concept of a network consisting of several agents representing sub-populations/healthcare facilities with a rich internal structure built using SD is similar to Vincenot and Moriya (2011) and Barnes et al. (2011). In these models, persons/patients move between sub-population/facility agents and spread the epidemics across a network. Their movement was modelled implicitly via behavioural rules of agents (i.e., how

[28] The description of the modules (sections 9.3.1 – 9.3.3) has been taken from the Model Structure section in Nguyen et al. (2022).

sub-population/facility agents exchange their persons/patients) in the network. These exchanged persons/patients were still considered homogeneous. However, the nature of such movement is different from the movement of bank/agency staff across care homes. Therefore, we find it essential to consider bank/agency staff in a separate module (i.e., Temporary Staff Module). We explain the choice of an appropriate simulation modelling method for each module in the following subsections.

9.3.1 Network module

The Network module models the constituent care homes in a network that share bank/agency staff. In this module, care home agents are characterised by their resident population size, staffing level, bank/agency staff use, and intra-facility transmission rates (Table 9.1). ABM is appropriate to build this module to address our questions as it can capture the heterogeneity in care homes' ingress risk and intra-facility transmission dynamics, which affect the homes' risk of experiencing outbreaks. Bank/agency staff shared between care homes can spread the virus from one facility with a current outbreak to other facilities with no cases of infection, causing them to experience outbreaks. ABM is also more flexible than SD for reflecting any changes in network composition and enables the explicit modelling of interventions such as creating bubbles of care homes. The composition of a network and such interventions may affect the extent to which the virus spreads across constituent care homes.

9.3.2 Temporary staff module

In the Temporary Staff module, bank/agency staff members are modelled as agents whose state variables are described in Table 9.1. As they are scheduled to work in different care homes on a daily basis, following specific rules affected by their decisions and care homes' preference and demand, it is important to consider them at the individual level to capture the stochasticity of their movement across care homes. Chance events such as a number of care homes having outbreaks in low community infection prevalence may emerge from the collective movement actions of bank/agency staff agents. Furthermore, while the aforementioned models did not consider interventions targeting persons/patients moving between sub-populations/facilities, ABM offers more flexibility in our study for explicitly incorporating the restriction of movement on bank/agency staff within a bubble of care homes.

9.3.3 Intra-facility module

A stochastic SD Intra-facility module is embedded within each care home agent of the Network module and represents the transmission dynamics of COVID-19 in each care home. In this module, individuals were aggregated based on their role (residents or staff members), state of infection, testing, and isolation status (Figure 9.2). Although we appreciate that the heterogeneity of individual traits and behaviours and the detailed operational structure are important in characterising the transmission dynamics within settings such as care homes, investigating the extent of their impact on the spread of the virus is not the purpose of this hybrid model and has been studied in our agent-based model discussed in Chapter 8. To address our questions on transmission across a heterogeneous network mediated by bank/agency staff, it is preferable to simplify the model by reducing the transmission dynamics complexity within each care home. The use of stochastic SD in this case also leads to lower computational intensity while still allowing for the stochastic transmission dynamics and the extinction of the virus, and thus, capturing the risk of outbreaks in each care home. Furthermore, as the investigated problem focuses on the transmission via bank/agency staff across care homes in a network, each care home is viewed as a sub-system from a holistic perspective. Each care home's macro characteristics and behaviours, rather than individuals' characteristics and behaviours, are of importance for decision-makers who manage a network of care homes at a regional level. We described the equations for stocks and flows of this module in Table 9.4.

9.4 Hybrid Model: Overview, Design Concepts, and Details

A complete, detailed model description, following the ODD protocol (Grimm et al., 2006; Grimm et al., 2010; Grimm et al., 2020) is provided in Appendix F. This section first describes the SD component of the hybrid model (section 9.4.1). The model assumptions are described in the Entities, state variables, and scales section – section 9.4.2 and the design choices in the Design concepts section (section 9.4.3). The links between the SD and ABM components and relevant assumptions are described in sections 9.4.4 and 9.4.5.

9.4.1 Intra-facility Module[29]

Figure 9.2 describes the structure of the Intra-facility sub-model developed using stochastic SD. This sub-model represents the transmission dynamics within a care home agent. Parameters used in the model are described in Table 9.1[30]. Table 9.2 summarizes the equations for stocks of residents and permanent staff in different states of infection and flows between stocks. This module implicitly accounts for the asymptomatic, pre-symptomatic, and

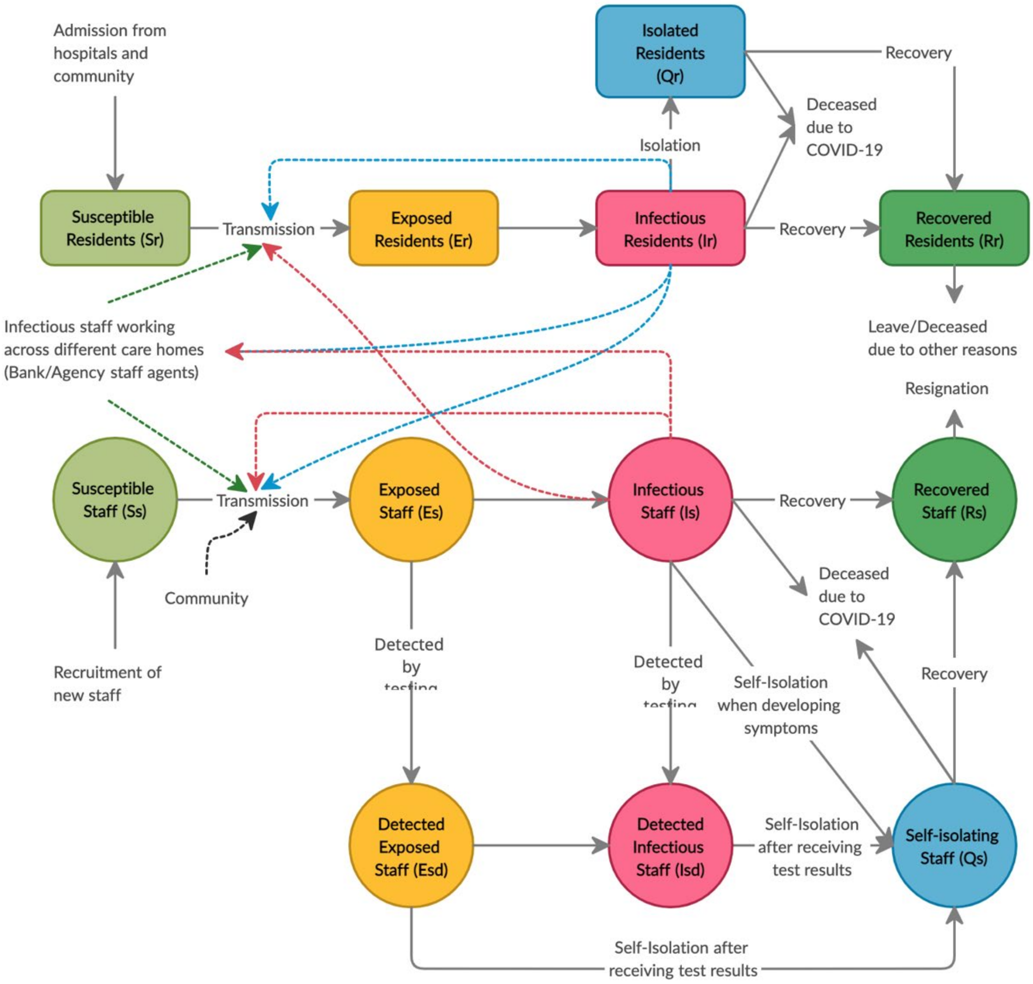

Figure 9.2: The structure of Intra-facility module embedded in each care home agent.

This sub-model developed using stochastic system dynamics represents the transmission dynamics of COVID-19 within a care home. Dash red, blue, and green lines represent transmissions caused by infectious permanent staff, residents, and temporary bank/agency staff respectively.

[29] Taken from the Intra-facility section under the Sub-models section in the ODD protocol (S1 Appendix in Nguyen et al. (2022))

[30] The same as Table S1-4 in the ODD protocol (S1 Appendix in Nguyen et al. (2022))

symptomatic states via flows ($Flow_{I_R Q_R}$ and $Flow_{I_S Q_S}$) to keep the structure of the SD module simple, reduce the number of equations, and keep the equations for the transmission flows simple.

Table 9.1: Parameters used in the model

Parameter name	**Meaning and rationale**	**Default Value**	**Sensitivity Analysis**	**Source**
β_C	Incidence rate in the community	Daily incidence in the UK	Triangular distribution (min = $5x10^{-5}$, max = 0.002, mode = 0.0005)	(GOV.UK, 2021a)
d_R	Infection fatality rate among residents	35.9%	Triangular distribution (min = 29.1%, max = 43.4%, mode = 35.9%)	(Ferguson et al., 2020; Knock et al.)
d_S	Infection fatality rate among staff	0.07%	Triangular distribution (min = 0.003%, max = 0.315%, mode = 0.070%)	(Ferguson et al., 2020; Knock et al.)
c_{RR}	The number of contacts that a resident has with other residents per day	4.1 contacts per resident per day	Triangular distribution (min = 1, max = 5, mode = 4.1)	(van den Dool et al., 2008; Chamchod and Ruan, 2012; Simon et al., 2013)
c_{SS}	The number of contacts that a staff has with other staff per day	9.6 contacts per staff member per day	Triangular distribution (min = 5, max = 15, mode = 9.6)	(van den Dool et al., 2008; Chamchod and Ruan, 2012; Simon et al., 2013)
c_{RS}	The daily number of contacts that a resident has with staff per day	7.9 contacts per resident per day	Triangular distribution (min = 5, max =15, mode = 7.9)	(van den Dool et al., 2008; Chamchod and Ruan, 2012; Simon et al., 2013)
c_{SR}	The daily number of contacts that a staff has with residents per day	A function of the daily staff-per-resident ratio	N/A	
μ_S	Staff turnover rate	24% per year	Triangular distribution (min = 14.0%, max = 37.7%, mode = 24.0%)	(Scottish-Care, 2018; Fenton et al., 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
μ_R	The rate at which residents leave the care home because of deaths caused by other reasons, moving to another facility, admitted to hospitals, or returning to their own home (rare)	0.004 deaths or discharges per resident per day	Triangular distribution (min = 0.001, max = 0.005, mode = 0.004)	(ISD, 2018; ONS, 2020c)
δ_R	The probability that an infected resident will develop symptoms	0.7	Triangular distribution (min = 0.5, max = 0.9, mode = 0.7)	(Ferguson et al., 2020; Verity et al., 2020) (Based on the age distribution of care home population in the UK)
δ_S	The probability that an infected staff member will develop symptoms	0.6	Triangular distribution (min=0.4, max=0.8, mode=0.6)	(Ferguson et al., 2020; Verity et al., 2020) (For a population like the UK or US)
ν	The risk of transmission per susceptible–infectious contact	0.02	Triangular distribution (min = 0.001, max = 0.05, mode = 0.02)	(Wang et al., 2020c; Tang et al., 2020a; Tang et al., 2020c; Tang et al., 2020b; Ferguson et al., 2020; Zhang and Enns, 2020; Sun et al., 2021)
τ_e	The time elapsed between first exposure and becoming infectious	4.6 days	No (This parameter does not significantly affect number of infections as exposed individuals are not infectious. Also, values for this parameter are relatively consistent across studies.)	(Lauer et al., 2020; Li et al., 2020a; Qin et al., 2020; McAloon et al., 2020; Nishiura et al., 2020) (Lognormal (μ = 1.16, σ = 0.85))
τ_p	The time elapsed between becoming infectious and onset of symptoms	2 days	Uniform (1,3)	(NHS, 2020; He et al., 2020; Gatto et al., 2020; Byrne et al., 2020)

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
τ_i	The time elapsed between onset of symptoms and recovery (or recovery time for those who remain asymptomatic)	9.8 days	Lognormal (mean = 9.769, std = 2.44)	(Wölfel et al., 2020; Kerr et al., 2020) (Lognormal (μ = 2.249, σ = 0.246))
τ	Isolation period of infected residents and staff	14 days	N/A	(Scottish-Government, 2020b)
ρ_{sd}	The reduction of resident-resident and staff-staff interactions (i.e. Compliance rate to social distancing)	0.75	Triangular distribution (min = 0.2, max = 0.9, mode = 0.75)	Assumed (based on other models' assumption (Ferguson et al., 2020; Matrajt and Leung, 2020) and discussions with care home staff and managers)
ρ_{pcr}	The compliance to routine PCR testing in permanent staff	0.8	No (Relative compliance to testing in permanent staff to bank/agency staff is important for the purpose of the model and explored by scenarios)	Scottish Government Data Analysis and Research Group
θ_{pcr}	The sensitivity of RT-PCR test	0.9	Triangular distribution (min = 0.7, max = 0.98, mode = 0.9)	(Watson et al., 2020; FDA, 2020; Arevalo-Rodriguez et al., 2020)
$\rho_{B,pcr}$	The compliance to routine PCR testing in bank/agency staff	0.6	Varied by scenario	Scottish Government Data Analysis and Research Group
τ_{pcr}	The interval of routine testing of staff	7 days	N/A	(Scottish-Government, 2020b; GOV.UK, 2021b)
τ_{trt}	The turnaround time of the test	2 days	Triangular distribution (min = 1, max =4, mode = 2)	Social Care Working Group

Parameter name	Meaning and rationale	Default Value	Sensitivity Analysis	Source
α	The proportion of bank/agency staff to total staff (i.e. the level of bank/agency staff use)	10%	Varied by scenario	(SSSC, 2020; Fenton et al., 2020; Allan and Vadean, 2017)
η	The probability that a bank/agency staff member is randomly allocated to a care home	0.5	Varied by scenario	Discussion with care home managers and representatives from Public Health Scotland and Health and Social Care Partnership Lanarkshire

Table 9.2: Summary of equations for stocks and flows in the Intra-facility module

Stock/ Flow	Equation	Assumption or Comment
Residents		
Susceptible residents	$\frac{d(S_R)}{dt} = Inflow_{S_R} - Flow_{S_R E_R}$	
Exposed residents	$\frac{d(E_R)}{dt} = Flow_{S_R E_R} - Flow_{E_R I_R}$	
Infectious residents	$\frac{d(I_R)}{dt} = Flow_{E_R I_R} - Flow_{I_R Q_R} - Flow_{I_R R_R} - Outflow_{I_R}$	
Recovered residents	$\frac{d(R_R)}{dt} = Flow_{Q_R R_R} + Flow_{I_R R_R} - Outflow_{R_R}$	
Isolated residents	$\frac{d(Q_R)}{dt} = Flow_{I_R Q_R} - Flow_{Q_R R_R} - Outflow_{Q_R}$	
Admission of new residents	$Inflow_{S_R} = Outlow_{I_R} + Outflow_{Q_R} + Outflow_{R_R}$	All residents admitted to a care home are susceptible as they receive two compulsory tests and are isolated for 14 days upon admission (Scottish-Government, 2020c). Care homes operate at a full capacity.

Stock/ Flow	Equation	Assumption or Comment
Transmission to susceptible residents	$Flow_{S_R E_R} = vc_{RR}(1-\rho_{sd})(1+F_1\xi_1)S_R\frac{I_R}{N_R} + vc_{RS}(1+F_2\xi_2)S_R\frac{(I_S+I_{SD})(N_W-N_B)}{N_S(N_W-N_U)} + vc_{RS}S_R\frac{I_B}{N_W-N_U}$	$F_i\xi_i$: heterogeneous parameter noise, representing parameter fluctuations caused by individual variation (unitless) (Keeling and Rohani, 2008) $\xi_i = \xi_i(t) = \frac{Normal(0,1)}{\sqrt{\delta \mathrm{t}}}$ (δt = 1/2[7] days) $F_1 = \frac{1}{\sqrt{I_R}}$ $F_2 = \frac{1}{\sqrt{I_S + I_{SD}}}$
Residents become infectious	$Flow_{E_R I_R} = (1+F_3\xi_3)\frac{E_R}{\tau_e}$	$F_3 = \frac{1}{\sqrt{E_R}}$
Isolation of residents when developing symptoms	$Flow_{I_R Q_R} = \delta_R(1+F_1\xi_4)\frac{I_R}{\tau_p}$	We assume perfect effectiveness of resident isolation in the model.
Recovery of infected residents	$Flow_{I_R R_R} = (1-\delta_R)(1-d_R)(1+F_1\xi_5)\frac{I_R}{\tau_i}$ $Flow_{Q_R R_R} = DELAY\left((1-d_R)Flow_{I_R Q_R}, \tau, 0\right)$	DELAY (input, delayTime, initialValue): discrete or pipeline. Use of this function means that all delays that it creates take exactly the same length of time, which is delayTime. However, until delayTime is reached, the function will return the initialValue.
Death of residents due to COVID-19	$Outflow_{I_R} = (1-\delta_R)d_R(1+F_1\xi_6)\frac{I_R}{\tau_i}$ $Outflow_{Q_R} = DELAY\left(d_R Flow_{I_R Q_R}, \tau, 0\right)$	

Stock/ Flow	**Equation**	**Assumption or Comment**
Death/Discharge of residents due to other reasons	$Outflow_{R_R} = \mu_R R_R$	
Staff		
Susceptible staff	$\frac{d(S_S)}{dt} = Inflow_{S_S} - Flow_{S_S E_S}$	
Exposed staff	$\frac{d(E_S)}{dt} = Flow_{S_S E_S} - Flow_{E_S I_S} - Flow_{E_S E_{SD}}$	
Exposed staff who are detected by testing	$\frac{d(E_{SD})}{dt} = Flow_{E_S E_{SD}} - Flow_{E_{SD} I_{SD}} - Flow_{E_{SD} Q_S}$	
Infectious staff	$\frac{d(I_S)}{dt} = Flow_{E_S I_S} - Flow_{I_S Q_S} - Flow_{I_S R_S} - Flow_{I_S I_{SD}} - Outflow_{I_S}$	
Infectious staff who are detected by testing	$\frac{d(I_{SD})}{dt} = Flow_{I_S I_{SD}} + Flow_{E_{SD} I_{SD}} - Flow_{I_{SD} Q_S}$	
Recovered staff	$\frac{d(R_S)}{dt} = Flow_{Q_S R_S} + Flow_{I_S R_S} - Outflow_{R_S}$	
Self-Isolating staff	$\frac{d(Q_S)}{dt} = Flow_{I_S Q_S} + Flow_{E_{SD} Q_S} + Flow_{I_{SD} Q_S} - Flow_{Q_S R_S} - Outflow_{Q_S}$	
Recruitment of new permanent staff to replace staff who have left	$Inflow_{S_S} = Outflow_{I_S} + Outflow_{Q_S} + Outflow_{R_S}$	Permanent staff who leave a care home are replaced by new recruited permanent staff. All new recruited staff are susceptible.
Transmission to susceptible staff	$Flow_{S_S E_S} = \nu c_{SS}(1 - \rho_{sd}) S_S \frac{N_W - N_B}{N_S}\left((1 + F_2 \xi_7)\frac{(I_S + I_{SD})(N_W - N_B)}{N_S(N_W - N_U)} + \frac{I_B}{N_W - N_U}\right) + \nu c_{SR}(1 + F_1 \xi_8) S_S \frac{I_R}{N_R}\frac{N_W - N_B}{N_S} + \beta_C (1 + F_4 \xi_9) S_S$	$F_4 = \frac{1}{\sqrt{S_S}}$

Stock/ Flow	**Equation**	**Assumption or Comment**
Staff becoming infectious	$Flow_{E_S I_S} = (1-\theta)(1+F_5\xi_{10})\frac{E_S}{\tau_e}$ $Flow_{E_{SD} I_{SD}} = (1-k)(1+F_6\xi_{11})\frac{E_{SD}}{\tau_e}$	$F_5 = \frac{1}{\sqrt{E_S}}$ $F_6 = \frac{1}{\sqrt{E_{SD}}}$ t = 0: {*TestOn = 95;* *TestReturn = TestON +* τ_{trt}} t = TestON: $\theta = \theta_{pcr}\,\rho_{pcr}$ t ≠ TestON: $\theta = 0$ t = TestReturn: {$k = 1$; *TestON = TestON +* τ_{pcr}; *TestReturn = TestON +* τ_{trt}} t ≠ TestReturn: $k = 0$
Infected staff detected by testing	$Flow_{E_S E_{SD}} = \theta E_S$ $Flow_{I_S I_{SD}} = \theta I_S$	
Self-isolation of staff when developing symptoms or tested positive	$Flow_{I_S Q_S} = (1-\theta)\delta_S(1+F_7\xi_{12})\frac{I_S}{\tau_p}$ $Flow_{I_{SD} Q_S} = (1-k)\delta_S\frac{I_{SD}}{\tau_p} + kI_{SD}$ $Flow_{E_{SD} Q_S} = kE_{SD}$	$F_7 = \frac{1}{\sqrt{I_S}}$
Recovery of infected staff	$Flow_{I_S R_S} = (1-\theta)(1-\delta_S)(1-d_S)(1 + F_7\xi_{13})\frac{I_S}{\tau_i}$ $Flow_{Q_S R_S} = DELAY\left((1-d_S)\left(Flow_{I_S Q_S} + Flow_{E_{SD} Q_S} + Flow_{I_{SD} Q_S}\right), \tau, 0\right)$	
Death of staff due to COVID-19	$Outflow_{I_S} = (1-\theta)(1-\delta_S)d_S(1+F_7\xi_{14})\frac{I_S}{\tau_i}$	

Stock/ Flow	Equation	Assumption or Comment
	$Outflow_{Q_S} = DELAY\big(d_S\big(Flow_{I_S Q_S} + Flow_{E_{SD} Qs} + Flow_{I_{SD} Q_S}\big), \tau, 0\big)$	
Staff turnover	$Outflow_{R_S} = \mu_S R_S$	

9.4.2 Entities, State Variables, and Scales[31]

The following entities are included in the model: two types of agents, namely care homes and bank/agency staff agents, respectively representing the care homes and temporary bank/agency staff who work in more than one care home within the network. Each agent entity is characterized by a unique set of state variables which are described in greater detail in Table 9.3. An SD module embedded in each care home agent represents the intra-facility transmission dynamics of COVID-19.

Table 9.3: The state variables of care homes agents and bank/agency staff agents

Variable name	Variable type, units and range	Meaning and rationale
Care home agent specific state variables		
ID	Integer, static; no unit; > 0	The identity of the care home
GroupID	Integer, static; no unit; > 0	The identity of the care home sub-group to which a care home belongs
N_R	Integer, static; residents; > 0	The capacity of the care home
N_S	Integer, static; staff members; > 0	The number of permanent staff members of the care home
N_W	Integer, static; staff members; > 0	The desired number of staff members on duty per day when the home operates at full capacity
N_U	Integer, dynamic; staff members; ≥ 0	The daily number of unfilled staff positions
N_B	Integer, dynamic; staff members; ≥ 0	The daily number of bank/agency staff members working in the care home
I_B	Integer, dynamic; staff member; ≥ 0	The daily number of bank/agency staff member that are infectious working in the care home
S_B	Integer, dynamic; staff member; ≥ 0	The daily number of bank/agency staff member that are susceptible working in the care home

[31] Taken from the Entities, State Variables, and Scales section in the ODD protocol (S1 Appendix in Nguyen et al. (2022))

Variable name	**Variable type, units and range**	**Meaning and rationale**
Intra-Facility Module	System dynamic module including the following stocks: S_R, E_R, I_R, Q_R, R_R: susceptible, exposed, infectious, isolated, recovered residents S_S, E_S, I_S, Q_S, R_S: susceptible, exposed, infectious, isolated, recovered permanent staff E_{SD}, I_{SD}: exposed and infectious permanent staff who have been tested and will be detected by PCR testing. They will self-isolate when testing results return.	The transmission dynamics within the care home. The levels of stocks in the SD module are the number of residents and permanent staff in different states of health and disease.
Bank/agency staff agent specific state variables		
ID	Integer, static; no unit; > 0	The identity of a staff member in the bank/agency staff pool among care homes
GroupID	Integer, static; no unit; > 0	The identity of the care home bubble to which a bank/agency staff member belongs. The staff member can only work at the care homes with the same GroupID.
WorkID	Integer, dynamic; no unit; ≥ 0 0 = Not at work yet	The identity of the care home where a bank/agency staff member works
WorkRecord	Array [i]: integers, dynamic; no unit; i ∈ [1, 2, …]	The work record of a bank/agency staff member across care homes i = care homes' ID WorkRecord [i] = the number of times that the staff member works in care home i
InfectionState	Integer; dynamic; no unit; 0 = susceptible 1 = exposed Infectious (2 = asymptomatic 3 = pre-symptomatic 4 = symptomatic) 5 = recovered	The state of infection of a member of bank/agency staff

Variable name	Variable type, units and range	Meaning and rationale
Tested	Boolean, dynamic; no unit; true/false	Indicates whether a bank/agency staff member has a RT-PCR test in the last 7 days
Isolation	Boolean, dynamic; no unit; true/false	Indicates whether a bank/agency staff member is self-isolating because of having COVID-19

9.4.3 Design Concepts[32]

Basic principles:

The model simulates the spread of COVID-19 within a network of care homes via staff who work at multiple facilities. Staff members who work across several care homes (bank/agency staff) can acquire COVID-19 via contacts with other individuals, including residents and staff in one care home, and spread the virus to other care homes. They can also contract the infection from the community and import it to the care homes where they work.

The risk at which susceptible bank/agency staff contract COVID-19 in a care home depends on the transmission dynamics within that facility which is modelled using SD. In the SD module, residents and permanent staff who only work in that care home are grouped into stocks based on their state of infection (susceptible, exposed, infectious, and recovered). Individuals (either residents or staff members) within a stock are assumed to be homogenous. Infections can be imported into the care home by asymptomatic staff acquiring the infection somewhere else. The guidance on controlling COVID-19 in care homes in the UK requires new residents to have two negative tests prior to admission to a care home and compulsory isolation of 14 days upon admission (Scottish-Government, 2020c; Scottish-Government, 2020b). We, therefore, assume that all newly admitted residents are susceptible for simplification.

The progression of COVID-19 infection after transmission occurs has been described in the basic principle of section 8.4.3. The resident population size, staffing level, operational and managerial features of care homes in the network, and how staff are shared among these homes can affect the inter-facility spread of the virus. Such information is obtained through

[32] Taken from the Design Concepts section in the ODD protocol (S1 Appendix in Nguyen et al. (2022))

discussions and interviews with stakeholders including HSCP, Public Health and care homes in Lanarkshire, and Scottish Government Data Analysis and Research Group. Infection control measures that target healthcare staff who work at multiple care homes are implemented to contain inter-facility transmission.

Emergence

The key outcomes of the model are patterns for the occurrence of outbreaks and the scope of affected care homes. These outcomes emerge from the use of bank/agency staff in care homes, infection control interventions targeting this group of staff, infection control measures implemented in care homes, and their resident and staffing characteristics.

Adaptation

Staff that exhibit symptoms or are tested positive for COVID-19 are required to self-isolate at home. Care homes also isolate their residents who exhibit symptoms. When social distancing is implemented, care homes adapt to the situation by decreasing rates of staff-staff and resident-resident contacts. In intervention scenarios, care homes that experience an outbreak can either increase the use of bank/agency staff to cover the permanent staff members absent due to COVID-19-related reasons. When the intervention of creating bubbles of care homes within which bank/agency staff are restricted to work is implemented in the network, care homes are adaptive to the new situation by using only eligible bank/agency staff members.

Prediction

The staff's adaptive behaviour is based on implicit predictions that leaving when exhibiting symptoms will disrupt transmission chains in the care home and across care homes. Care homes that continue to operate as normal during an outbreak need to increase their use of bank/agency staff as they expect a shortage of permanent staff absent due to having to self-isolate.

Sensing

Bank/agency staff agents who develop symptoms can sense their own state of health and do not go to work the next day. In intervention scenarios, staff agents can sense which care home(s) they are allowed to work for, and in reverse, care home agents can sense whom they can schedule.

Interaction

Residents can interact with other residents and staff. Staff can interact with other staff members in a care home. The rates of interactions between residents and staff are defined based on the management policy of a care home agent and the implemented infection control interventions such as social distancing. Bank/agency staff agents do not interact with each other outside care homes. Regarding interactions between bank/agency staff and care home agents, bank/agency staff agents are allowed to work in all care homes in the base case and are restricted to work in a bubble of care homes in intervention scenarios.

Stochasticity

Stochasticity is used to describe variability in the parameters that determine the transitions of individuals between different states of infection, including the incubation time and the transmission probability. This represents variations in the risk of acquiring the infection and the progression and outcome of the infection among people, influenced by factors such as their health status, underlying conditions, and immune system. Another stochastic element is contact rates between individuals in a care home that affects the spread of the infection. The movement of bank/agency staff between care homes in the network is also a stochastic process as randomness exists in which care homes they come to work on a particular day. This also leads to the stochasticity in the time at which bank/agency staff become infected and introduce the infection into a care home.

Collectives

In intervention scenarios, the model has collectives of care homes and bank/agency staff agents. The collective referred to as a bubble of care homes to which agents belong restricts them to only work within that bubble.

9.4.4 Module Interfaces

Interface between Network Module and Temporary Staff Module

Care home i seeks to recruit $N_{B,i}$ bank/agency staff each day. For each care home agent i, chosen randomly, bank/agency staff agents who have not been allocated to any other care home and are not self-isolating are allocated based on the following two rules one by one until the demand of this care home is fulfilled.

- Rule 1 with probability η: A randomly chosen bank/agency staff agent is allocated. In base case simulations, η is set to 0.5 based on discussion with bank/agency staff members and care home managers in Lanarkshire.
- Rule 2 with probability $(1 - \eta)$: The bank/agency staff agent with the largest value of *WorkRecord[i]* is allocated. The rule describes a desire by care homes to utilise the same bank/agency staff and by these staff to work in the same care home. *WorkRecord* is initiated by a warm-up period of 90 days without infections in each simulation run. It reaches a steady state after this period.

If the number of available bank/agency staff is insufficient to fill the required positions, care homes will be understaffed for that day.

Interface between Network Module (ABM) and Intra-facility Module (SD)

Agents' state variables affect flows: Care home agents' daily staffing level determined by the state variables N_W, N_U, and N_R affects $Flow_{S_S E_S}$ and $Flow_{S_R E_R}$. The number of contacts with staff per resident remains unchanged based on the implicit assumption that the overall care home workload does not change and, therefore, is not affected by the daily staff-to-resident ratio. This means that staff on duty will have to carry out extra workload to maintain the quality care delivered to residents. Therefore, the daily number of contacts with residents per staff member at work, calculated as $c_{SR} = \frac{c_{RS} N_R}{N_W - N_U}$, is used in $Flow_{S_R E_R}$ in the SD Intra-facility module.

Stock levels affect agents' state variables: The number of permanent staff members self-isolating due to COVID-19 (i.e., the level of the stock $Q_{S,i}$) in care home i affect the demand for bank/agency staff on a given day during the pandemic defined by the state variable $N_{B,i}$. This state variable is calculated as follows:

$$N_{B,i} = N_{BN,i} + \frac{Q_{S,i}(N_{W,i} - N_{BN,i})}{N_{S,i}}$$

$$N_{BN,i} \sim Poisson(\alpha N_{W,i})$$

$N_{BN,i}$ *describes* the number of bank/agency staff required in normal circumstances prior to the COVID-19 pandemic due to ongoing staff shortage and absence of staff for reasons such as holidays, unfilled vacancies, and sickness. The parameter α is the average percentage usage level of bank/agency staff in all care homes in the network. The value of α is between 5% and 20% across various areas in the UK (SSSC, 2020; Fenton et al., 2020; Allan and Vadean, 2017). In base case scenarios, we set α to 10%. $N_{W,i}$ denotes the desired number of staff members on duty per day when care home *i* operates at full capacity. $N_{S,i}$ is the number of permanent staff members of care home *i*. The component $Q_{S,i}(N_{W,i} - N_{BN,i}) / N_{S,i}$ represents the number of bank/agency staff agents required to cover for permanent staff members self-isolating due to COVID -19.

Interface between Temporary Staff Module (ABM) and Intra-facility Module (SD)

Aggregate measures of agents affect flows: The daily number of infectious bank/agency staff members (I_B) increase the forces of infection for susceptible residents and susceptible permanent staff ($Flow_{S_R E_R}$ and $Flow_{S_S E_S}$) in the Intra-facility module.

Stock levels affect agents' state variables: The levels of stocks I_R and I_S affect bank/agency staff agents' state variable *InfectionState*. At the end of the day (ABM time-step), susceptible bank/agency staff acquire infection via interactions with infectious residents and other staff members at a rate that is equal to the force of infection in staff in the care home where they have worked. The force of infection among staff is calculated as below:

$$vc_{SR}\frac{I_R}{N_R} + vc_{SS}\left(1 - \rho_{sd}\right)\frac{I_W}{N_W - N_U} \qquad (1)$$

$$I_W = I_{SW} + I_B \qquad (2)$$

$$I_{SW} = \frac{(I_S+I_{SD})(N_W-N_B)}{N_S} \qquad (3)$$

In which,

$I_W - N_U$: The daily number of staff members at work (permanent and bank/agency staff)

$N_W - N_B$: The daily number of permanent staff members at work

I_W: The number of infectious staff members at work

I_{SW}: The number of infectious permanent staff members at work

Replace (2) & (3) into (1), the rate becomes:

$$vc_{SR}\frac{I_R}{N_R} + vc_{SS}(1-\rho_{sd})\frac{\frac{(I_S+I_{SD})(N_W-N_B)}{N_S}+I_B}{N_W-N_U}$$

9.4.5 Updating Rules

Table 9.4 shows the updating rules between the modules. The agent-based modules Network and Temporary Staff run at a daily time step as epidemiological data are collected on a daily basis and this is also the unit of time commonly used to describe clinical characteristics of COVID-19 in the literature. The stochastic SD module Intra-facility is theoretically based on continuous time in which the time step *dt* represents an infinitesimal time-step (Ossimitz and Mrotzek, 2008). In practice, the module runs at a small finite time step *dt* of $1/2^7$ days for good numerical results for a continuous model. The modules exchange information daily to capture transmission dynamics across care homes. As bank/agency staff are rostered daily, it is important to update their infection state and the state of SD modules in affected care homes on this time scale. Simulations are 90-day time steps long as this covers the period for planning response strategies to contain the spread of COVID-19. However, we also ran the model for 180 days to assess the robustness of the findings for a longer time period.

Table 9.4: Updating rules at each time step (daily)

Execution Order	**Sending Module**	**Receiving Module**	**Information**
At the beginning of each time step			

1	Network (ABM)	Temporary Staff (ABM)	Request bank/agency staff based on the daily demand
2	Temporary Staff (ABM)	Network (ABM)	Schedule job – Allocate bank/agency staff into care home agents
3	Network (ABM)	Intra-facility (SD)	Daily staffing level affects the number of contacts with residents per staff member
	Temporary Staff (ABM)	Intra-facility (SD)	Ingress of virus – The number of infectious bank/agency staff members (an aggregated measure) allocated to a care home agent affect the force of infection for susceptible residents and staff (flows) in that facility.
At the end of each time step			
4	Intra-facility (SD)	Temporary Staff (ABM)	Bank/agency staff acquire infection from infectious residents and other staff members
	Intra-facility (SD)	Network (ABM)	The number of permanent staff members self-isolating due to COVID-19 determine the need of additional bank/agency staff in the next time step.

9.5 Experimentation

9.5.1 Experiment Scenarios[33]

Base-case scenario: We considered the impact of different intervention scenarios on the spread of COVID-19 within a network of 12 care homes (network A), which consists of a total of 780 residents, 960 permanent staff members, and 107 (10%) bank/agency staff members. The proportions of bank/agency staff were varied by scenario, but the total number of staff remained the same across scenarios. Sizes and staff-to-resident ratios of constituent care homes were determined based on the empirical distributions of 84 care homes in Lanarkshire, and the same characteristics were used for all simulations (Table 9.5). Data in Lanarkshire also reflected the proportions of care homes by size ranges in the UK (Shallcross et al., 2021; ISD, 2018). All residents and staff were susceptible at the beginning of the simulations. Furthermore, Table 9.5 includes three other hypothetical networks B, C, and D that comprise the same number of

[33] This section includes Experiment Scenarios under Material and Methods in Nguyen et al. (2022) and additional information in the ODD protocol (S1 Appendix in Nguyen et al. (2022)).

residents and staff members but have different compositions. We described these networks in more detail later in this section.

Table 9.5: Resident population size and staffing level in care homes within a network

Network	Care Home ID	Resident Population Size (N_R)	Total Permanent Staff (N_S)
Network A	1	10	22
	2	24	31
	3	32	47
	4	40	49
	5	46	73
	6	50	63
	7	65	80
	8	73	90
	9	80	90
	10	90	103
	11	110	110
	12	160	202
Network B	1 – 12	65	80
Network C	1	65	50
	2	65	55
	3	65	60
	4	65	65
	5	65	70
	6	65	75
	7	65	80
	8	65	90
	9	65	95
	10	65	100
	11	65	105
	12	65	115
Network D	1	10	12
	2	21	30
	3	30	39
	4	40	49
	5	46	57
	6	50	63
	7	65	80
	8	75	90

Network	Care Home ID	Resident Population Size (N_R)	Total Permanent Staff (N_S)
	9	82	98
	10	92	110
	11	109	135
	12	160	197

We assumed that care homes operate at their full capacity for the entire simulated period. The assumption helped avoid any distortion to the network composition in terms of constituent care homes' sizes and staff-to-resident ratios. Each care home in a network implemented the following interventions: hand hygiene and use of PPE, social distancing, testing and isolation upon admission and re-admission of residents, closure to visitation, and weekly PCR testing of permanent staff (80% compliance) (Scottish-Government, 2020b; PHE, 2020). We assumed that bank/agency staff and permanent staff have the same risk of infection acquiring in the community.

Different levels of staff usage: Staff under other contract types (bank, agency, temporary, casual, and non-guaranteed hours contracts) constitutes 5 – 20% of total care home staff across various areas in the UK (SSSC, 2020; Fenton et al., 2020; Allan and Vadean, 2017). Thus, we examined the impact of different average usage levels of bank/agency staff with no pandemic (*α):* 0%, 5%, 10%, 15%, and 20%. When the usage level of bank/agency staff is different from the base-case value (107 bank/agency staff agents – 10% of total staff), the levels of permanent staff in each care home and bank/agency staff shared among care homes are adjusted accordingly so that the total staff in a network remains constant ($N_{S,total} = 1067$).

- The number of permanent staff members in care home *i*: $N_{S,i} = \frac{(1-\alpha)N_{S,i,base-case}}{(1-\alpha_{base-case})}$
- The number of bank/agency staff agents in a network initialized: $\alpha N_{S,total}$

Creating bubbles of care homes: We considered interventions that create similarly sized care home bubbles of size two, three, four, or six care homes. Care homes were grouped into bubbles randomly in the base-case simulations under the assumption that this would be done based on care homes' geographic location in reality. We also explored a scenario in which care homes are grouped based on their resident population sizes and staff-to-resident ratios. Bank/agency staff agents were grouped into these bubbles so that the ratios of bank/agency staff to total staff were as equal as possible across the bubbles. In the scenarios of creating bubbles of care homes, care homes are grouped into m bubbles with similar sizes. Care homes can be allocated into bubbles randomly or based on their size or staff-to-resident ratio. The number of bank/agency staff members of bubble i ($n_{B,i}$) was calculated as $n_{B,i} = \frac{\alpha n_i}{1-\alpha}$

- n_i: Total number of permanent staff in bubble i
- $n_{B,i}$ bank/agency staff agents with *GroupID* = 0 are randomly assigned to group i (their *GroupID* changes to i).

Staff shortage: Additionally, we examined the effect of different levels of staff shortage (α_s: 0%, 5%, 10%, 15%, and 20% of total staff) and compared scenarios in which bank/agency staff were used to compensate for the shortage and ones in which they were not. The number of permanent staff members in care home i was adjusted as $N_{S,i} = \frac{(1-\alpha_S)N_{S,i,base-case}}{(1-\alpha_{S,base-case})}$.

We also explored the impact of these interventions given different compliance rates to weekly PCR testing among bank/agency staff ranging from 0% to 80% in 20% increments.

Furthermore, we assessed how sharing bank/agency staff affects individual care homes' COVID-19 outcomes and how care home characteristics affect these outcomes. We performed the experiments for three other hypothetical networks B, C, and D (Table 9.5). Network B, which consists of homogeneous care homes in terms of size and staff-to-resident ratio, was used to examine the effect of using bank/agency staff on individual care homes with different intra-facility transmission risks drawn from a distribution. This heterogeneity represents different levels of adherence to care home interventions and other care home characteristics (e.g., architecture and operation) that we abstract from the SD Intra-facility module. Care homes in network C are homogeneous in size and heterogeneous in staff-to-resident ratio, and those in network D are heterogeneous in size and homogeneous in staff-to-resident ratio. We used networks C and D to disaggregate the impact of the heterogeneity in size and staff-to-resident ratio on the model results. Experiments with these networks also helped examine the robustness of model results to changes in network composition.

9.5.2 Outcomes[34]

We considered the cumulative number of infections in residents, permanent and bank/agency staff (medians and CIs, IQRs, and distributions) and the probabilities of outbreak occurrence (i.e., the presence of at least two infected residents) in m care homes (m = 1, 2, ..., 12). The model is stochastic and yields a distribution of possible outputs for each outcome for each set of input parameters, describing first-order uncertainty, and thus requires a large number of simulations to capture the system behaviour. We ran 1,000 simulations for each scenario since the median outputs of each outcome converged after this number of simulations. With this number of simulations, the 95% CIs of the median outputs for the cumulative number of infections was ± one infection per 1,000 people and the probability of outbreak occurrence was ± 5%.

9.5.3 Statistical Analysis[35]

We used the Wilcoxon test at a significance level of $\alpha = 0.05$ to perform hypothesis testing for the difference between scenarios in the median cumulative numbers of infections in residents after 90 days. We also adopted the Bonferroni correction method in which the *p*-values were multiplied by the number of tests to counteract the potential for type 1 error in multiple comparisons. When there was no statistical significance in median outputs of this outcome between scenarios, we performed the Kolmogorov-Smirnov [KS] test to identify the difference in distributions of the outputs (Sheskin, 2007). We also calculated the relative risk [RR] of infection for residents and the RR of outbreaks for different pairs of scenarios and the RR of infection in bank/agency staff to permanent staff for each scenario.

[34] Taken from the Outcomes section (under Materials and Methods) in Nguyen et al. (2022)

[35] Taken from the Statistical Analysis section (under Materials and Methods) in Nguyen et al. (2022)

9.6 Confidence Building[36]

9.6.1 Approaches

Evidence from a review indicated that the processes of verification and validation are not commonly reported for hybrid simulation models (Brailsford et al., 2019). Only a minority of these hybrid simulation modelling studies verified and validated the individual single-method modules using existing standard approaches for single-method models. However, the links between modules were rarely verified, and the overarching hybrid model was not validated. Mostafavi et al. (2014) verified the links between modules by matching the exchanged information with the expected values.

Our simulation model was built in Anylogic PLE 8.7.5, a multimethod simulation modelling tool that combines graphical modelling and Java code, and analysis was carried out in R version 1.4.1717. We gained confidence in the modules and the overall hybrid model using several approaches: code verification (Appendix F), white-box validation (including face validation, interface validation), black-box validation, and sensitivity and uncertainty analysis. We adapted these methods from both SD and ABM practices responding to the lack of systematic approaches for building confidence in hybrid simulation models (Brailsford et al., 2019).

In white-box validation, we developed individual modules and the hybrid model by triangulating insights from the literature, secondary data, and interviews and discussions with care home stakeholders, including representatives from HSCP, Public Health, and staff and managers of care homes in Lanarkshire. The model was presented to and challenged by the Scottish Government Data Analysis Research Group, SCWG, and DHSC. This helped ensure that the model structure and parameters sufficiently represented the investigated system and that our assumptions were appropriate for the model's purposes. We, in consultation with the stakeholders, continuously assessed the selection of SD and ABM for each module and the design of the hybrid model throughout the modelling process to ensure the appropriate level of abstraction for each part of the system. For instance, we compared the stochastic SD Intra-

[36] Section 9.6.1, excluding the first paragraph, has been taken from the Confidence Building (Verification and Validation) section (under Materials and Methods) in Nguyen et al. (2022). Section 9.6.2 has been taken from the Validation Results section (under Results).

Facility module with parallel deterministic SD and ABM models providing complementary representations of the same system at a different level of abstraction (Appendix F). This approach helped gain plausible explanations of the system behaviour and understand any differences in outcomes resulting from the use of these different simulation modelling methods. Additionally, we assessed the design of the SD–ABM interfaces—in terms of what and how information is exchanged between the modules—and updating rules to ensure the synchronisation of the modules.

In black-box validation, we adopted the pattern-oriented modelling approach (Grimm et al., 2005) to assess the model's ability to reproduce the following patterns observed in care homes in the UK: i) the higher risk of infection for residents and staff in care homes that frequently use bank/agency staff compared with ones that do not use them (Shallcross et al., 2021), ii) the higher risk of infection for bank/agency staff compared with permanent staff in care homes that frequently use bank/agency staff (Ladhani et al., 2020; Shallcross et al., 2021), iii) the higher risk of outbreaks in care homes that frequently use bank/agency staff compared with ones that do not use them (Green et al., 2021; Shallcross et al., 2021; Baister et al., 2021), and iv) the risk of outbreak occurrence in care homes specified by their size and staff-to-resident ratio (Green et al., 2021; Burton et al., 2020a; Scottish-Government, 2020a). Patterns i, ii, and iii, which reflect the impact of agency/bank staff use upon the spread of COVID-19 across care homes within a network, are important to clarify that our model is useful for its purposes. Patterns i, ii, and iii help validate the behaviours of the overall system. Pattern iv addresses the validity of the sub-systems' behaviour (care homes) when accounting for their interactions via bank/agency staff. We identified the studies to which we compared our modelling results by a systematic search of PubMed, the WHO COVID-19 database, and medRxiv on June 25, 2021 (Appendix F).

We performed a global sensitivity analysis for parameter uncertainty in the base case scenario and uncertainty analyses for structural and characteristic changes of the model to establish the robustness of the results and their uncertainty. The global sensitivity analysis parameter probability distributions are summarised in Table 9.3. We ran ten iterations for each of the 10,000 sets of samples generated using the LHS method (i.e., 100,000 simulations in total). The calculated PRCC determined the strength of the relationship between each LHS parameter and each outcome measure. For model structural and characteristic uncertainty, we examined the impact of different network compositions (networks A, B, C, and D) as described above and the heterogeneity of care homes' intra-facility transmission risk upon the model outcomes, which we explain below. We also explored the model sensitivity to different network sizes by considering networks of 24 and 6 care homes.

We conducted each experiment in three different scenarios of intra-facility transmission risk. In the first scenario, care homes in a network have the same average per-contact transmission probability of 0.02 calibrated for a single care home in Lanarkshire. The studies of transmission risk in similar settings reported similar values (Sun et al., 2021). The corresponding R_o of 4.02 in a care home was in line with the base case R_o of 4.04 used in a study of COVID-19 spread in a long-term care facility in France (Smith et al., 2020). The intra-facility transmission risk is affected by institutional and operational factors such as physical layout, ventilation, provided care services, cohorting, and adherence to interventions and, therefore, likely to be heterogeneous among care homes. For example, care homes providing nursing care have been more likely to have infected residents, possibly owing to their residents' higher level of dependency requiring closer contact with care staff (Green et al., 2021). In the second scenario, to reflect this heterogeneity, the average per-contact transmission probability in each care home was drawn from a Beta distribution (Toth et al., 2021; Knock et al.) (shape 1 = 5, shape 2 = 266). In the third scenario, we used Beta (shape 1 = 2, shape 2 = 117) to incorporate greater heterogeneity in the transmission risk across care homes. To obtain these distributions, we calibrated the hybrid model with heterogeneity in transmission risk to the time series of average daily infection prevalence produced by the baseline model with homogeneous transmission risk (Figure F.3 in Appendix F). The objective function minimizes the sum of squared errors and uses Tabu search and scatter search, which make less use of randomization and greater use of strategic choices and, therefore, is unlikely to be trapped in a locally optimal solution (Kleijnen and Wan, 2007). We varied the two Beta distribution parameters and held other parameters constant.

9.6.2 Validation Results

Black-Box validation

Pattern i: Our modelling results on the RR of infection for residents and staff in care homes that used bank/agency staff compared to ones that did not were consistent with other studies. The Vivaldi study, conducted in more than 9,000 care homes in England, reported that the odds ratio [OR] of infection for staff in care homes using bank/agency staff compared with care homes not using these staff was 1.88 (95%CI 1.77 – 2.00) among care homes in London. Bank/agency staff constitute 20% of the adult social care workforce in the London region (Shembavnekar, 2020). This study did not include information on the compliance rate to weekly testing in bank/agency staff. The HSCP Lanarkshire and Public Health Scotland advised that the compliance of bank/agency staff was likely to be lower than among permanent staff, which ranges between 70% and 90%. For the same level of bank/agency staff use, the corresponding OR in our model was very close to the Vivaldi study's finding (OR 1.81, 95%CI 1.77 – 1.86) for 60% testing compliance among bank/agency staff. Our model also approximated well the increased risk of infection for residents (Model: OR 2.20, 95%CI 2.14 – 2.27 (60% testing compliance); OR 1.67, 95%CI 1.65 – 1.70 (80% testing compliance); Vivaldi: OR 1.58, 95%CI 1.50 – 1.65) (Shallcross et al., 2021).

Pattern ii: Our model reproduced a similar increase in the risk of infection for staff working across multiple care homes compared to staff working in single care homes. A study conducted in April 2020 in six London care homes where 10.6% of staff had worked across multiple care homes reported that these staff had a three-fold higher risk of infection than staff working in single care homes (95%CI 1.90 – 4.79) (Ladhani et al., 2020). During this period, no testing was conducted and the intra-facility transmission risk was likely higher due to PPE shortages and a lack of clear and consistent IPC guidance. For a similar level of bank/agency staff use and when neither permanent nor bank/agency staff were tested weekly, the corresponding RR in our study was 3.09 (95%CI 3.03 – 3.15).

Pattern iii: Our model also reproduced a similar increase in the risk of outbreaks due to using bank/agency staff (Model: OR 3.42, 95%CI 3.25 – 3.60 (60% testing compliance); OR 2.53, 95%CI 2.40 – 2.66 (80% testing compliance); Vivaldi: OR 2.33, 95%CI 1.72 – 3.16) (Shallcross et al., 2021). This finding was in line with another study in 34 Liverpool care homes. The study reported that care homes employing agency staff had an increased risk of COVID-19 outbreaks (RR 8.4, 95%CI 1.2 – 60.8) (Green et al., 2021). Due to these study results' wide confidence intervals, we only compared the trend qualitatively. This finding coincided with the results from Baister et al. (2021), who used a compartment model to simulate the spread of COVID-19 in the Lothian health board (Scotland).

Pattern iv: The association between care home characteristics, including resident population size and staff-to-resident ratio, and COVID-19 outbreaks in our model echoed the results from other observational studies. Our model results showed that the care home population size was strongly associated with a COVID-19 outbreak (OR per 20-bed increase 2.32, 95%CI 2.15 – 2.51). This finding was consistent with the trend observed in the data of care homes in the UK and the finding from the investigation of 189 care homes in Lothian (OR per 20-bed increase 3.35, 95%CI 1.99 – 5.63) (Burton et al., 2020a; Scottish-Government, 2020a). We found no association between the staff-to-resident ratio and the risk of outbreaks (Pearson's correlation coefficient –0.17, 95%CI –0.45 – 0.68) (Appendix F). This finding was in line with the finding in care homes in Liverpool (Green et al., 2021).

Sensitivity and uncertainty analyses

We summarize the outputs from the PRCC analyses in Table F.4 (Appendix F). The per-contact transmission risk and the infection incidence in the community were the most significant contributors to the uncertainty in the number of infections in residents and staff. Increasing these parameters increased the number of infected residents and staff. These parameters were positively associated with the number of infected residents and staff. The number of infections was also sensitive to the staff-resident contact rate and the duration of pre-symptomatic disease but to a significantly lesser extent. The RR of infection for bank/agency staff to permanent staff was only sensitive to the per-contact transmission risk.

The relative effectiveness of interventions targeting bank/agency staff remained robust to modifying network composition in terms of care home size and staff-to-resident ratio, heterogeneity in intra-facility transmission risk, and the number of care homes in the network. The only exception was that forming bubbles of care homes was no longer effective in the scenario with no weekly testing for bank/agency and different intra-facility transmission risks drawn from the Beta distributions (KS tests: $p>0.1$).

9.7 Results[37]

9.7.1 Impact of Different Usage Levels of Bank/Agency Staff

The usage level of bank/agency staff had a statistically significant impact on the risk of infection for residents and the risk of outbreaks across care homes (Figure 9.3; Table F.3 in Appendix F). There was a statistically significant difference in the RR of infection and outbreak between the scenarios tested. When bank/agency staff were not tested weekly, the RR of infection for residents in care homes using an average of 10% bank/agency staff compared with those in care homes not using bank/agency staff was 2.65 (95%CI 2.57 – 2.72). When we set the average level of bank/agency staff to 20% of total staff, this RR of infection almost doubled (5.17, 95%CI 5.03 – 5.30). The RRs of outbreaks in care homes using 10% and 20% bank/agency staff to those not using bank/agency staff were 3.76 and 5.64 respectively (95%CI 3.58 – 3.96 and 5.37 – 5.92).

[37] Taken from the Results section, excluding Validation Results, in Nguyen et al. (2022)

The magnitude of the effect of using bank/agency staff significantly reduced when they were more compliant with the weekly PCR testing intervention. However, when bank/agency staff's compliance to weekly testing was as high as permanent staff's (80%), using bank/agency

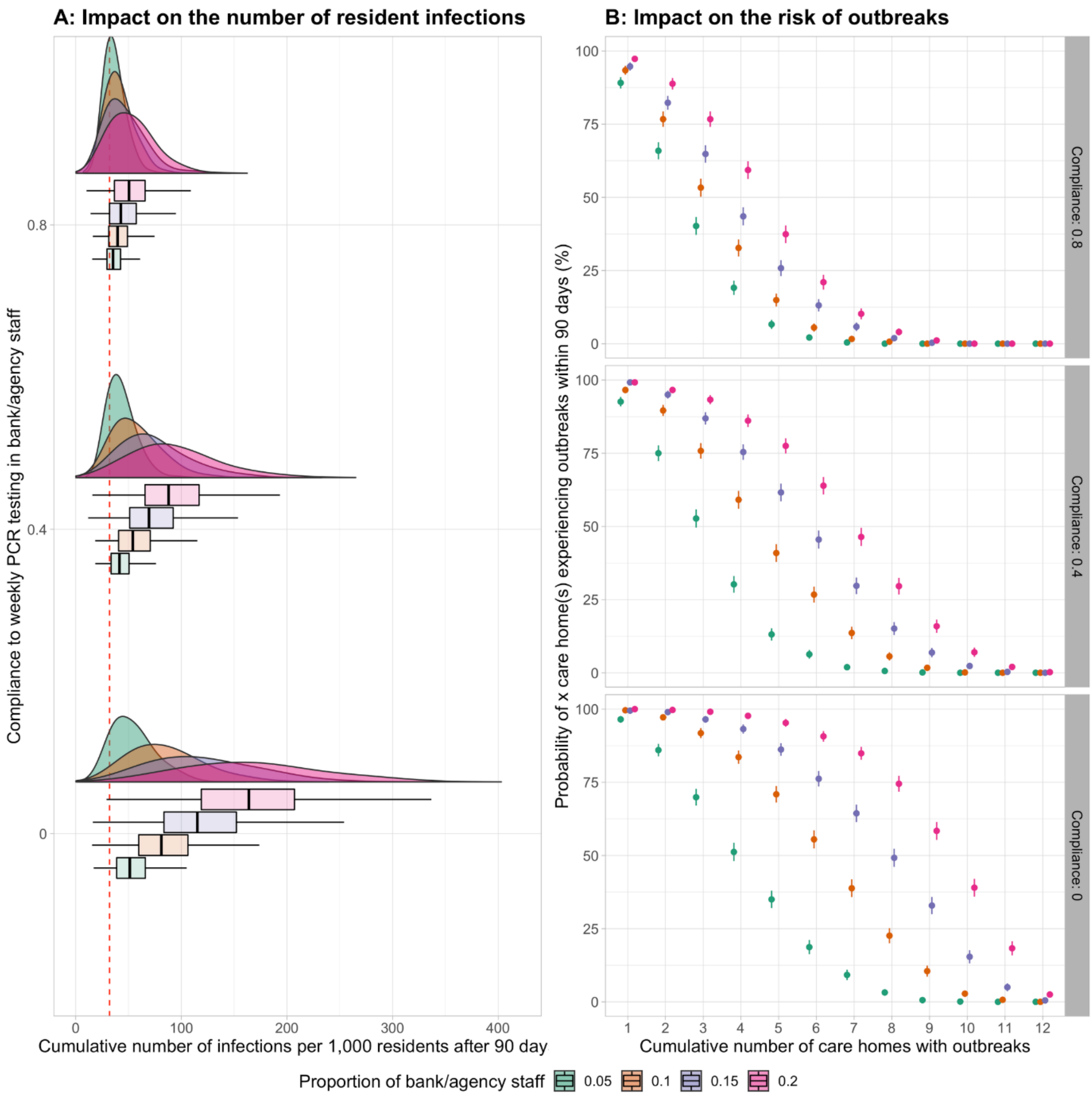

Figure 9.3: Impact of using bank/agency staff with different compliance rates to weekly PCR testing

*(A) On the cumulative number of infected residents after 90 days: Red dashed line denotes the median cumulative number of infected residents when care homes do not use bank/agency staff. Results are for 1,000 simulations in each scenario. Boxplot: middle – median; lower hinge – 25% quantile; upper hinge – 75% quantile; lower whisker = smallest observation greater than or equal to lower hinge - 1.5 * IQR; upper whisker = largest observation less than or equal to upper hinge + 1.5 * IQR. (B) On the risk of outbreak occurrence across care homes within 90 days. The risk of outbreak occurrence (point) is the proportion of simulations where outbreaks occur in 1,000 simulations for each scenario. Line range denotes the 95% CI of this outcome.*

staff still increased the risk of infection for residents and the risk of outbreaks in care homes. The RRs of infection for residents in care homes using an average of 10% and 20% bank/agency staff compared with those in care homes not using bank/agency staff were 1.28 (95%CI 1.25 – 1.31) and 1.64 (95%CI 1.60 – 1.68) respectively. The corresponding RRs of outbreaks were 1.83 (95%CI 1.73 – 1.94) and 2.48 (95%CI 2.35 – 2.61).

Bank/agency staff working across multiple care homes also had a higher risk of infection than permanent staff working in single care homes (Figure F.4 in Appendix F). When the average usage level of bank/agency staff was 10% of total staff, the RRs of infection for bank/agency staff compared with permanent staff were 1.55 and 1.35 in the scenarios of 0% and 80% compliance to weekly testing, respectively (95%CI 1.52 – 1.58 and 1.32 – 1.38). When the average usage of bank/agency staff increased to 20% of total staff, these RRs of infection were 1.98 and 1.48 in the scenarios of 0% and 80% compliance to testing, respectively (95%CI 1.95 – 2.01 and 1.46 – 1.51).

9.7.2 Impact of Using Bank/Agency Staff upon Individual Care Homes with Different Characteristics

The impact of using bank/agency staff on the risk of outbreaks varied across care homes with heterogeneous characteristics in a network. The use of bank/agency staff was more impactful in care homes with lower intra-facility transmission risk, higher staff-to-resident ratio, and smaller resident population size (Figure 9.4). The RR of outbreaks in care homes using bank/agency staff (at 10%) was negatively correlated to their intra-facility transmission risk (Figure 9.4A). The RR for the care home with the lowest transmission risk in the network was 17.3 (95%CI 9.47 – 31.5), whilst that for the care home with the highest transmission risk was 1.11 (95%CI 1.08 – 1.15). We observed a similar trend for the RR of care homes with different sizes (RR for ten residents 19.3, 95%CI 4.12 – 61.6; RR for 160 residents 1.75, 95%CI 1.64 – 1.86) (Figure 9.4C). By contrast, the RR of outbreaks in care homes using bank/agency staff was positively correlated to their staff-to-resident ratio (for the ratio of 0.77: RR 2.46, 95%CI 2.16 – 2.8; for the ratio of 1.77: RR 11.0, 95%CI 8.26 – 14.5) (Figure 9.4B).

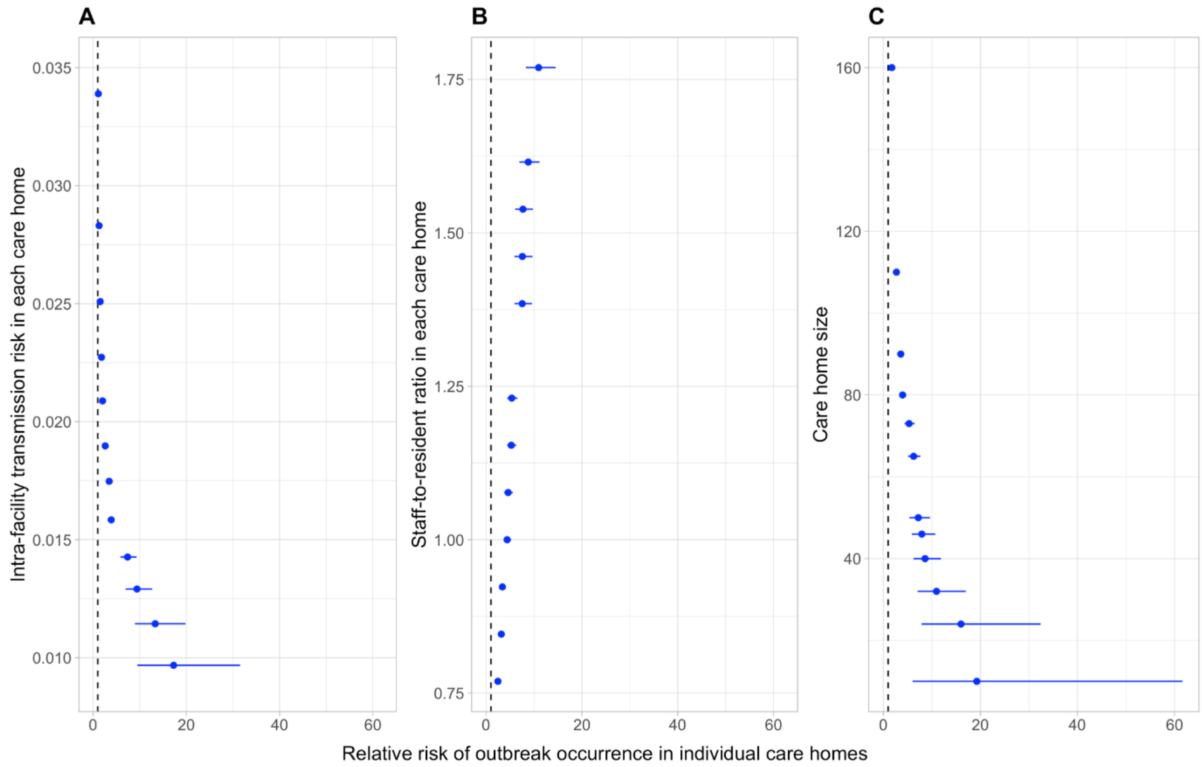

Figure 9.4: Impact of using bank/agency staff upon individual care homes with different characteristics

The plot illustrates the relative risk [RR] of outbreaks (points) within 90 days in individual care homes using 10% bank/agency staff compared with those care homes not using bank/agency staff. (A) Care homes in network B (homogeneous size & staff-to-resident ratio) with heterogeneous transmission risk drawn from a Beta distribution (shape 1 = 5, shape 2 = 266). (B) Care homes in network C (homogeneous size & heterogeneous staff-to-resident ratio) with homogeneous transmission risk. (C) Care homes in network D (heterogeneous size & homogeneous staff-to-resident ratio) with homogeneous transmission risk. No intervention in bank/agency staff is implemented. Line range denotes the 95% CI of the RRs. The dashed blacked vertical line denotes the RR of 1.00.

9.7.3 Impact of Forming Bubbles of Care Homes

Randomly grouping care homes into similarly sized bubbles

When bank/agency staff were not tested weekly, creating smaller bubbles of care homes and restricting bank/agency staff from working across these bubbles slightly reduced the spread of COVID-19 across care homes. Forming bubbles of two to four care homes reduced the cumulative number of infections by six (95%CI 5 – 7) per 1,000 residents after 90 days. When the weekly PCR testing of bank/agency staff was implemented, creating bubbles of care homes had no statistically significant effect on the cumulative number of infected residents (pairwise

Wilcoxon tests: $p>0.1$, KS tests: $p>0.05$ except for the pair of bubble size of two/three and 12 in the testing compliance of 20%: $p<0.001$).

Grouping care homes into bubbles by their size and staff-to-resident ratio

Grouping care homes into bubbles by their size and staff-to-resident ratio led to the same results as forming random bubbles.

9.7.4 Impact of Understaffing Due to not Using Bank/Agency Staff

Filling vacant positions with bank/agency staff led to more infections (Figure 9.5) and outbreaks (Figure 9.6) than leaving these positions unfilled. When 10% of positions in care homes were unfilled, the average cumulative number of infections after 90 days was 33 per 1,000 residents (95%CI 33 – 34). When filling these vacant positions with bank/agency staff, the average cumulative number of infections increased to 40 infections per 1,000 residents (95%CI 39 – 40). When the vacant positions increased to 20% of total staff, leaving these positions unfilled resulted in an average of 35 infections per 1,000 residents after 90 days (95%CI 34 – 35). Filling these positions with bank/agency staff led to an average of 51 infections per 1,000 residents (95%CI 50 – 52). The stochasticity of bank/agency staff movement across care homes in the network led to wider distributions of infections as compared to leaving these positions unfilled (Figure 9.5). The stochasticity of bank/agency staff movement also led to a larger variation in outbreak probabilities (Figure 9.6B as compared to Figure 9.6A) as the proportion of vacant positions to total staff increased.

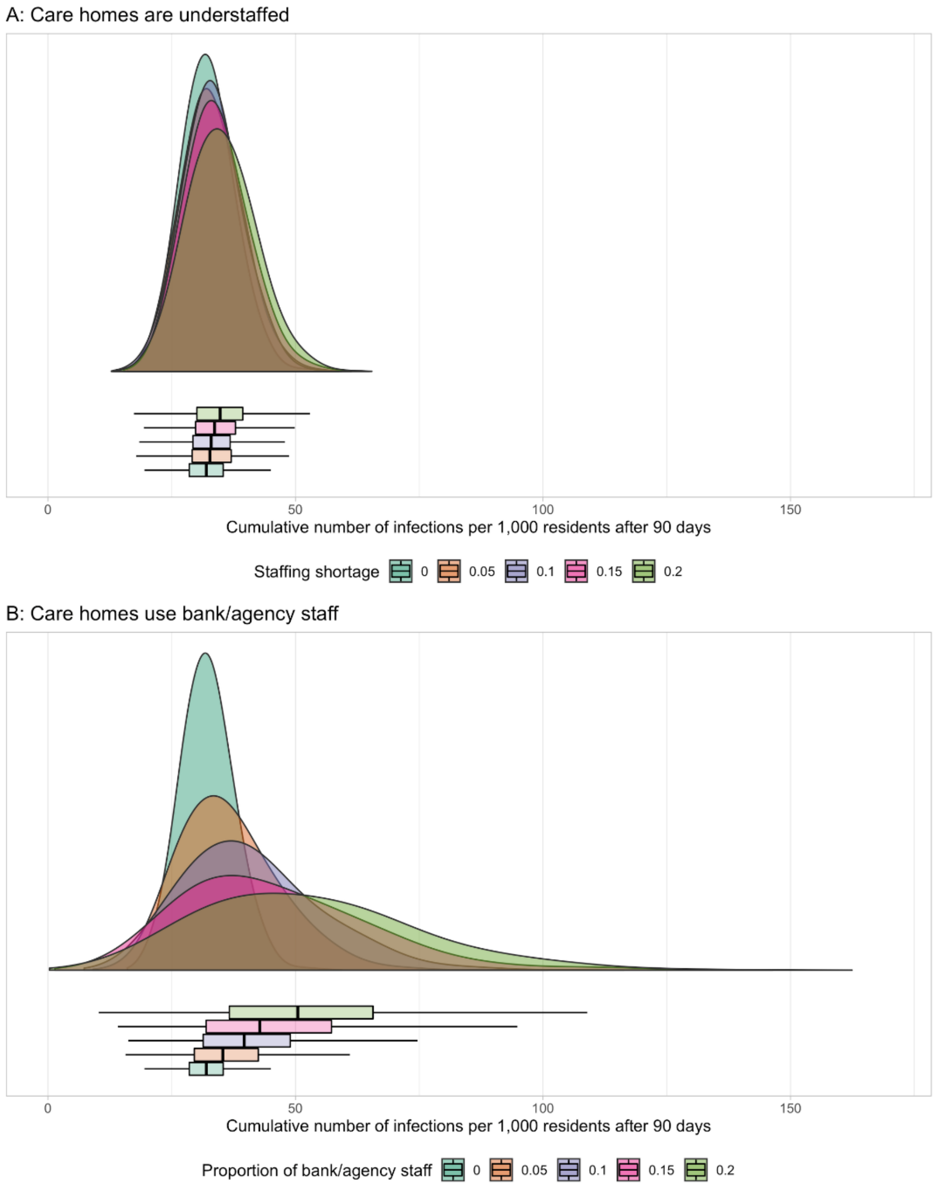

Figure 9.5: Impact of staffing shortage vs use of bank/agency staff on infections in residents

*The plots illustrate the distributions of the cumulative number of infected residents after 90 days. (A) in various levels of staff shortage. No bank/agency staff are used to cover the vacant positions. (B) in various usage levels of bank/agency staff. Bank/agency staff have 80% compliance to weekly PCR testing (α = 0.5). Boxplot: middle – median; lower hinge – 25% quantile; upper hinge – 75% quantile; lower whisker = smallest observation greater than or equal to lower hinge - 1.5 * IQR; upper whisker = largest observation less than or equal to upper hinge + 1.5 * IQR.*

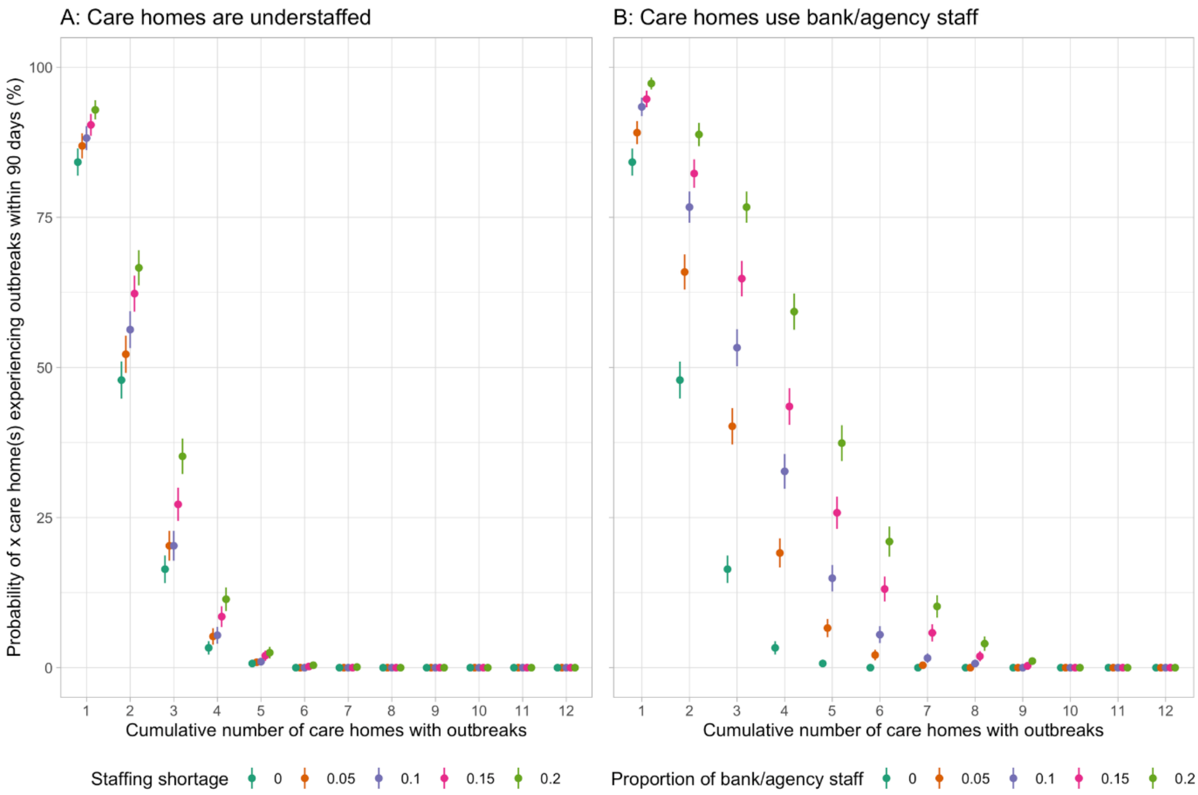

Figure 9.6: Impact of staffing shortage verse use of bank/agency staff on the risk of outbreak.

The plots illustrate the risk of outbreak occurrence across care homes within 90 days. (A) in various levels of staff shortage. No bank/agency staff is used to cover the vacant positions. (B) in various usage levels of bank/agency staff. Bank/agency staff have 80% compliance to weekly PCR testing (α = 0.5). The risk of outbreak occurrence (point) is the proportion of simulations where outbreaks occur in 1,000 simulations for each scenario. Line range denotes the 95% CI of this outcome.

9.8 Discussion[38]

Our model provides a unique perspective on exploring the impacts of bank/agency staff movement on the spread of COVID-19 across care homes in a network. Combining ABM for the inter-facility transmission and SD for the intra-facility transmission allows us to effectively address research questions that are difficult to study with a single method. ABM enables the heterogeneity of care homes and the stochasticity of bank/agency staff's movement that characterise the inter-facility spread of COVID-19 to be captured. This bottom-up modelling method is also more flexible than SD to reflect changes in the network composition, and it

[38] Sections 9.8 and 9.9 have been taken from the Discussion section, excluding the last two paragraphs, in the Nguyen et al. (2022).

allows us to explicitly model interventions such as creating bubbles. Meanwhile, stochastic SD, with a lower computational intensity than ABM, provides a holistic perspective of the transmission dynamics in each care home which sufficiently meets our modelling objectives.

Consistent with other COVID-19 prevalence surveys in care homes in the UK (Green et al., 2021; Shallcross et al., 2021; Ladhani et al., 2020), our findings generally support policies limiting the movement of staff working across multiple care homes if their testing compliance is low. Our modelling study found that the usage level of bank/agency staff in care homes significantly impacts the risk of SARS-CoV-2 infection in residents and the risk of outbreaks in care homes. Bank/agency staff working across multiple care homes can act as vectors that facilitate the inter-facility transmission of COVID-19. Additionally, the lack of infection control training and accountability among bank/agency staff and their unfamiliarity with various practice protocols across care homes potentially limit their capability to adhere to the IPC procedures (Travers et al., 2015). This undermines the implementation of IPC and increases the risk of infection for residents and staff.

We explored weekly testing of bank/agency staff in this paper, and we found that it reduced the spread of COVID-19 across care homes. Increasing compliance to routine testing among these staff reduces the risk of infection among residents and the risk of outbreaks in the care homes. Our previous study showed that increasing the frequency of routine testing for staff within care homes is likely even more effective in reducing infections (Nguyen et al., 2020a), though it may lead to reduced compliance. Despite the effectiveness of testing when compliance is high, residents in care homes using bank/agency staff are still exposed to a slightly higher risk of infection compared with those care homes not using bank/agency staff.

The effect of using bank/agency staff on the risk of an outbreak varies with a care home's relative – compared to other care homes in the network – intra-facility transmission risk, staff-to-resident ratio, and size. Bank/agency staff are more likely to acquire the infection in care homes with a higher transmission risk and then spread it into care homes with a lower transmission risk than in the reverse direction. Care homes with higher transmission risks are also more likely to experience an outbreak before exporting the virus via bank/agency staff. Therefore, the simulation results indicated that using bank/agency staff increased the risk of outbreaks in care homes with a lower transmission risk more significantly than in ones with a higher transmission risk. The risk of outbreaks increases significantly with the increase of care home size due to the increased risk of infection ingress by a larger number of staff members.

Similar to the pattern observed in the network containing care homes with heterogeneous transmission risk, using bank/agency staff is more impactful on the risk of outbreaks in smaller care homes. Care homes with higher staff-to-resident ratios have a higher average daily number of bank/agency staff on duty, which increases the risk of infection ingress via this route and, thus, the risk of outbreaks.

Creating care home bubbles within which bank/agency staff work had a limited effect on simulation infection estimates. This intervention slightly reduces the number of infections when bank/agency staff's compliance with weekly testing is low. In other scenarios, forming bubbles adds no value to reducing the risk of infection for residents. Testing bank/agency staff weekly to quickly identify asymptomatic and pre-symptomatic staff prevents them from spreading the infection whether they are in bubbles or not. Whether care homes are grouped randomly or based on their characteristics, such as sizes and staff-to-resident ratios, does not affect the overall number of infections in the network. The latter approach shifts the risk of outbreaks and the number of infections, reducing them in smaller and higher staff-to-resident ratio care homes but increasing them further in larger and lower staff-to-resident ratio ones. However, this approach may cause a mismatch between the demand and supply of bank/agency staff. For example, bank/agency staff may resist working in bubbles where care homes have a higher risk of outbreaks or are distant from each other. The practicalities of this approach need to be explored and discussed with HSCP and care homes.

Our model estimates also suggest that staff shortages increase the risk of infection for residents and the risk of outbreaks across care homes to a lesser extent than using bank/agency staff to fill vacant positions. However, these estimates underestimate the impact of staff shortages as we did not account for their potential to reduce compliance to IPC measures leading to an increased transmission risk. Furthermore, staff shortages negatively impact the quality of care delivered to residents and undermine the effort to resume visitation, which affects residents' well-being (Spilsbury et al., 2011; Kim et al., 2009; McGilton et al., 2020). Staff shortages also increase the workload and pressure on staff, potentially causing them mental and psychological strain and can make them leave their positions. Staff burnout and its impact on controlling outbreaks and reducing compliance with IPC practices should be researched further.

Despite our findings, employing bank/agency staff is viable to care homes to avoid falling short of safe staffing levels and losing places for residents. The links between the use of bank/agency staff and poorer care outcomes and higher risks of infection have been reported in previous studies, and the latter is echoed by our modelling study. However, as other research has noted, care homes could potentially mitigate these risks by increasing wages, offering incentives for working in single care homes, and offering sick leave (Van Houtven et al., 2020; Nuño et al., 2008). As our model suggests that routine testing of bank/agency staff significantly reduces the risk of COVID-19, care homes utilising bank/agency staff and agencies supporting care homes during the pandemic may wish to consider protocols and support to enhance compliance to the testing intervention in this group of workers. In the longer term, better pay and training, including IPC training, will help create a higher quality and more stable workforce.

9.9 Limitations

This modelling study has a number of limitations. Firstly, we assumed that when bank/agency staff are in care homes, they have the same compliance level to IPC measures as permanent staff, including hand hygiene, wearing PPE, and social distancing. If bank/agency staff compliance is lower, our study underestimates the increased risk of COVID-19 transmission by them. Secondly, the model has not accounted for the activities that bank/agency staff undertake within the care homes. These activities would affect their contact rates and the nature of their contacts, which in turn influences the per-contact transmission risk with residents. The evidence remains uncertain on the difference in the risk of SARS-CoV-2 infection between care home staff working in resident-facing roles compared with those not working in these roles. The estimates in a COVID-19 infection survey in England showed evidence of an increased level of infection amongst staff working in resident-facing roles (ONS, 2020a). However, other studies suggested infection rates among staff members within individual care homes do not statically differ when comparing different exposures to the residents, including those with no contact with residents (Ladhani et al., 2020; ONS, 2020b). Thirdly, our model has not accounted for the potential increased risk of SARS-CoV-2 infection in bank/agency staff who also work in other healthcare settings such as hospitals and/or carry out other care duties. Interactions in these settings typically require closer contact than in the community more broadly. Fourthly, the model has not considered scenarios in which bank/agency staff move across care homes multiple times per day. These factors would serve to increase the impact of using bank/agency staff. Fifthly, we have not modelled care homes' adaptive decisions about interventions which can also contribute to affecting the intra-facility transmission risk. For example, care homes that experience outbreaks may become more compliant with IPC measures, while the compliance in other care homes that have not had outbreaks may decrease over time. Finally, the model does not consider scenarios when vaccination is available or the effect of different variants of SARS-CoV-2 explicitly.

Several key parameters describing virus and disease characteristics are still uncertain and may also vary greatly from community to community. Similarly, a lot of relevant information about the characteristics of the care home resident population and staff are not readily available. Therefore, we performed sensitivity and uncertainty analyses for a wide range of parameter values and various model characteristics, respectively. The purpose of this modelling study was not to project the absolute number of SARS-CoV-2 infections and deaths in residents and staff in care homes but rather to compare the relative effectiveness of different interventions targeting staff working across multiple care homes. Although the absolute values of the model outcomes are sensitive to some parameters and changes in model structure, the relative findings which have been our focus are robust to uncertainty in model parameters and structure. Our results also help understand how heterogeneity in network composition affects individual care homes. Our base case model reflected characteristics of care homes in the UK, but it could be tailored to a specific network of care homes in other countries to evaluate the impacts of policies targeting staff working across multiple care homes. The model can also be updated and extended to reflect the heterogeneity in care homes' adaptive decisions about interventions.

9.10 Chapter Summary[39]

In conclusion, this modelling study has implications for policymakers considering developing effective interventions targeting staff working across multiple care homes during the ongoing and potential future pandemics. The use of bank/agency staff working in multiple care homes increases the risk of SARS-CoV-2 infection for residents and the risk of outbreaks across these facilities. Our results suggest that the movement of staff across care homes should be limited, and care homes should use bank/agency staff at a minimum possible level to reduce infections. Where using bank/agency staff is unavoidable, they must be encouraged to comply with routine testing. They should also be inducted into new care home environments to enhance their

[39] The first paragraph has been taken from the Conclusion section in Nguyen et al. (2022).

compliance with other IPC interventions. Forming bubbles of care homes shows little value in reducing the risk of inter-facility transmission and may be resource-consuming to implement and monitor.

Besides the model findings' implications for policy, the learning from performing the modelling in this chapter has several implications for the framework in Chapter 7. First, the modelling process provided insights into when modellers should plan for different validation activities throughout the framework. Second, it revealed that determining the relative hierarchical level of one module to other modules does not aid in choosing a simulation method for each module. Third, iterations between different steps in the framework help clarify modules' linkages. Fourth, it highlighted that the high-level designs of hybrid simulation models discussed in the literature could not be considered until the flows of information, interface, and updating rules had been defined. Fifth, the modelling has highlighted the importance of understanding the impact of updating frequency on model outputs and specifying the order of updates occurring at a pre-defined time point. Previous studies have not discussed these aspects of updating rules between modules. Finally, the reflection upon the modelling process has led to two new interface designs that are potentially useful in developing hybrid simulation models (see section 7.2.4.2).

Chapter 10. Conclusion

10.1 Introduction

This chapter first summarizes the research agenda and subsequently presents a precis of the main conclusions reached through this research. The theoretical, methodological, and empirical contributions of this research to the fields of HAI prevention and control, and management science and operational research are then described. Furthermore, implications for practice and policy are discussed. The limitations of the research are presented, and finally, opportunities for further research are suggested.

10.2 Research Summary

Chapter 2 presented a review of the burden of HAIs and IPC evidence and practice in care homes and discussed how simulation models have been used to study HAIs in this setting. How the COVID-19 pandemic has highlighted the issues of IPC in care homes was discussed. The first research objective was identified, which is to evaluate the effect of different intervention strategies to prevent and control the spread of COVID-19 within and across care homes.

Chapter 3 introduced and compared different simulation modelling methods, focusing on SD and ABM, which are the two commonly used methods in infectious disease modelling. The comparison of SD and ABM in terms of theories underlying the methods, assumptions, stochasticity, inputs, outputs, data dependency, and typical case uses in healthcare provided a ground for consideration of why and when they can be combined. This chapter also reviewed how simulation models have been used to investigate HAIs and their mitigation and how these models have evolved. This review enabled the identification of the research gap that was explored in this research: a lack of simulation modelling studies for transmission dynamics in the care home setting.

Chapter 4 discussed the benefits of hybrid simulation for modelling HAIs in-depth. These benefits included the provision of richer insights beyond single simulation methods, the capability of supporting decision-makers at different levels of management, and balancing simulation performance and result accuracy. This chapter also highlighted challenges in the development and use of hybrid simulation models. This included a lack of methodological clarity for combining different simulation methods, especially SD and ABM combinations, which was explored in detail in Chapter 5.

Chapter 5 focused on one of the challenges of developing hybrid simulation models highlighted in Chapter 3. This chapter reviewed the literature that guides the combination of SD and ABM and identified the unanswered questions in this field. The second research objective was determined, which is to develop comprehensive and practical guidance on combining SD and ABM in a hybrid simulation model.

Chapter 6 presented the philosophical standpoint underpinning this research (i.e., critical realism) and the methodology (i.e., case study) and methods undertaken to address the research gaps highlighted in Chapter 4 and Chapter 5.

Chapter 7 proposed a detailed stepwise framework for combining SD and ABM in the conceptual model development process including four main stages: i) exploring the problem, ii) assessing the appropriateness of combining SD and ABM, iii) designing the modules, and iv) designing the links between modules. The hybrid model of inter-facility transmissions in networks of heterogeneous care homes described in Chapter 9 was referred to, where appropriate, to demonstrate the use of the framework. This framework was based on the review of the existing guidance on combining SD and ABM in Chapter 5 and the researcher's reflection on the modelling process of the case study. It addressed the gap with respect to a lack of methodological clarity on mixing SD and ABM identified in Chapter 5.

Chapter 8 presented an ABM that simulated the transmission dynamics of COVID-19 via contacts between individuals in a care home setting to evaluate the effectiveness of a range of intervention strategies relating to testing staff and residents, using PPE, visiting policy, and cohorting. The model addressed the gap around IPC in care homes identified in Chapter 4. ABM was selected to capture the heterogeneity and stochasticity of individuals' disease progression and the interaction patterns between different types of staff, residents, and visitors. Additionally, care homes are diverse in terms of their resident population, structure, and management, and ABMs have more flexibility compared to simpler epidemiological compartment models to reflect this variation and examine how it impacts findings. This model provided insights to refine the research question about inter-facility transmissions and contributed to informing the experiment design of the hybrid model presented in Chapter 9. It also helped build confidence in one of the modules constituting the hybrid model.

Chapter 9 presented the case study of hybrid simulation modelling of networks of heterogeneous care homes and the inter-facility spread of COVID-19 by sharing staff. The model contains three modules using either SD or ABM: the Network module representing a network of heterogeneous care home agents, the Intra-facility module (stochastic SD) embedded within each care home agent to capture its intra-facility transmission, and the movement of bank/agency staff agents in the Temporary Staff module spreading COVID-19 across care homes. Combining SD and ABM provided a comprehensive appreciation of the complexity and multi-scale characteristics of the problem that are difficult to achieve with a single simulation method and offered richer insights. The model findings addressed the gap in knowledge with respect to the spread of epidemics across care homes identified in Chapter 4. This chapter explained the choice of simulation modelling methods and described the hybrid model structure informed by the proposed framework for combining SD and ABM discussed in Chapter 7.

10.3 Key Contributions

10.3.1 Theoretical Contribution

From a theoretical perspective, this research has two key contributions. First, it provides **a conceptualisation of the care home environment with characteristics that are crucial for infection control**. Care homes, where the majority of residents are elderly and have complex medical and care needs, have suffered devastating outcomes from HAI outbreaks (Burton et al., 2021; Lee et al., 2020). Suspension of visiting due to these outbreaks (Currie et al., 2016) has also caused substantial unintended harm to the health and wellbeing of residents. However, there is a lack of understanding of what characterizes transmission within a care home and across care homes and what interventions are practical to implement in this environment. This has led to a lack of context-specific best practice IPC guidance for this setting. This research fills these gaps of knowledge by triangulating insights from different sources, including a review of literature, data on national databases, data provided by care homes, and discussion and interview of various care home stakeholders. This research provides a better understanding of different routes of infection ingress into a care home, how staff in different roles, visitors, and residents interact, how care homes adapt to staff shortages by using bank/agency staff, and what IPC interventions are infeasible to implement and may affect the quality of care provided to residents or the mental health and wellbeing of residents. This understanding of the care home setting can hopefully serve as a ground for future modelling and empirical research.

The second theoretical contribution of this research is **the development of a multi-layer simulation for modelling interactions in a network that can be tailored and applied in different contexts**. The majority of existing simulation modelling studies have focused on the transmission dynamics of HAIs within a single healthcare facility and the ingress of infection from the wider community into a healthcare facility. These studies neglect that healthcare facilities are connected via patient transfer and sharing staff and the importance of inter-facility transmission via these routes. The concept of a network consisting of several agents representing healthcare facilities with a rich internal structure built using SD, which the hybrid model of this research adopts, is similar to Barnes et al. (2011). In Barnes et al.'s model, patients' movement (i.e., transfer) that causes the spread of HAIs across a network of facilities is modelled implicitly via behavioural rules of facility agents. These transferred patients are still considered homogeneous and presented by an aggregated measure. However, the stochasticity of individual movement across facilities is important to explain emergent events such as healthcare facilities (e.g., care homes in the UK during the COVID-19 pandemic) continuing to suffer outbreaks even when community infection rates decline. This research addressed this issue by considering those moving across facility agents at the individual level. This approach also offers more flexibility for explicitly incorporating interventions targeting this group of individuals, such as the restriction of their movement within a bubble of facilities, which could not be considered in the aforementioned models.

10.3.2 Methodological Contributions

From a methodological perspective, this research has three key contributions to the field of modelling and simulation in management science. The first contribution is **the proposal of a stepwise, detailed, and practical framework for developing a conceptual hybrid simulation model.** The framework is developed based on a review of existing guidance for combining SD and ABM and the researcher's reflection upon the process of building a hybrid simulation model for a case study. It addresses a lack of methodological clarity on combining simulation methods, especially SD and ABM combinations revealed through the literature review. It focuses on the conceptual modelling process for hybrid models, which has been identified as "the least developed stage in the modelling cycle, despite its importance" (Brailsford et al., 2019). Conceptual modelling also helps the structural modelling and validation processes and is considered as an important tool for model confidence building in healthcare (Roberts et al., 2012). In particular, this research addressed the following issues: i) a description of when SD and ABM should be combined, ii) an explanation of why SD and ABM combinations are required, iii) an explanation of how information is exchanged between SD and ABM modules at their interfaces, iv) a description of the elements including modules, their interfaces, and updating rules that are essential for reporting a conceptual hybrid model, and v) a description of how modellers can plan the confidence-building process for the individual modules and the overarching hybrid model at different stages of the framework.

The second methodological contribution of this research is **new practices for modelling interfaces between SD and ABM modules in a hybrid simulation model**. Previous frameworks for hybrid simulation have described different modes of interaction between simulation methods focusing on the system view, method dominance, and direction and frequency of interaction. Examples include the Hierarchical, Process Environment, and Integrated modes in Chahal and Eldabi (2008) and the Sequential, Enriching, Interaction, and Integration models in Morgan et al. (2017), Swinerd and McNaught (2012), and Martinez-Moyano et al. (2007). Swinerd and McNaught (2012) expand the concept of the Integration mode into three generic designs of combining SD and ABM, namely agents with rich internal structure, stocked agents, and parameters with emerging behaviours. However, the description of these interaction modes is still abstract and has not explicitly explained how the information is passed between different simulations. This research addresses this issue by categorizing the designs of an interface between SD and ABM modules and defining how SD/ABM modules generate the information and how the receiving ABM/SD modules handle such information for each design. These interface designs also explain other forms of feedback that go beyond what has been generally discussed in previous hybrid models: i) the SD module generates information that shapes the agents' environment or affects their decision-making and ii) the aggregation of the agents' characteristics or actions represents a stock or parameter in the SD module. The research also proposes two new interface designs: i) a stock level defines the agents' network topology and ii) the agents' state variables affect flows.

The third methodological contribution is **the demonstration of confidence-building approaches for a hybrid model adapted from both SD and ABM practices**. The process of verification and validation is not commonly reported for hybrid modelling studies, and only a minority of these studies verified and validated the individual single-method sub-models using existing standard approaches for single-method models (Brailsford et al., 2019). Confidence building at the level of the overarching hybrid model is under-researched. This research showcases how the constituent modules and the overall hybrid model were verified and validated using several approaches adapted from both SD and ABM practice. For code verification, tracing of randomly chosen agents of each type via simulation output and using the debugger, bottom-up testing, stress testing, and regression testing were performed. These activities were carried out for each module, each pair of modules, and the overall hybrid model. The hybrid model was validated using three approaches: i) white-box validation (including face validation and interface validation by triangulating insights from the literature, secondary data, interviews and discussions with care home stakeholders and experts, and comparing the stochastic SD module with parallel deterministic SD and ABM models), ii) black-box validation (cross-validation to observed data in care homes in Lanarkshire and published literature for the ABM and pattern-oriented modelling approach for the hybrid model using observed data in care homes in the UK), and iii) sensitivity and uncertainty analyses.

10.3.3 Empirical Contributions

This research makes two empirical contributions to the field of HAI prevention and control. First, the ABM model has **improved understanding of the transmission dynamics of COVID-19 within a care home via interactions between staff, residents, and visitors and the effectiveness of a range of intervention strategies relating to testing of staff and residents, using PPE, cohorting, and visiting policy**. The COVID-19 pandemic has highlighted care homes' vulnerability to infectious disease outbreaks and the lack of context-specific best practice IPC guidance for this setting. Furthermore, at the time of the ABM study, no other published models considered elements specific to care homes, and interventions proposed by wider population models (e.g., closure and social distancing in schools) were not suitable for this setting—care homes act as a residence and staff interaction with residents is often unavoidable. The model predictions suggest that routine testing should target staff in care homes in conjunction with adherence to strict hand hygiene and using PPE to reduce the risk of transmission per contact. Routine testing of residents is no more effective as a reference strategy, while routine testing of both staff and residents only shows a negligible additive effect. Furthermore, the model results show that the likelihood of the presence of an outbreak in a care home is associated with the care home population size. Cohorting residents and staff into smaller, self-contained units reduces the spread of COVID-19. However, shielding residents in care homes is not as effective as predicted in a number of studies that have modelled the shielding of vulnerable populations in the wider communities.

Second, the integrated hybrid SD-ABM model has **shed light on the impact that temporary bank/agency staff, who work across multiple care homes, have on the spread of COVID-19 across care homes and the effectiveness of a range of interventions**. To the best of our knowledge, this hybrid model is the first study that evaluated the effects of different interventions targeting bank/agency staff working across multiple care homes. Our findings align well with existing observational study evidence, including that using bank/agency staff increases the risk of COVID-19 infection for residents and that bank/agency staff have a greater risk of infection compared with permanent staff working in single care homes. Using bank/agency staff has the greatest impact on infections in care homes with lower intra-facility transmission risks, higher staff-to-resident ratios, and smaller sizes. Testing bank/agency staff is particularly important, while forming smaller bubbles of care homes and restricting staff to only work within a bubble has limited impact on the spread of COVID-19.

10.3.4 Practical and Policy Implications and Implementation

The models in this research improved our understanding of what interventions work well in the environment of care homes and, therefore, contributed to supporting our government partners' decisions, as mentioned in section 6.4. The ABM model contributed to decisions on several interventions made by the Scottish Government, including who to test in care homes and at what interval, the creation of smaller cohorts of residents and staff, and the development of visitation policy. This work contributed to understanding the circumstances under which care homes could permit visits. The Scottish Government changing its visitation policy based on this evidence helped promote the mental health and well-being of residents and their families. The findings from the hybrid SD-ABM model have policy implications for care homes, which are heavily reliant on bank/agency staff due to staff shortages. The work has been supporting the UK Health and Social Care Department in shaping IPC policy and guidance relating to the use of bank/agency staff in the care home setting.

Working closely with partners from HSCP Lanarkshire and the Scottish Government during the modelling helped gain their buy-in and acceptance, which supports the implementation of the models' recommendations. The flexibility of ABM to capture the distinct structure and management features of individual care homes also helped us to build care home managers' and staff's trust and confidence in the model. The effective communication of the model structure and the validation approaches to the partners and other stakeholders through regular reports and presentations helped build their confidence in the robustness of the model findings. Due to this, although this work was initially intended to support decision-makers from HSCP Lanarkshire, it was then provided to other government partners and contributed to supporting their decisions, as mentioned earlier in this section.

10.4 Limitations and Future Research

This section will reflect on the limitations of this research relating to the research design and the generalizability of the research contributions. It will also discuss future research opportunities to address these limitations and other research opportunities that build on the contributions of this research.

10.4.1 Data for Care Homes

We have encountered challenges in obtaining relevant data for developing the models in this research and determining their inputs due to a lack of data in care homes. Although we have triangulated data relating to the characteristics of care homes and their staff and residents from various sources, we appreciate that such data have only revealed a small part of the whole picture on health and social care in this setting. Several uncertainties have led to various assumptions in the models. Hanratty et al. (2020) also indicate that UK care home residents are invisible in national datasets and that data failings exposed by the COVID-19 pandemic have hindered service development and research for years. The discussion in this section is limited to data gaps that are relevant to infectious disease dynamics and infection control.

First, individual-level data on the demographics of resident and staff populations are essential but unavailable (Burton et al., 2020b). The ABM model in this research has captured the heterogeneous characteristics of residents in terms of age and age-stratified disease progression. However, the model could not account for other characteristics such as comorbidity and frailty that will affect residents' disease progression and contact patterns due to the absence of these data. National and regional mortality data and analyses are reported at an aggregated level (NRS, 2021; ONS, 2020d; Burton et al., 2020a; Stow et al., 2020). While these provide valuable insights, they cannot account for the heterogeneity in care home populations and, therefore, cannot offer insights into who lives and works in this setting. Without such knowledge, it is difficult to assess and predict how outbreaks and their outcomes are related to resident comorbidities and frailty, and staffing skill-mix.

Second, individual-level interactions in care homes are not well-understood. Interactions between different individuals in care homes are highly heterogeneous in terms of contact rates, contact nature (e.g., social or close/physical contact), and contact patterns (e.g., contacts with a specific cohort of staff and residents). The characteristics of individual interactions have a significant impact on how the infection spreads across a care home. Although this research has tried to capture some of these important characteristics by reviewing literature and interviewing care home managers and staff in different roles, further empirical research such as observational studies can offer a better understanding of individual interaction in this setting. This will help design better-targeted interventions.

Third, how bank/agency staff are shared between care homes and the flow of residents between hospitals and care homes have not been well-understood. Before interviews with relevant care home stakeholders, there is no data on how staff move between care homes. We still do not know whether staff in specific roles are more likely to work across care homes and whether their skills and infection control knowledge are different from those who work in a single care home. Furthermore, tracking residents who are admitted into and discharged from care home settings and transferred to other healthcare settings is an issue due to a lack of a systematic recording system (Burton et al., 2020b). Improving such knowledge will help design better-targeted interventions to prevent inter-facility transmissions.

10.4.2 Validating Hybrid Simulation Models

The literature review in this research has identified a lack of a framework for validating hybrid simulation models. Although we have adapted various approaches from both SD and ABM practices to validate the hybrid model of this research and discussed how modellers could plan for validation activities for a hybrid model in the framework, a comprehensive hybrid model validation guidance remains a major gap. The COVID-19 pandemic has also highlighted the need to validate simulation models used for analysis and decision-making in health systems. Real-world decision-makers must be able to trust the models' results as they inform decisions that significantly affect populations. Brailsford et al. (2019) emphasize, "the question of client trust, which is difficult enough in a DES model with an attractive animated visual display, is even more challenging in a hybrid model "glued together" with computer code." The lack of confidence in the model result will, in turn, affect real-world implementation. Katsaliaki and Mustafee (2011) and Brailsford et al. (2009) find that just above 5% of the simulation modelling studies in healthcare report being used in practice, and 2% of hybrid simulation modelling studies describe a real-world implementation (Brailsford et al., 2019).

10.4.3 The Generalization, Practicability and Potential Extension of the Framework

The framework for developing a conceptual hybrid SD-ABM model has been built on the reflection of a single modeller/researcher bound by a healthcare context, and its application is only demonstrated in a single case study. This significantly impacts the generalizability of the decisions on which methods to apply and the practicability of the framework. Further testing of the framework is necessary through applications in other contexts.

An extension of this research could explore the values of the proposed interface designs between SD and ABM modules which have not been applied in the existing hybrid models. Future research can also consider how to combine three simulation methods (i.e., SD, ABM, and DES) in a hybrid simulation model and what other OR methods can be combined using versions of this framework. There will be a need to explore further designs of interfaces between modules depending on the methods selected for combining.

10.4.4 Rationale of Decisions for Selecting Hybrid Simulation

This research has discussed different scenarios where hybrid simulation models are preferred compared to using single simulation methods and explained the benefits of using hybrid simulation for each application scenario based on reviewing and analysing existing models. However, it remains unclear how individual modellers or modelling teams decide on the use of hybrid simulation and what key factors affect their decision, as there is little discussion on the decision-making process in the literature. Therefore, analysing existing models is not sufficient to address these issues, and other research methods, such as in-depth interviews, will provide richer insights into the decision-making process of selecting hybrid simulations. Understanding this decision-making process would be helpful to draw generic lessons to aid the selection of appropriate methods.

10.4.5 Extending the Models

Future research can extend the ABM model by incorporating more detailed contact networks between individuals and health profiles of residents in care homes when data become available, or data collection is feasible. This can help identify the super-spreaders and the most vulnerable groups of residents for better-targeted interventions and allocation of resources. The model can also be extended to explore how the heterogeneity in compliance with infection control behaviours among staff and residents in care homes can influence the risk and magnitude of HAIs outbreaks in this setting.

Further research can also explore the transmission dynamics and the effectiveness of non-pharmaceutical interventions and vaccines in the scenarios where multiple SARS-CoV-2 variants of concern circulate in the community. Chapters 8 and 9 describe the historical situation in the spring/summer of 2020 when the alpha variant was dominant in the UK and before vaccines and lateral flow tests were available. Different variants may affect the virus' properties such as its transmissibility, disease severity, the performance of vaccines, diagnostic tools, therapeutic medicines, and other public health and social interventions (WHO, 2022).

The hybrid model can be expanded to examine the spread of COVID-19 across care homes under various scenarios of vaccination coverages among residents and staff. The network of healthcare facilities could also be extended to include hospitals and other health settings that connect with care homes via resident transfer. This research has identified that staff is the main route of COVID-19 ingress into a care home as the transfers of residents between facilities are restricted during the pandemic, and residents need to have two PCR tests before admission to care homes. However, when health services are back on track, transfers of residents/patients can cause the spread of infections, especially MDROs, across healthcare facilities. Understanding the vulnerability of each facility in the network will help design IPC interventions that account for the interconnectedness of healthcare facilities and target the most vulnerable facilities. Further, DES modules can be incorporated into this hybrid model to explore how HAI outbreaks occurring in one part of the healthcare system can affect access to services and transfers of patients across the system.

Appendix A. Systematic Review of Simulation Models in HAIs

Table A.1: Characteristics of the reviewed studies

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
(Sebille et al., 1997)	Not specified	ICU	SD	No	MRSA	Hand hygiene, antibiotic stewardship, isolation	N/A	Yes	No	No	Yes	Yes	No
(Lipsitch et al., 2000)	Not specified	ICU	SD	No	Not specified	Hand hygiene, barrier precautions	N/A	No	Yes	No	Yes	No	No
(D'Agata et al., 2002)	The US	General ward	SD	No	VRE	HCW cohorting, hand hygiene	N/A	No	No	No	Yes	No	No
(Cooper and Lipsitch, 2004)	UK and Denmark	Hospital*	SD	No	MRSA	Isolation	N/A	No	No	No	Yes	No	No
(D'Agata et al., 2005)	The US	Hospital*	SD	No	VRE	Hand hygiene, antibiotic stewardship, HCW cohorting	N/A	No	No	No	Yes	No	No
(Hotchkiss et al., 2005)	Not specified	ICU	ABM	No	MRSA, VRE	Isolation, patient cohorting, HCW cohorting	Nurses, primary physicians, and consultant physicians	No	No	No	Yes	No	No
(Webb et al., 2005)	Not specified	Hospital*	SD	No	Not specified	N/A	N/A	No	No	No	Yes	Yes	No
(Bootsma et al., 2006)	Netherlands	Hospital	DES	No	MRSA	Isolation, screening and combined interventions	N/A	No	No	No	Yes	No	Yes (ICUs and general wards)
(Basu et al., 2007)	South Africa	General ward	SD	No	Multi-drug resistant tuberculosis	Isolation, HIV treatment, air ventilation, facial mask	N/A	No	No	No	Yes	No	No
(Boldin et al., 2007)	Not specified	ICU	SD	No	Pseudomonas Aeruginosa, enteric Gram-negative bacteria,	Barrier precautions (improved hygiene, gloves, gowns), antibiotic prophylaxis	N/A	No	Yes	No	Yes	No	No

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
					MRSA and enterococci								
(D'Agata et al., 2007)	Not specified	Hospital*	Hybrid (SD + ABM)	No	Anti-biotic resistant nosocomial pathogens	Antibiotic stewardship	N/A	No	No	No	Yes	No	No
(Hotchkiss et al., 2007)	The US	Dialysis unit	ABM	No	Not specified	Environment disinfection, patient cohorting	N/A	No	No	No	Yes	Yes	No
(McBryde et al., 2007)	Australia	ICU	SD	No	MRSA	Hand hygiene, HCW cohorting, decolonization, patient cohorting	N/A	No	No	No	Yes	No	No
(Nuño et al., 2008)	Not specified	LTCF	SD	No	Influenza	Non-pharmaceutical interventions	N/A	No	No	No	No	No	No
(Ueno and Masuda, 2008)	Japan	Hospital*	SD	No	Not specified	Isolation, HCW cohorting, vaccination	Nurses and medical doctors	Yes	Yes	No	Yes	No	No
(van den Dool et al., 2008)	Netherlands	LTCF	Hybrid (SD + DES)	No	Influenza	Vaccination	N/A	Yes	Yes	Yes	Yes	No	Yes (LTCF and community)
(Wolkewitz et al., 2008)	Germany	General ward	SD	No	VRE	Hand hygiene, antibiotic stewardship, screening, patient cohorting, environmental cleaning	N/A	No	No	No	Yes	Yes	No
(D'Agata et al., 2009)	The USA	Hospital*	SD	No	HA-MRSA, CA-MRSA	Hand hygiene, screening, decolonization	N/A	No	No	No	Yes	No	No
(Greer and Fisman, 2009)	Canada	ICU	ABM	No	Pertussis	Vaccination strategies	N/A	Yes	No	Yes	Yes	No	No
(Hagtvedt et al., 2009)	The USA	ICU	DES	Yes	MRSA, VRE	Hand hygiene, isolation	Doctors and nurses	No	No	Yes	Yes	No	No
(Temime et al., 2009)	Not specified	ICU	ABM	No	Staphylococcus aureus, Enterococci, MRSA, VRE	Hand hygiene	Nurses, physicians, and Peripatetic HCWs	Yes	No	No	Yes	No	No
(Vanderpas et al., 2009)	Belgium	LTCF	SD	No	Viral nosocomial gastroenteritis	N/A	Nurses and medical staffs	No	No	Yes	Yes	Yes	No

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
(Barnes et al., 2010)	Not specified	Hospital*	ABM	No	MRSA	Hand hygiene, isolation, screening, decolonization	Physicians, nurses, rogue HCWs	No	No	Yes	Yes	No	No
(D'Agata et al., 2010)	The US	ICU and general ward	SD	No	HA-MRSA and CA-MRSA	Hand hygiene, decolonization	N/A	No	No	No	Yes	No	No
(Donker et al., 2010)	The Netherlands	Hospital network	ABM	No	MRSA	Referral patterns	N/A	No	No	No	No	No	Yes (Different categories of hospitals)
(Meng et al., 2010)	UK	Hospital ward	ABM	No	MRSA	Isolation, decolonization	Doctors, nurses	No	Yes	No	Yes	Yes	No
(Temime et al., 2010)	Not specified	ICU	ABM	No	Not specified	Hand hygiene	Nurses, physicians, and Peripatetic HCWs	No	No	No	Yes	No	No
(Webb et al., 2010)	Not specified	Hospital	SD	No	HA-MRSA, CA-MRSA	Hand hygiene, decolonization, and combination of these interventions	N/A	No	No	No	Yes	No	No
(Barnes et al., 2011)	The US	Hospital and LTCF	Hybrid (SD + ABM)	No	MRSA	Screening, decolonization	N/A	No	No	No	No	No	Yes (Hospitals and LTCFs)
(Chow et al., 2011)	Not specified	Hospital*	SD	No	Antibiotic-resistant pathogens (not specified)	Antibiotic stewardship	N/A	No	No	No	No	No	No
(Greer and Fisman, 2011)	Canada	ICU	ABM	Yes	Pertussis	Vaccination strategies	N/A	Yes	No	Yes	Yes	No	No
(Hubben et al., 2011)	Netherlands	Hospital	DES	Yes	MRSA	Screening, isolation	N/A	No	No	No	Yes	No	Yes (ICUs and general wards)
(Kardas-Sloma et al., 2011)	EU countries and the US	ICU and general ward	ABM	No	MRSA	Antibiotic stewardship	N/A	No	No	No	No	No	No
(Kouyos et al., 2011)	The US and Ireland	A setting in which several hospitals	SD	No	Not specified (Dataset from Ireland	Antibiotic stewardship	N/A	No	Yes	No	No	Yes	Yes

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
		interact with the community			included MRSA)								
(Lanzas et al., 2011)	The US	Hospital ward	SD	No	Clostridium difficile	N/A	N/A	No	No	No	No	No	No
(Lee et al., 2011)	The US	Hospitals (Excluding pediaetric hospitals)	ABM	No	MRSA	N/A	N/A	No	No	No	No	No	Yes (Within a hospital, between hospitals and between hospitals and community)
(Milazzo et al., 2011)	UK	Vascular unit	ABM	No	MRSA	Hand hygiene, HCW cohorting	N/A	No	No	No	Yes	No	No
(Robotham et al., 2011)	UK	ICU	ABM	Yes	MRSA	screening, isolation, and decolonization	N/A	No	No	No	No	No	No
(Wang et al., 2011)	China	Hospital*	SD	No	MRSA	Hand hygiene	HCWs in general and volunteers	No	No	No	Yes	Yes	No
(Barnes et al., 2012)	Not specified	ICU	ABM	No	Antibiotic-resistant bacteria (e.g., MRSA) or airborne diseases (e.g., Influenza or tuberculosis)	HCW cohort	Nurses, physicians	Yes	Yes	No	Yes	No	No
(Chamchod and Ruan, 2012)	Not specified	LTCF	SD	No	MRSA	Hand hygiene, screening, decolonization and isolation	N/A	No	Yes	No	Yes	No	No
(Gurieva et al., 2012)	Netherlands	Hospital	DES	No	MRSA	Decolonization, isolation	N/A	No	No	No	Yes	No	No
(Lee et al., 2012)	The US	Hospitals (Excluding pediaetric hospitals)	ABM	No	MRSA	Active surveillance, contact isolation (wearing gloves and gowns), combination of interventions	N/A	No	No	No	No	No	Yes

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
(Caudill and Lawson, 2013)	Not specified	Hospital ward	Hybrid (SD + ABM)	No	Staphylococcus aureus and Pseudomonas aeruginosa, MRSA	Antibiotic treatment	N/A	Yes	Yes	No	Yes	No	No
(Ferrer et al., 2013)	An EU country	ICU	ABM	No	Unspecified pathogens	N/A	Physicians and nurses	No	No	No	Yes	No	No
(Gurieva et al., 2013)	Netherlands	Hospital	DES	Yes	MRSA	Screening and isolation	N/A	No	No	No	Yes	No	Yes (ICUs and general wards)
(Jiménez et al., 2013)	The US	A floor of the hospital	ABM	No	Clostridium difficile	Antibiotic stewardship	Physicians, nurses, respiratory therapists, occupational therapists, speech therapists, physical therapists	Yes	Yes	No	Yes	No	No
(Kardas-Sloma et al., 2013)	France	ICU	Hybrid (SD + ABM)	No	MRSA	Antibiotic stewardship	N/A	No	No	No	Yes	No	No
(Lee et al., 2013a)	The US	Hospitals (Excluding pediatric hospitals)	ABM	No	VRE	N/A	N/A	No	No	No	No	No	Yes
(Lee et al., 2013b)	The US	Hospitals (Excluding pediatric hospitals) and LTCFs	ABM	No	MRSA	N/A	N/A	No	No	No	No	No	Yes
(Lee et al., 2013c)	The US	Hospitals (Excluding pediatric hospitals) and LTCFs	ABM	No	MRSA	Contact precautions	N/A	No	No	No	No	No	Yes

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
(Rubin et al., 2013)	Not specified	Hospital	ABM	No	Clostridium difficile	isolation, hand hygiene, barrier precautions (gloves), environmental disinfection	Physicians, nurses	No	No	No	Yes	Yes	No
(Sadsad et al., 2013)	Australia	Hospital	Hybrid (SD + ABM)	No	MRSA	HCW cohorting, screening, isolation, hand hygiene, ward staffing level	Nurses	No	No	No	Yes	No	Yes (Wards and rooms)
(Ciccolini et al., 2014)	UK and The Netherlands	Multiple hospitals	SD	No	MRSA, VRE	screening	N/A	No	No	No	Yes	No	Yes (Between hospitals)
(Ferrer et al., 2014)	An EU country	ICU	ABM	No	MRSA, VRE, influenza	HCW cohorting	Physicians and nurses	No	No	No	Yes	No	No
(Codella et al., 2015)	The US	Hospital	ABM	No	Clostridium difficile	Antibiotic, hand-hygiene, isolation, environment disinfection and mixed strategies	N/A	No	Yes	Yes	Yes	Yes	Yes (HCWs can travel to different wards when not servicing patients)
(Jaramillo et al., 2015)	Spain	Emergency department	ABM	No	MRSA	Hand hygiene, isolation material	Doctors, triage nurse, clinical nurses, admission personnel, auxiliary personnel, and cleaning staffs	No	No	No	Yes	Yes	No
(Wendelboe et al., 2015)	Mexico	LTCF	Hybrid (SD + DES)	No	Influenza	Vaccination	N/A	Yes	Yes	Yes	Yes	No	Yes (LTCF and community)
(Nelson et al., 2016)	The US	Hospital*	ABM	Yes	Clostridium difficile	Bundle including testing, isolation, hand hygiene, contact precautions, soap and water for hand hygiene, and environmental cleaning		No	No	No	Yes	Yes	No
(Robotham et al., 2016)	UK	Hospital*	ABM	Yes	MRSA	Screening	N/A	No	No	No	No	No	
(Caudill and Lawson, 2017)	Not specified	Hospital ward	Hybrid (SD + ABM)	No	Staphylococcus aureus	N/A	N/A	Yes	Yes	No	Yes	No	No
(Lei et al., 2017)	China	Two hypothetical	SD	No	MRSA	Environment disinfection	N/A	No	No	No	Yes	Yes	No

Reference	Country of Research	Setting	Type of Simulation Model	Cost-Effectiveness Analysis	Pathogen	Intervention	Type of HCWs included	Inclusion of Direct HCW-HCW Contact	Inclusion of Direct Patient-Patient Contact	Inclusion of Patient-Visitor Contact	Inclusion of HCW-Patient Contact	Inclusion of Transmission via Contaminated Environment	Inclusion of Interactions Between Settings
		patient rooms											
(Pérez et al., 2017)	The USA	ICU	DES	No	Not specified (Catheter-associated urinary tract infections)	N/A	Nurses	No	No	No	No	No	No
(Shenoy et al., 2017)	The US	Hospital ward	DES	No	MRSA/VRE	N/A	N/A	No	Yes (Roommates)	No	No	No	No
(Shin et al., 2017)	South Korea	Hospital	SD	Yes	MERS	Operational interventions	N/A	No	Yes	Yes	Yes	Yes	No
(Stephenson et al., 2017)	The USA	Hospital*	SD	Yes	Clostridium difficile	Vaccination	N/A	No	No	No	No	No	No
(Wang and Ruan, 2017)	China	Hospital*	Hybrid (SD + stochastic continuous-time Markov chain)	No	MRSA	Hand hygiene, environment disinfection	N/A	No	No	No	Yes	Yes	No
(Luangasanatip et al., 2018)	Thailand	ICU	SD	Yes	MRSA-BSI	Hand hygiene	N/A	No	Yes	No	Yes	No	No

Hospital*: A hospital that lack any further ward structure
N/A: Information is not available

Appendix B. Guidance on Mixing SD and ABM

Table B.1: Detail of the existing theoretical guidance/framework in published papers

References	Concepts	Details
(Shanthikumar and Sargent, 1983)	Hybridizing simulation and analytical methods	Class I – "A model whose behaviour over time is obtained by alternating between independent analytic and simulations models." Class II – "A model in which a simulation model and an analytic model operate in parallel over time with interactions through their solution procedure." Class III – "A model in which a simulation model operates in a subroutine way for an analytic model of the total system." Class IV – "A model in which a simulation model is used as an overall model of the total system, and it requires values from the solution procedure of an analytic model representing a portion of the system for some or all of its input parameters."
(Bennett, 1985)	Comparison, Enrichment and Integration (Apply to mixed operation	Comparison: Using different methods wholly separately to solve different aspects of a problem which either method adopted on its own could not handle. Enrichment: Using elements of one method to enhance the main method. Integration: Treating the methods on an equal footing and combining elements of each method to create an entirely new hybrid method.

References	Concepts	Details
	research (OR) methodologies)	
(Kim and Juhn, 1997)	Multi-Agent Dynamics	They constructed a hybrid model with the principles of SD and using array variables to represent the individual agents. As causal structures that relate many intelligent agents in most models of multi-agent systems are simple, array variables in SD can be used to incorporate several similar agents without cluttering these casual structures.
(Parunak et al., 1998)	Individuals and observables	Observables are measurable features of interest associated with the collection of individuals as a whole or with separate individuals. Individuals' actions can affect the values of observables. Individuals' behaviours inform interactions among themselves; and equations relate observables with one another. An agent in an ABM can be modelled using SD. The evaluation of equations over particular observables can drive behavioural decisions within an individual agent. An agent can be part of a bigger SD model. An agent with global view which can access system-level observables and make them visible to local agents can drive an ABM with system level information System elements including "equations describing observables" and "individual behaviors" can be decomposed into SD and ABM respectively for designing a hybrid model.
(Akkermans, 2001)	The Renga approach	Using SD to model the logic of individual agents but not specifying how the agents interact with each other
(Schieritz and GroBler, 2003)	Mental models or internal schemata	They presented a hybrid model using SD to model the internal decision logic or cognitive structure of the agents in an ABM. The internal structure of an agent is considered as its *mental model* in SD terms or *schemata* in ABM terms.

References	Concepts	Details
(Borshchev and Filippov, 2004)	Multi-Paradigm Model architectures	SD sub-models inside discretely communicating agents. Many hybrid simulation models on supply network use this design (Schieritz and GroBler, 2003). E.g., SD is used to model the processes inside a company whereas the communication among the companies is modelled using ABM. Agents such as people and households in an ABM live in an environment such as housing, jobs and infrastructure whose dynamics is modelled using SD.
(Lorenz and Jost, 2006)	“Alternative environment” in ABM	Using SD structures to create entities for an ABM. Using SD to create a dynamic environment for agents of an ABM. Three distinguishing categories of environments in an ABM include: - A “zero” environment: Environment does not interact with agents but may hold some aggregate parameters for use in an ABM. SD structure is not needed. - A “passive’ environment: Environment does not have any inherent dynamics but contains some variables or structures with which agents interact. SD structure is not needed. - An “active” environment: SD is used to model the environment’s own dynamics. Environment is, therefore, an active part of the ABM.
(Bobashev et al., 2007)	Hybrid threshold model	A hybrid threshold model switches between SD and ABM descriptions at a threshold. The concept of this design originates from the application of the law of large numbers and central limit theorem when the number of active agents in an ABM is large and reaches a threshold. In this case, aggregating the behaviour of similar agents and modelling their behaviour through mean-field approximations should be possible. Conversely, when the number of agents becomes small, the SD model is switched back to the ABM to avoid artifacts possibly caused by the SD.

References	Concepts	Details
(Martinez-Moyano et al., 2007)	Three types of interaction between modules, relating to different modes of usage of the hybrid model	Scenario exploration: The domain ABM is run first and its results are passed onto the SD model. Intertwined models: The domain AB and SD models potentially exchange information and alternate. Crisis response: The domain ABM is run first using empirical input data and results it produces are sent to the SD model.
(Chahal and Eldabi, 2008)	three-layer framework of "formats".	Hierarchical format: This design consists of two separate models where one model uses the outputs of the other as its inputs. Process - Environment format: This design also consists of two models where a DES model is embedded inside a SD model. The two models run in parallel and exchange information and data at runtime in a cyclic manner. Integration format: This design combines two simulation modelling methods into one single model without explicit distinction between discrete and continuous components.
(Brailsford et al., 2010)	The "Holy Grail"	The "Holy Grail" refer to a fully integrated hybrid simulation models which combines the benefits and virtues of each simulation modelling method with no distinction or demarcation between the DES part and the SD part.
(Lättilä et al., 2010)	Methods for creating a hybrid	The journal proposed five approaches to create a hybrid simulation model - Low-level programming - SD programming

References	Concepts	Details
	simulation model	- SD with middleware - Hybrid toolset - Constructing simulation software
(Vincenot et al., 2011)	The spatial structure of AB-SD models	Case 1: Individuals interacting within a single SD model. Case 2: SD sub-models embedded in individuals. Case 3: Individuals interacting with spatially disaggregated instances of a SD model. Case 4: Components swapping between the SD and the AB paradigm.
Swinerd and McNaught (2012 and 2014)	Sequential, interfaced and integrated classes	Sequential class: The output of a module is used as input for another module which produces the final model output. Each model is implemented in a different simulation modelling method. Interfaced class: Modules which are modelled using different simulation modelling methods can be run concurrently or sequentially but they do not directly affect one another. The final model output is the combination of the output of each module. Integrated class: The output of modules and model are fully integrated. Connections between any of them provides the opportunity for a continuous flow of information and feedback. Three designs which belong to the integrated class include: - The SD model is within an agent ("agents with rich internal structure"). - A stock in a SD model bounds the behaviour of agents ("stocked agents").

References	Concepts	Details
		- An emergent property of an ABM affects a parameter in the SD model ("parameters with emergent behaviour").
(Chahal et al., 2013)	Cyclic or parallel interactions	Cyclic interaction: SD and DES models do not interact during run time, but only after individual model completes its own run. Parallel interactions: SD and DES models are run in parallel whilst exchanging information during run time.
(Onggo, 2014)	Modules, module interface and updating rules	A hybrid simulation model consists of multiple modules modeled by different simulation methods. The module interfaces define the information that will be exchanged between them. The updating rules determine how the information sent by one module influences other modules.
(Mustafee et al., 2017)	Domain-specific hybrid simulation	The proposed domain-specific hybrid simulation approach involves the following three processes - Step 1: Identify relevant levels of abstraction or subclasses of the considered domain. - Step 2: Horizontal paradigm linking involves in coupling abstraction levels and appropriate simulation modelling methods. - Step 3: Vertical paradigm linking defines the connection between different subclasses or the interaction between different simulation modelling methods.
(Wallentin and Neuwirth, 2017)	Dynamically switching hybrid simulation model	System entities can be represented as agents, stocks, super-agents (stocks embedded in agents), and spatial stocks (stock embedded in cells of a cellular automaton). A static hybrid model combines different representations into a certain SD-ABM configuration. For example, agents represent one entity while stocks represent another entity. By contrast, a dynamic hybrid model offers a design where the model can reversibly switch between two or more alternative configurations.

References	Concepts	Details
(Morgan et al., 2017)	A toolkit of designs for mixing SD and DES	Parallel: A design for combining two or more simulation modelling methods that provide two potential representations of the same system, offering complementary insights of the system. Sequential: A design for combining two or more simulation modelling methods that can capture different parts/behaviors of the same system or at different levels of detail. The simulation models that are hybridized interact with one another in a way that information or data is passed from one model to the next model. Enrichment: A design for combining two or more simulation modelling methods to form a single model in which one method remains the core method that defines the system and other enhancing methods are transferred into and embedded within the primary method. Interaction: A design for combining two or more simulation modelling methods in which individual models can operate independently but work together to capture interactive influences within the system. Integration: A design for combining two or more simulation modelling methods to form a single model which presents one coherent and concise view of the system, and captures interactive influences within the system.

Appendix C. Interview Outline

Participant Information Sheet (Consent for Interview)

Participant Information Sheet (Consent for Interview)

[FOR USE WITH STANDARD PRIVACY NOTICE FOR RESEARCH PARTICIPANTS]

Name of department: Management Science (Strathclyde Business School)
Title of the study: Hybrid systems simulation modelling: controlling healthcare-associated infections

Introduction
I am Le Khanh Ngan Nguyen, a PhD student in Management Science at the University of Strathclyde in Glasgow. I am doing research on healthcare-associated infections (HAIs), which is a critical public health issue. This sheet provides you with information about, and invites you to be part of, this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

What is the purpose of this research?
HAIs pose a serious risk for patients and providers as they cause increased morbidity and mortality, prolonged length of stay in healthcare facilities, increased multi-drug resistant organisms and tremendous psychological and financial burdens to patients, their families, and the healthcare system. Implementing a combination of strategies to control HAIs without understanding their potential outcomes, knock-on effects, and overlapping impacts and effects, including unexpected ones, can be costly. The objective of this research is to develop a simulation model to evaluate the effectiveness of interventions to prevent and control HAIs in the context of the Scottish healthcare system.

Do you have to take part?
It is the participant's decision whether to take part in the research or not (i.e. participation is voluntary), and refusing to participate or withdrawing participation will not affect any other aspects of the way a person is treated.

What will you do in the project?
The research will involve an interview which will only take 30-45 minutes of your time. The interview will be undertaken via an online-platform such as Microsoft Teams and Zoom and on a date and time that suits you best.

Why have you been invited to take part?
As the research aims to find the best practice for infection prevention and control in Scottish long-term care facilities, it involves interviewing different stakeholders (e.g., healthcare workers, managers, and infection control team members) to achieve in-depth understanding of current infection control practice in long-term care facilities and their thoughts regarding the challenges in implementing and complying to IPC strategies.

What information is being collected in the project?
In order to understand the transmission of HAIs in your healthcare setting, information including, but not limited to, your daily activities of care delivery to patients, current IPC strategies and policies, and factors influencing your compliance to IPC practice will be collected in the project.

Who will have access to the information?
We will not share the identity of the facilities and the individuals participating in the research. The information that we collect from this research project will be kept confidential, and no-one but the researchers will be able to access it.

Where will the information be stored and how long will it be kept for?
Personal information will only be retained until the end of my PhD studies. Anonymous research data will be retained indefinitely by depositing it in a suitable data repository.

Thank you for reading this information – please ask any questions if you are unsure about what is written here.

What happens next?
If you would like to participate in this project, I kindly ask you to sign a consent form to confirm this. If you need to find out more about this project, please do not hesitate to contact myself.

Your interview will be recorded. You have the right to put your own name to your interview recording and transcript or, if you prefer, to be anonymous. In order to use information you provide in any publications, we must ask you to sign a Recording Agreement Form. We will not use your name or other identifying information in publication. Please also read our Data Protection Privacy Notice at the following link: https://www.strath.ac.uk/whystrathclyde/universitygovernance/accesstoinformation/dataprotection/.

We ask that you consider these issues and if you agree to be interviewed, we ask you to complete a Recording Agreement Form prior to the interview taking place. This protects your legal rights, ensures that your interview recording and transcript are properly and professionally archived and looked after and enables us as researchers to utilize your information in our research provided you agree. A copy of your interview will also be sent to you (securely under arrangements agreed with yourself) for checking, giving you the opportunity to indicate if you wish anything to be taken out or changed from your interview. This procedure is in line with your legal rights and we operate strictly to the moral, ethical and legal requirements laid down by the UK Oral History Society.

Researcher contact details:
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The University of Strathclyde is a charitable body, registered in Scotland, number SC015263

Chief Investigator details:
This research was granted ethical approval by the University of Strathclyde Ethics Committee.

If you have any questions/concerns, during or after the research, or wish to contact an independent person to whom any questions may be directed or further information may be sought from, please contact:

Secretary to the University Ethics Committee
Research & Knowledge Exchange Services
University of Strathclyde
Graham Hills Building
50 George Street
Glasgow
G1 1QE

Telephone: 0141 548 3707
Email: ethics@strath.ac.uk

Consent Form for Interview

Name of department: Management Science (Strathclyde Business School)
Title of the study: Hybrid simulation modelling in healthcare-associated infection prevention and control

- I confirm that I have read and understood the Participant Information Sheet for the above project and the researcher has answered any queries to my satisfaction.
- I confirm that I have read and understood the Privacy Notice for Participants in Research Projects and understand how my personal information will be used and what will happen to it (i.e. how it will be stored and for how long).
- I understand that my participation is voluntary and that I am free to withdraw from the project at any time, up to the point of completion of interview, without having to give a reason and without any consequences.
- I understand that I can request the withdrawal of some personal information from the study, and that researchers will comply with my request. This includes the following personal data:
    - audio recordings of interviews that identify me;
    - my personal information from transcripts.
- I understand that anonymised data (i.e. data that do not identify me personally) cannot be withdrawn once they have been included in the study.
- I understand that any information recorded in the research will remain confidential and no information that identifies me will be made publicly available.
- I consent to being a participant in the project.

(PRINT NAME)	
Signature of Participant:	Date:

Interview Questions

Role and Responsibility

(Questions with * are the questions that we added based on reflection of some initial interviews)

1. Could you please describe your position in this care home and the responsibilities you have?
2. How long have you been working in this care home?
3. What is your employment contract type in this care home? (E.g., full-time/part-time/casual)
4. What qualification(s)/training course(s) have you taken to do this job?
5. *Are you also working in other care homes? (If yes, how many other care homes?)
6. *Did you work in other care homes before COVID-19?
7. Are you working in other healthcare settings? (If yes, which settings? For how long? Your roles and responsibilities in these settings?)

8. Did you work in other healthcare settings before COVID-19? (If yes, which settings? For how long? Your roles and responsibilities in these settings?)
9. *Have you worked in other positions in care homes?
10. How many hours do you do per week in this care home (and others, if any)?
11. What is your roster in this care home?

General Operation

12. How many units are there in this care home?
13. How many beds and residents per unit are there?
14. *Do staff members from one unit usually go to the other units to work or cover someone else? (How frequently and under what circumstances does this happen?)
15. *Is there a group of staff members shared between units? If yes, could you explain how this sharing of staff works?
16. Could you explain how a working day is split into shifts and what the staffing level for each shift is? (E.g., the number of nurses, nursing/care workers, and other staff members per shift per unit)
17. Apart from nurses and nursing/care workers, who else can provide direct care to residents, and what types of care do they provide?
18. How are nursing/care staff members assigned to provide care to residents? (E.g., each resident has a key nurse and nursing/care worker and other workers can also provide care to them throughout the day)
19. *Are nurses and other nursing/care workers allocated into teams within a unit that cares for a group of residents? If yes, what is the average team, and how many residents does each team care for?
20. *Is it correct to say that any nurse or nursing/care worker can care for any resident in the same unit?

Interactions

21. How are residents assigned to you and other colleagues (in your team/unit)?
22. *Is your work confined in one unit (for one shift or shifts on different days)? Do you need to carry out your duty across the units?
23. How many residents do you provide care per shift? (Day/night shifts)
24. How do you describe your typical working day in this care home?
25. What types of direct care do you provide to the residents?
26. What other duties that do not involve direct care do you carry out?

27. How do you describe a typical day of the residents staying at this care home?
28. How have residents' daily routines and life changed since the pandemic started?
29. How often do residents come into contact with other residents? (Before and after COVID-19)
30. *Does a resident often interact with a particular group of other residents?
31. *How often do residents in a unit interact with residents in other units?
32. Do family visitors often come individually or in a group? (If it is the latter case, how many people are there approximately in a group? (E.g., 2-3 visitors per group))
33. How often do you come into contact with visitors? (E.g., discussing care plans with residents' family members, casual conversations in residents' rooms)
34. How many other colleagues do you often come into contact with per day/night shift? (E.g., shift change meetings, sharing information about residents, de-briefing, chatting during a break)

IPC

Managers/Deputy Managers

35. How has the COVID-19 pandemic impacted this care home?
36. What changes in the IPC protocol have been made in this care home to prevent and control COVID-19? (E.g., closure to admissions from community/hospitals, restriction on visitors, mandatory testing before admission) (It would be helpful if you could provide the timeline for these changes)
37. What challenges have you experienced when implementing such changes?
38. *What challenges have you experienced in implementing IPC interventions in this care home before the pandemic?
39. What support for IPC practice (E.g., advice, guidance, staff training) has this care home received before and after the pandemic started?
40. What support would you wish to receive to facilitate the implementation of IPC interventions during the pandemic?

Care-home Staff

41. *How have IPC interventions implemented in this care home been communicated to you before and after COVID-19?
42. From whom would you seek advice on IPC issues? (E.g., IPC team/key worker, manager, NHS)
43. How has your IPC practice changed since the pandemic started?

44. What changes in the IPC protocol have been made in this care home to prevent and control COVID-19?
45. What challenges have you experienced when these changes in IPC protocol are implemented?
46. What support have you received relevant to IPC practice during the pandemic?
47. What support would you wish to receive to facilitate your IPC practice during the pandemic?
48. Do you have any suggestions about how IPC could be improved in this care home?
49. *(If the interviewee is working in other healthcare facilities) What are the differences in IPC between this care home and other facilities where you are working?

Staff Sharing

Managers/Deputy Managers (Follow-up Interviews)

50. Could you describe how the care home uses bank/agency staff?
    a. How many bank/agency staff members per day/week on average does the care home require?
    b. How frequently does the care home need to use bank/agency staff?
    c. What shift (day/night) does the care home often have to use bank/agency staff?
    d. Under what circumstances does the care home need to use additional bank/agency staff?
    e. What does the care home do if it could not have the sufficient number of bank/agency staff members it requires?
51. How have the demand and use of bank/agency staff changed since the pandemic began? What are the main reasons explaining such changes?
52. How does the care home get bank/agency staff? (E.g., agencies, contractors)
53. When requesting bank/agency staff, does the care home specify any requirements? (E.g., someone has worked in this care home before, someone with certain skills)

Bank/Agency Staff (Follow-up Interviews)

54. How do you receive care homes' requests? (E.g., via agencies, self-employed)
55. If he/she is employed by a bank staff agency,
    a. How many agencies do you work for?
    b. How do you receive bookings? (E.g., via apps, emails, phone)
56. How do you decide to accept or decline a booking? (e.g., location, familiarity)
57. How many different care homes do you work in per day?

58. How many different care homes do you usually work in per week?
59. How has the pandemic affected your job?

Bank Staff Agencies

60. Could you describe how the booking system works?
    a. How do you receive care homes' bookings?
    b. How do you decide on assigning bank staff to these bookings? (E.g., based on the proximity, availability, and ensuring that bookings are allocated to staff as equally as possible)
61. How has the pandemic affected your agency?
62. How has the pandemic changed the way that the booking system works?
63. What are the IPC measures that your agency has required bank/agency staff to adhere to during the pandemic?

Appendix D. Review of Hybrid SD-ABM Models in Various Application Areas

Table D.1: Overview of hybrid SD-ABM models in various application areas excluding hybrid models in HAIs

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
(Asif et al., 2016)	Supply chain	Consider complex connections between individual consumer behaviour and overall social dynamics	Stock levels affect agents' behaviours Aggregated measures of agents affect flows
(Baki et al., 2012)	Management of urban water systems	Use ABM to zoom in on specific socio-economic sub-sections of the urban water system modelled in SD	Stock levels affect agents' behaviours Agents' behaviours affect flows
(Barbosa and Azevedo, 2019; Barbosa and Azevedo, 2018)	Supply chain	Model rich internal dynamics of different agents in a supply chain network	Agents' behaviours affect flows Stock levels define agent-specific state variables
(Bergman et al., 2008)	Transitions	Capture interactions of individual agents and sub-systems, as well as cumulative effects on system structures	Aggregate measures of agents affect flows Agents' behaviours affect flows Stock levels define agent-specific state variables
(Block and Pickl, 2014; Block, 2016)	Human resources management	Capture both the macro and micro views of the system	Stock levels affect agents' behaviours Agents' behaviours affect flows
(Caiani et al., 2016; Caiani et al., 2019)	Economics	Model internal dynamics of agents playing in the economic dynamics	Agents' behaviours affect flows Stock levels define agent-specific state variables
(Cernohorsky and Voracek, 2012a)	Public health policy	Cope with centralized aspects of markets, such as institutions and regulation, as well as decentralized components of the markets, such as patients	Stock levels affect agents' behaviours Agents' behaviours affect flows

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
(Cernohorsky and Voracek, 2012b)	Health services	Develop a model that can serve both policy makers and hospital managers	Stock levels affect agents' behaviours Agents' behaviours affect flows
(Chen and Desiderio, 2020)	Economics	Capture the centralized and decentralized aspects of job markets	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Choong and McKay, 2014)	Supply network	Model complex behaviour of each agent in a network	Stock levels define agent-specific state variables Agents' behaviours affect flows
(Darabi et al., 2012)	Transportation science	Capture both feedback loops inside the maritime system and interactions between entities	Aggregate measures of agents affect flows Stock levels affect agents' behaviours
(Djanatliev and Meier, 2016)	Health services	Capture different views of a system	Generating a crowd of agents from stocks Stock levels affect agents' behaviours
(Elia et al., 2016)	Waste collection	Not discussed	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Flynn et al., 2014)	Workforce	Understand the link between individual choice behaviours to workforce supply and demand dynamics	Stock levels bound aggregated measures of agents Aggregated measures of agents affect flows
(Gao et al., 2014)	Non-communicable disease modelling	Secure computational economies while supporting upstream intervention investigation	Generating a crowd of agents from stocks
(Glock et al., 2016)	Large socio-technical large infrastructure systems	Model different sub-systems with their own dynamics that require different levels of abstraction in a more natural way Address and satisfy different views of stakeholders on the system	Agents' behaviours affect flows Stock levels affect agents' behaviours Aggregated measures of agents affect flows

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
(Goh and Askar Ali, 2016)	Construction safety management	Allow a more natural presentation of the complex dynamics in construction activities Using SD to model the cognitive processes and physiological aspects of agents	Stock levels affect agents' behaviours Agents' behaviours affect flows
(Haase et al., 2012)	Urban policy and planning	Integrate social science dimensions and consider urban systems, characterized by causal relationships and feedback, in a spatially explicit fashion.	Stock levels bound aggregated measures of agents Aggregated measures of agents and their behaviours affect flows
(Jo et al., 2015)	Project management	The SD part elucidates the relationships among system elements that constitute project's benefits and costs, while the ABM part depicts users' emergent behaviour with their heterogeneity.	Aggregated measures of agents affect flows Stock levels affect agents' behaviours
(Kieckhäfer et al., 2009)	Product strategy decisions	Model actors with individual goals in the automobile market, whose behaviour is influenced by a dynamic, uncertain macro-economic environment	Aggregated measures of agents affect flows Stock levels affect agents' behaviours
(Kieckhäfer et al., 2014)	Market share evolution of sustainable transport	Study the interdependencies between the evolution on the macro level and (1) individual replacement purchases as well as (2) heterogeneous consumer behaviour	Stock levels affect agents' behaviours Aggregated measures of agents affect flows
(Kolominsky-Rabas et al., 2015; Djanatliev et al., 2012b; Djanatliev and German, 2013b; Djanatliev et al.,	Health technology assessment	Present interdisciplinary processes in a more natural way Model the system in a more natural way Harmonize interdisciplinary expertise of experts whose views may be rooted in either SD or ABM Optimize trade-off between the computational and the predictive performance of the model	Aggregated measures of agents affect flows Generating a crowd of agents using a stock level

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
2012a; Djanatliev and German, 2013a)			
(Łatuszyńska and Fate, 2019)	Public management	Capture both macro- and micro-aspects of the phenomenon of poverty	Stock levels affect agents' behaviours Aggregate measures of agents affect flows
(Mackay et al., 2013)	Health services	Capture different levels of abstraction of the complex healthcare system	Stock levels affect agents' behaviours
(Martin et al., 2020)	Ecology	Model different parts of a multi-disciplinary problem	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Mazhari et al., 2009)	Energy generation capacity planning	Provide richer insight into the interdependences between the behaviours of a system at a macro level and the behaviours of multiple agents involved at the micro level Contribute to explaining why a strategic policy may fail to improve operational performance Offer flexibility to model different operational circumstances or intervention scenarios explicitly	Agents' behaviours affect flows
(Meijers et al., 2019)	Economics	Assess how the behaviours of individuals affect the macroeconomic business cycle	Agents' behaviours affect flows Stock levels define agent-specific state variables Aggregate measures of agents affect flows
(Mostafavi et al., 2014)	Infrastructure systems management	facilitate incorporation of uncertainties and complex adaptive behaviours of stakeholders in the analysis of infrastructure policies	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Muravev et al., 2021)	Transportation and supply chain	Capture both feedback loops inside the system and interactions between entities	Aggregate measures of agents affect flows Stock levels affect agents' behaviours
(Nikolic et al., 2013)	Water resources management	Capture both feedback system structure and spatial dynamics of the water resources problems	Agents' behaviours affect flows

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
			Stock levels define agent-specific state variables
(Páez-Pérez and Sánchez-Silva, 2016)	Infrastructure development	Model different sub-systems with their own dynamics that require different levels of abstraction in a more natural way Address and satisfy different views of stakeholders on the system	Aggregated measures of agents affect flows Stock level bounds aggregated measures of agents
(Robledo et al., 2013)	University management	Support decision-making at strategic and operational levels	Stock levels bound aggregated measures of agents Aggregated measures affect flows
(Ruiz et al., 2016)	Public policy management	Incorporate social and psychological factors into the feedback dynamics of a public policy	Agents' behaviours affect flows
(Shafiei et al., 2013)	Supply chain	Capture the combination of heterogeneous and homogenous components observed in the transportation system Lead to a satisfying computation time and accuracy	Stock levels affect agents' behaviours Aggregated measures of agents affect flows
(Swinerd and McNaught, 2015; Swinerd and McNaught, 2014)	Technology forecasting	Exploit the complementary benefits available from using different simulation methods Capture coherently the detail of individual and aggregate measures within a system	Aggregated measures of agents affect flows Stock levels define agent-specific state variables Agents' behaviours affect flows
(Taghikhah et al., 2021)	Supply chain	Allow different levels of abstractions to interact with each other and increase the flexibility of the model for users	Stock levels affect agents' behaviours

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
(Verburg and Overmars, 2009)	Land use	Capture the macro-level dynamics of land use with spatial variations between local areas	Stock levels bound aggregated measures of agents
(Viana et al., 2012)	Health and social care	Use the 'best tools for the job' rather than rigidly sticking to one paradigm	Stock levels define agent-specific state variables Agents' behaviours affect flows
(Vincenot and Moriya, 2011)	Infectious disease dynamics	Model spatial interactions in a network of agents with rich internal structures	Network topology affects flows Stock levels define agent-specific state variables
(Wallentin and Neuwirth, 2017)	Ecology	Optimise trade-offs between the computational and the predictive performance of a model Present systems in a more natural way	Agents are generated from stocks Aggregated measures of agents affect flows
(Wang et al., 2013)	Supply chain	Perform strategic analysis that needs the flexibility to model different operational circumstances	Stock levels affect agents' behaviours Aggregated measures of agents affect flows
(Wang et al., 2013)	Supply chain	Capture multiple aspects of the system	Stock levels affect agents' behaviours Agents' behaviours affect flows
(Wang et al., 2014)	Product lifecycle assessment	Refine parts of the aggregated system structure where necessary	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Wu et al., 2010)	Technological innovation risks	Help model stochastic/uncertain elements in casual relationships explicitly by entering variation into the appropriate sources/ decision levels of the model Provide richer insight by capturing parameters with emergent behaviours	Agents' behaviours affect flows Stock levels affect agents' behaviours
(Xu et al., 2016)	Supply chain	Provide a coherent and comprehensive simulation platform that supports hierarchical manufacturing planning and control	Agents' behaviours affect flows Stock levels affect agents' behaviours

Article	Domain	Hybrid simulation use rationale (Inferred/Extracted from the paper)	Interfaces
(Zhao et al., 2011)	Policy evaluation of solar power generation systems	Study strategic policy with consideration of a range of operational circumstances	Stock levels affect agents' behaviours Agents' behaviours affect flows

Appendix E. Supplementary Materials for the ABM Model

ODD Protocol

Purpose and Patterns

See section 8.4.1

Entities, State Variables, and Scales

See 8.4.2

Process Overview and Scheduling

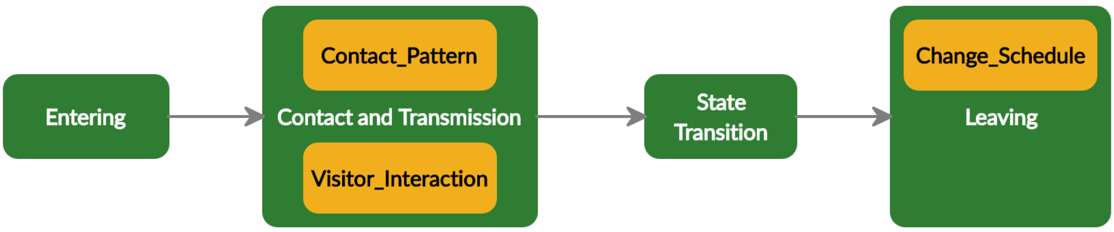

Figure E.1: The process overview and scheduling of the model at each time step

The model includes five actions executed in the following order at each time step (Figure E.1):

Entering:

Resident agents: New residents (AdmissionScheduled is "true") are admitted. Residents could be admitted from either hospitals or the community at equal probabilities based on discussions with care homes. Their ResidentInState is set to "exposed" at the corresponding probability determined by the parameters InfectionPrevalenceHospital and InfectionPrevalenceCommunity; otherwise, it is set to "susceptible". AdmissionScheduled is returned the value "false". The variable Age is drawn from an empirical distribution. Other state variables are reset as in *Initialization*.

Staff agents: If a staff agent's state variable Replaced is "true", it is altered to "false". If its variable AtWork is "false", it is set to "true" and vice versa. Susceptible permanent staff agents whose state variable AtWork is "true" and casual staff can introduce infections into the care home at the probability defined by (InfectionPrevalenceCommunity x RelativePrevalence). Infected staff agents can either be exposed or infectious (asymptomatic or presymptomatic) at equal probabilities.

Contact and Transmission: Agents (residents and staff agents whose state variable AtWork is "true") interact with one another following the corresponding contact rates and the rules described in the sub-model *Contact_Pattern*. Transmission occurs at the transmission probability per contact determined by the parameter InfectionProbability when a susceptible agent comes into contact with an infectious agent. When transmission occurs, the infection status of the susceptible agent (i.e., ResidentInState or StaffInState) changes to "exposed". Interactions between residents and visitors are described in the sub-model *Visitor_Interaction*. Interactions with isolated residents will result in no infection. The order of agents coming into contact with one another is executed randomly within this process.

State Transition:

Exposed → Pre/Asymptomatic: Exposed residents and staff agents transit to either the pre-symptomatic state at the probability pSymptomatic and pStaffSymptomatic respectively, or the asymptomatic state at the end of the period determined by the parameter ExposedTime.

Presymptomatic → Symptomatic: Presymptomatic agents develop symptoms (the infection status changes to "symptomatic") at the end of their pre-symptomatic period defined by the parameter PresymptomaticTime. The probability that a symptomatic agent has severe symptoms is defined by the parameter pSevere and pStaffSevere for resident and staff agents respectively. Symptomatic residents are isolated (Isolation = "true') without delay. Staff agents who develop symptoms have to self-isolate at home in the next time step until they recover and be covered by another staff member described in the sub-model *Change_Schedule*.

Asymp/Symptomatic → Recovered: Asymptomatic and symptomatic agents recover at the probability of (1 – DeathProbability) or (1 – StaffDeathProbability) for residents and staff respectively at the end of their Infectiousness duration corresponding to the severity of their symptoms (i.e. asymptomatic, mild or severe symptoms). Their state of infection changes to "recovered". The variable Isolation of resident agents and SelfIsolation of staff agents are set to "false". If such staff agents' state variable Employment is "casual" implying that they have been covered by Bank/Agency staff, it is changed back to "permanent".

Leaving: The AdmissionScheduled variables of residents who die or leave the care home are set to "true". These agents represent residents admitted to the care home in the next time step to replace those dying or leaving in this time step. Infected residents die at the end of their infectiousness period at the probability DeathProbability specific to their Age. Residents in other states of infection could die or leave the care home for other reasons at the rate determined by the parameter LeavingRate. Infected staff could die at the probability StaffDeathProbability. Permanent staff could leave the care home for non-covid reasons at a rate defined by the parameter StaffTurnover. Staff who die or leave are replaced by new "susceptible" staff agents with other state variables being set as in Initialization.

Design Concepts

See section 8.4.4

Initialization

The number of residents and staff and the operational structure in the base case model are informed by discussions with the manager of a representative care home for older people. The model is initialized with 80 resident agents and 72 staff agents in the base case. The first unit (UnitID = 1) has 40 resident agents and 33 staff agents. The second unit (UnitID = 2) has 40 resident agents and 32 staff agents. A group of seven staff agents are shared between the two units (UnitID = 3). The number of staff agents present in the care home is 16 and 15 for Unit 1 and 2 respectively. All shared staff are on duty. There are two Bank/Agency staff in Unit 1 and one in Unit 2.

The variable Age of residents is drawn from an empirical distribution based on the demographic data of older people adult care homes in North Lanarkshire. Initial values of variables and parameters for the baseline scenario (no intervention) are summarized in Table E.1. In intervention scenarios, interventions start on day 1 and remain for the entire simulated time. How relevant state variables and parameters are altered for each intervention is described in greater details in the sub-model *Intervention.*

Depending on the aims, in some simulations one random resident is exposed to the virus at the beginning of the simulation and others are susceptible. In other simulations, no agents are infected at the beginning of simulation. Instead, infection in the care home occurs through visitor and care worker interactions with the community.

Table E.1: Initial values of entities' state variables and parameters

Variable/ Parameter	**Initial value**	**Sources**
Resident-agent-specific state variables		
unitID	1 for 40 resident agents 2 for the remaining 40 resident agents	Discussions with the manager of a Scottish care home for older people
Age	Drawn from empirical distribution: 18-64 years old: 3% 65-74 years old: 13% 75-84 years old: 39% 84-94 years old: 39% 95 and older: 6%	(ISD, 2018) (Calculated from data for older people care homes in North Lanarkshire)
ResidentInState	“susceptible” with one resident assigned “exposed”	
Severity	0	
AdmissionScheduled	False	
Isolation	False	
Tested	False	

Staff-agent-specific state variables		
unitID	1 for 33 staff agents 2 for the other 32 staff agents 3 for the remaining seven staff agents	
Employment	"casual" for two staff from unit 1 and one staff from unit 2 "permanent" for the rest	Discussions with the manager of a Scottish care home for older people
StaffInState	"susceptible"	
AtWork	True for all causal staff and 14 permanent staff agents from each unit False for the rest	
SelfIsolation	False	
Replaced	False	
Tested	False	

Input Data

A time-series of Covid-19 infection prevalence in Scotland adjusted for undetected cases describes prevalence in the community. We adopted the worse situation that the undetected cases represent 80% of the total cases in the community (Perez-Reche and Strachan, 2021; PHS, 2020). The adjusted prevalence is, therefore, calculated by multiplying the infection prevalence reported by Public Health Scotland by five.

Submodels

Parameters used in the model are described in Table 8.2.

Intervention

Parameter values dependent on interventions are described in Table E.2.

Table E.2: Infection control measures and how model parameters are modified when a measure is adopted

Infection Control Intervention		**Modified Parameter**
Temporary closure to admissions	Closed to admissions	ClosedToAdmission = true;
	Opened to admissions	ClosedToAdmission = false;
Social distancing		The parameter SDCompliance is used to control the compliance rate to the social distancing measure. ContactRateRR and ContactRateSS are reduced by (1 – SDCompliance). Residents in different units do not interact with each other (ContactAcrossUnits = 0).
Testing upon admission		Residents can be admitted after two negative tests (Scottish-Government, 2020c). The probability of identifying true positive after two tests equals to (1 - (1 -TestSensitivity)^2)
Isolation of infected residents		Their state variable Isolation is set to "true". Interactions between isolated residents and other individuals result in no infection at the probability *IsolationEffectiveness*. The model assumes no delay between onset of symptoms and isolation.
Testing of staff		Staff members who are tested have their state variable Tested set to "true". After the time delay from testing to test result determined by the parameter TestDelay, the state variable Tested is set to "false" and infected staff are detected at the probability TestSensitivity and have to self-isolate.
Change of visiting policy		The parameter VisitorsPerDay is changed depending to the care home's visiting policy. The contact rate between staff and visitors (i.e., ContactRateSV) also changes accordingly.
Cohorting		Staff and residents in the same cohort are assigned the same UnitID. Interactions only occur between individuals with the same UnitID. When there are some contacts across cohorts, residents and staff can contact with other residents and staff in any other cohorts at a predefined probability *ContactAcrossUnits*.

Contact_Patterns:

The patterns for interactions between individuals are informed by discussions with the manager and care staffs in a representative care home, in the base case:

- A staff member (UnitID = 1 or 2) can interact with any random staff in the same unit at the rate *ContactRateSS*.
- A staff member (UnitID = 1 or 2) can interact with any random resident in the same unit at the rate *ContactRateRR*.
- A resident can interact with any random resident in the other unit at the probability *ContactAcrossUnits*.
- A staff member in the shared group (UnitID = 3) can interact with any random resident or staff member from any unit at the rate *ContactRateSR* and *ContactRateSS* respectively.
- Isolation of infected residents is assumed to be 100% effective at preventing further transmission (i.e., interactions with isolated residents result in no infection).
- Only staff agents that are present in the care home (the state variable AtWork = true) can interact with other agents.

Visitor_Interaction:

Susceptible residents could acquire the infection when coming into contact with visitors who are asymptomatic. Visitors are not explicitly represented as agents in the model as there is no need to consider visitors at an individual level. The model only considers the transmission from visitors to residents. Whether visitors may acquire the infection from residents or staff in the care home and how they spread it elsewhere are not within this model's scope. In each time step, the number of infectious visitors that come into contact with each susceptible resident are drawn from a Poisson distribution with a mean that equals to (VisitorsPerDay x InfectionPrevalenceCommunity). Similarly, the number of infectious visitors that interact with a staff member are drawn from a Poisson distribution with the mean of (ContactRateSV x InfectionPrevalenceCommunity). Transmission of such contacts occurs at the probabilities InfectionProbabilityRV and InfectionProbability respectively.

Change_Schedule:

A staff agent who develops symptoms and self-isolates will be covered by another staff member. Its state variable SelfIsolation is set to “true”. The replaced staff agent is randomly chosen from the corresponding staff pool including staff agents that have the same UnitID, are not already on duty (AtWork = false) or in self-isolation (SelfIsolation = false), and have not been scheduled to replace someone else (Replaced = false). The state variables Replaced of both replacing and replaced agents are altered to “true”. If none of staff agents in the pool satisfies these conditions, the agent’ Employment is set to “casual”.

Statistical Analyses

Table E.3: Summary of statistics of the cumulative number of infected residents after 90 days in different intervention scenarios

Intervention	***Mean***	***Median***	***Interquartile range***
Inter0	74	75	70 – 79
Inter1	53	53	49 – 57
Inter2	50	50	47 – 53
Inter3	42	43	39 – 46
Inter4	42	42	38 – 46
Inter5	53	53	49 – 57
Inter6	32	32	28 – 36
Inter7	31	31	27 – 36
Inter8	29	29	25 – 33
Inter9	30	30	26 – 33
Inter5 (every day)	52	52	48 – 55
Inter6 (14 days)	44	44	40 – 48
Inter6 (20 days)	47	47	43 – 51
Inter6 (30 days)	50	50	46 – 54
Inter6 (compliance 75%)	38	38	34 – 42
Inter6 (compliance 50%)	43	43	39 – 48
Inter6 (compliance 25%)	49	49	46 – 53

Table E.4: The results of hypothesis testing for the difference in mean cumulative numbers of infected residents after 90 under different intervention strategies using Welch's t-test (Bonferroni correction)

Interventions for hypothesis testing		***Welch's t-test results***			
		Outcomes after 90 days		***Outcomes after 180 days***	
Intervention 1	***Intervention 2***	***p-value adjusted (2-tailed)***	***95% CI of the difference***	***p-value adjusted (2-tailed)***	***95% CI of the difference***
Inter0	Inter1	< 2.2E-16	20.4 , 22.4	< 2.20E-16	27.6 , 30.3
Inter1	Inter2	2.1E-07	1.9 , 3.8	3.9E-08	2.3 , 4.4
Inter2	Inter3	< 2.2E-16	6.8 , 8.6	< 2.20E-16	7.0 , 9.0
Inter3	Inter4	1.0	-0.7 , 1.1	1.0	0.0 , 1.9
Inter1	Inter5	1.0	-0.5 , 1.3	1.0	-0.9 , 1.4
Inter4	Inter6	< 2.2E-16	9.4 , 11.2	< 2.20E-16	10.1 , 12.0
Inter1	Inter6	< 2.20E-16	20.1 , 22.0	< 2.20E-16	22.4 , 24.5
Inter6	Inter7	1.0	-0.1 , 1.8	1.0	-0.3 , 1.7
Inter6	Inter8	5.4E-05	2.0 , 3.9	8.1E-07	2.1 , 4.1
Inter8	Inter9	1.0	-1.4 , 0.3	1.0	-1.6 , 0.2
Testing intervals					
Inter1	Inter5 (every day)	1.0	0.3 , 2.2	1.0	-0.1 , 2.1
Inter1	Inter6 (14 days)	< 2.2E-16	8.5 , 10.4	< 2.20E-16	10.2 , 12.3
Inter1	Inter6 (20 days)	< 2.2E-16	5.0 , 6.8	< 2.20E-16	6.4 , 8.4
Inter1	Inter6 (30 days)	7.9E-07	1.8 , 3.7	3.8E-12	3.0 , 5.1
Inter2	Inter6 (30 days)	1.0	-1.0 , 0.8	1.0	-0.3 , 1.7
Compliance to routine testing					
Inter1	Inter6 (compliance 75%)	< 2.2E-16	13.8 , 15.8	< 2.20E-16	15.6 , 17.7

Interventions for hypothesis testing		***Welch's t-test results***			
		Outcomes after 90 days		***Outcomes after 180 days***	
Inter1	Inter6 (compliance 50%)	< 2.2E-16	8.9 , 10.9	< 2.20E-16	10.2 , 12.4
Inter1	Inter6 (compliance 25%)	1.7E-14	3.0 , 4.9	< 2.20E-16	4.0 , 6.0

Additional Plots of Modelling Results

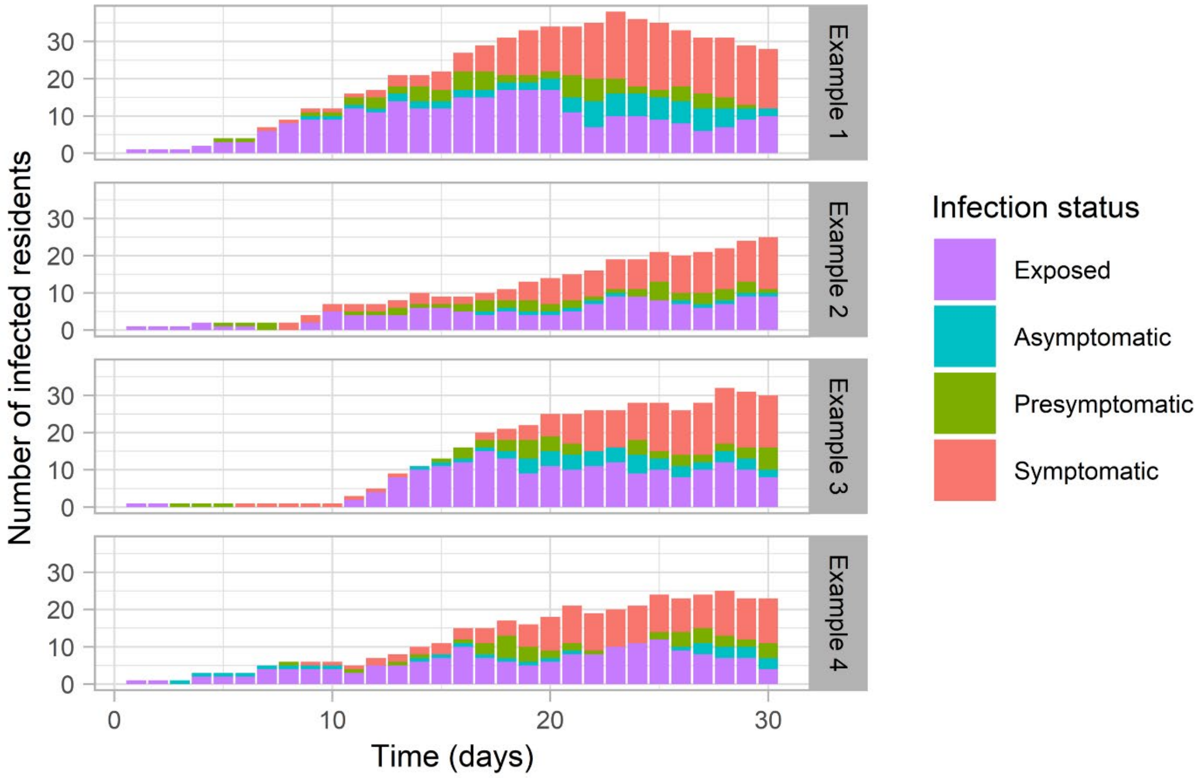

Figure E.2: Four simulation examples of prevalence of infected residents in different infection states over time

No intervention is implemented (Inter0) using base case parameters. This figure displays variations of data due to stochastic uncertainty of interactions within the care home and disease progression; parameter uncertainty was not considered in this figure.

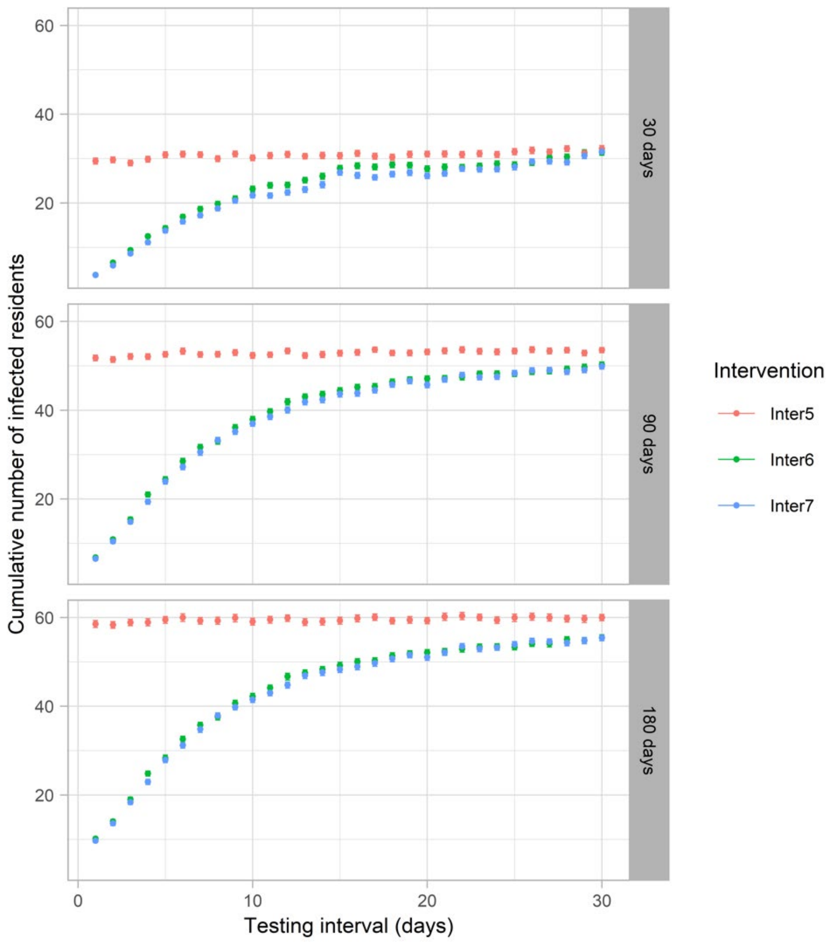

Figure E.3: Impact of different testing intervals in routine testing scenarios on the cumulative number of infections after 30, 90, and 180 days

(Inter5: Inter1 + Weekly testing for residents; Inter6: Inter1 + weekly testing for staff; Inter7: Inter1 + weekly testing for staff and residents; Inter8: Inter6 + isolation upon admission; Inter9: Inter7 + isolation upon admission)

Table E.5: Percent of simulations in which an outbreak occurs 30, 60, and 180 days after the simulation starts. The results presented are for care homes with different capacities in reference intervention and weekly staff testing scenarios (1,000 runs for each scenario). Base case values are used for other parameters.

Population Size (residents)	**Percent of simulations with the presence of an outbreak (%)**					
	Reference Intervention			**Weekly Staff Testing**		
	Infection probability per contact					
	0·005	**0·02**	**0·05**	**0·005**	**0·02**	**0·05**
	After 30 days					
10	0·1	1·1	1·9	0·2	0·3	1·1
20	0·3	2·2	4·8	0·2	0·8	3·2
30	0·3	3·4	6·1	0·3	2·3	5·0
40	0·4	3·7	10·4	0·3	2·6	5·2
50	0·7	5·3	13·8	0·3	2·7	7·1
60	1·2	6·3	15·1	0·8	3·7	10·0
70	1·8	7·5	16·7	0·9	4·1	10·8
80	1·9	9·2	20·1	1·0	5·1	12·1
90	1·9	9·7	22·2	1·2	5·3	15·9
100	2·6	12·4	24·7	1·3	6·5	14·0
	After 60 days					
10	4·2	21·5	42·6	1·5	9·1	23·1
20	8·5	42·5	65·0	2·0	16·5	43·0
30	12·2	57·0	81·0	3·4	27·7	53·8
40	20·6	69·5	88·8	6·0	37·1	63·2
50	23·1	75·8	94·0	9·9	45·7	73·5
60	32·9	83·8	97·0	12·9	53·6	82·4
70	38·5	89·5	98·6	15·2	57·9	86·9
80	41·9	91·9	99·0	17·4	63·7	90·4
90	48·2	95·0	99·6	22·1	69·9	92·9
100	53·8	96·1	99·5	22·2	71·7	95·0
	After 90 days					
10	11·4	52·7	80·4	4·2	24·6	53·0
20	26·0	82·5	96·1	7·0	45·4	80·3
30	41·0	92·0	99·5	13·4	62·6	89·4
40	52·8	97·3	99·7	20·5	76·4	95·2
50	65·0	99·4	100·0	29·4	82·5	97·4
60	74·5	99·7	100·0	34·6	88·8	99·4
70	80·4	100·0	100·0	41·8	93·8	99·8
80	85·7	100·0	100·0	46·0	95·5	99·9

90	89·5	100·0	100·0	55·0	96·9	100·0
100	93·2	100·0	100·0	59·5	98·7	100·0
			After 180 days			
10	29·3	91·7	99·7	12·0	55·6	88·1
20	59·9	99·7	100·0	25·6	84·3	99·2
30	81·5	99·8	100·0	38·9	95·8	99·9
40	90·7	100·0	100·0	53·3	98·3	100·0
50	96·9	100·0	100·0	66·6	99·5	100·0
60	98·5	100·0	100·0	73·4	99·9	100·0
70	99·2	100·0	100·0	83·6	100·0	100·0
80	99·7	100·0	100·0	86·7	100·0	100·0
90	99·9	100·0	100·0	92·6	100·0	100·0
100	100·0	100·0	100·0	95·1	100·0	100·0

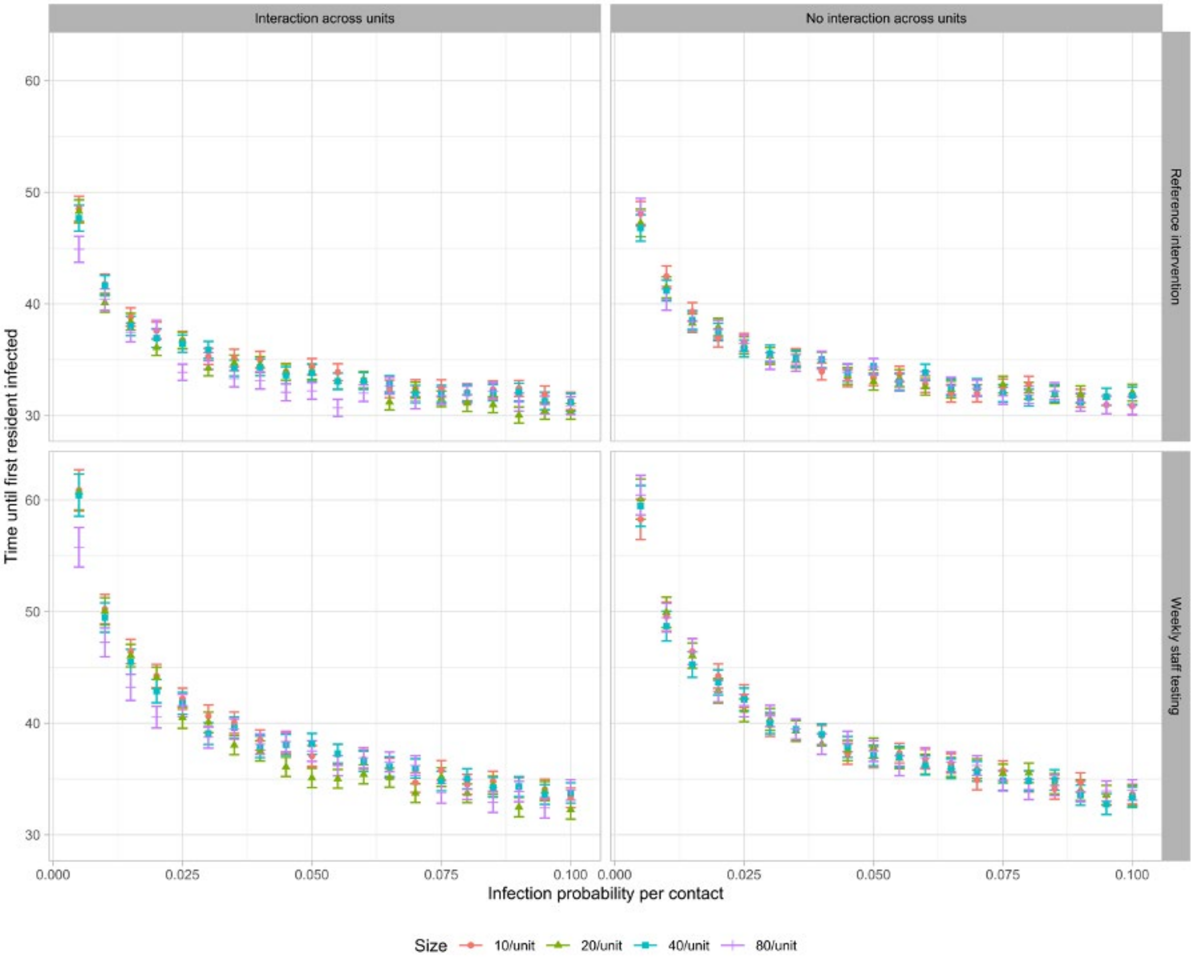

Figure E.4: Impact of unit size on the elapsed time until the first resident is infected

The impact of splitting the care home with size of 80 residents into one, two, four, and eight units with 80, 40, 20, and 10 residents per unit respectively on the elapsed time until the first resident is infected across a range of values of infection probability per contact in the reference intervention and weekly staff testing scenarios. Interactions of residents and staff across units of the care home occur at zero and 20% of total contacts for the "no interaction across units" and "interaction across units" scenarios respectively. Points represent the mean values of 1000 simulations; error bars represent 95% CIs of the means.

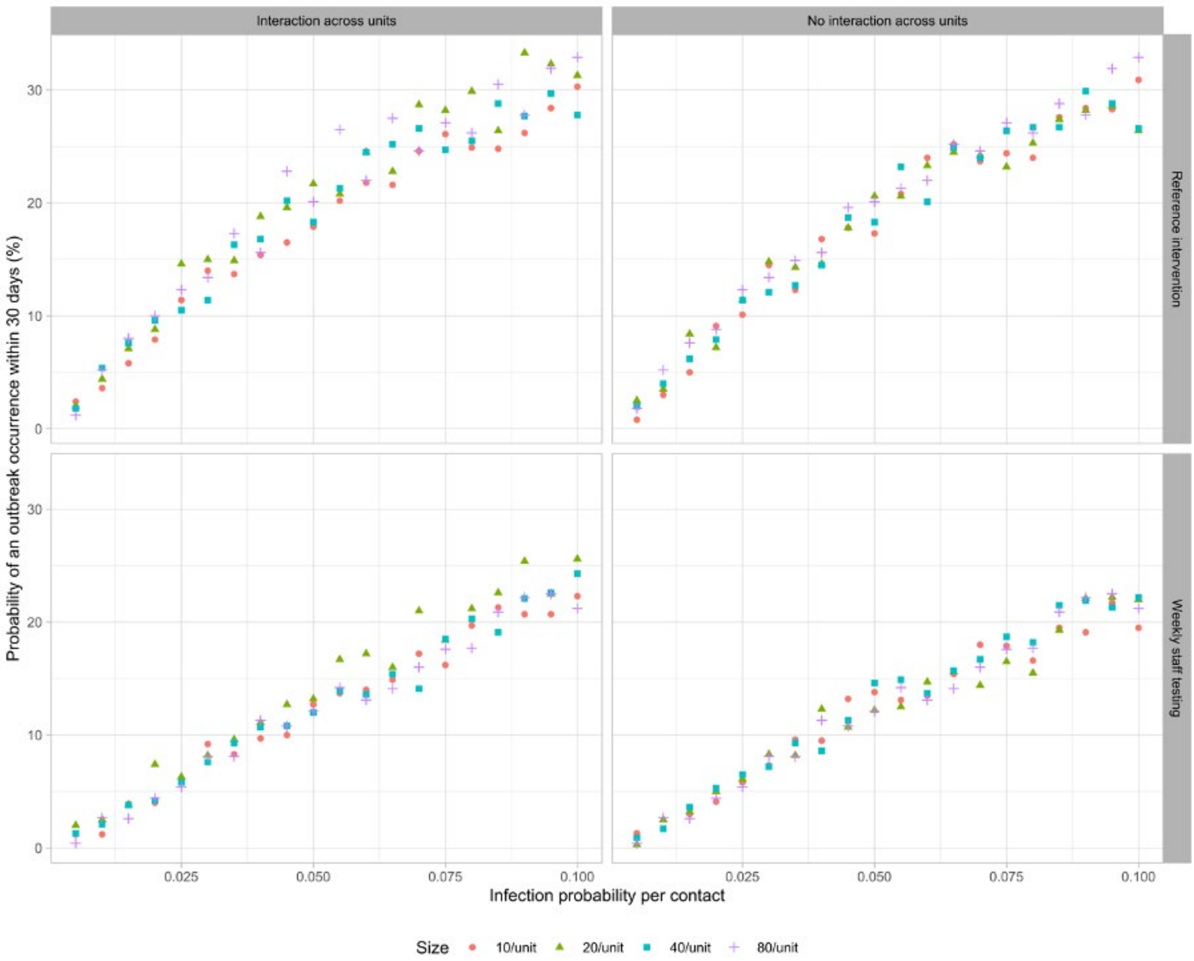

Figure E.5: Impact of unit size on the risk of an outbreak occurrence

The impact of splitting the care home with size of 80 residents into one, two, four, and eight units with 80, 40, 20, and 10 residents per unit respectively on the probability that an outbreak occurs across a range of values of infection probability per contact in the reference intervention and weekly staff testing scenarios. Interactions of residents and staff across units of the care home occur at zero and 20% of total contacts for the "no interaction across units" and "interaction across units" scenarios respectively. Points represent the mean values of 1000 simulations; error bars represent 95% CIs of the means.

Confidence Building

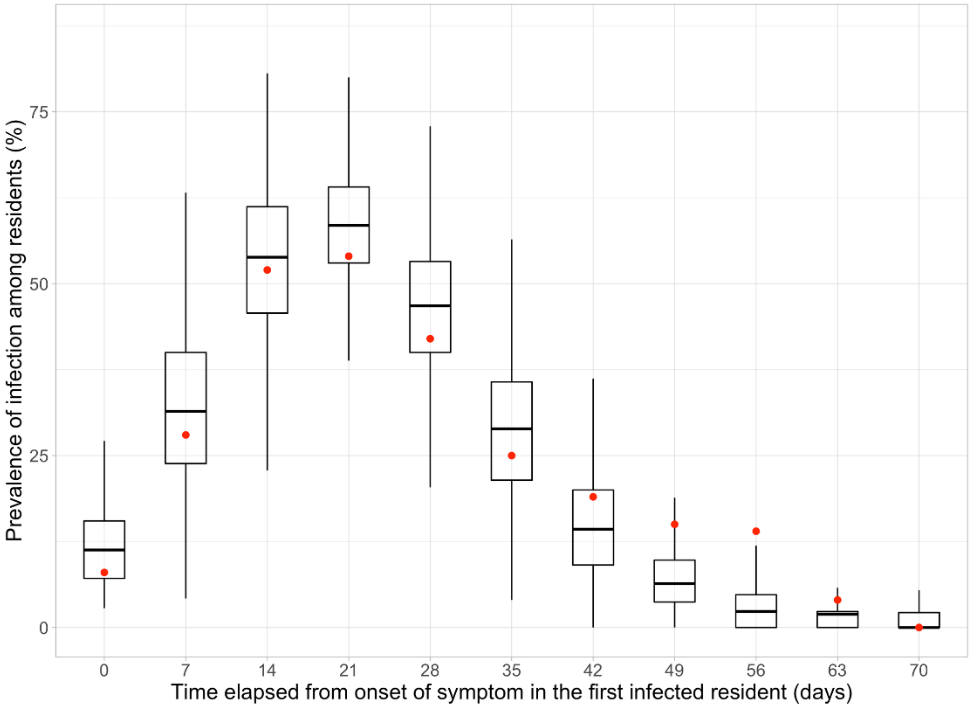

Figure E.6: Cross-validation for time series prevalence of infections among residents

The time series prevalence of infections among residents of the model over 1,000 runs (boxplot) is compared with that of the observed data from a care home in Lanarkshire (red points) where the reference intervention is implemented. The care homes are closed to admission of new residents and visitors 10 days after the first resident develops COVID-19 symptoms.

Boxplot: lower hinge: 25% quantile; lower whisker: smallest observation greater than or equal to lower hinge − 1.5×IQR; middle: median; upper hinge: 75% quantile; upper whisker: largest observation less than or equal to upper hinge + 1.5×IQR

Sensitivity and Uncertainty Analyses

Table E.6: Set up for uncertainty analyses of care home capacity, structure, and staff pool system

Capacity (Total residents)	Number of units	Unit size (Residents per unit)	Care staff member per units per day	Staff pooling system
Base case model				
80	2	40	16/15	33/32 staff members per unit
Population size				
30	2	15	6	12 staff members per unit
50	2	25	10	21 staff members per unit
120	2	60	24	50 staff members per unit
Number of units				
80	1	80	31	65 staff members
80	4	20	8	16 staff members per unit
80	8	10	4	8 staff members per unit
Residents per staff ratio *(Staff-resident contact rate is adjusted accordingly)*				
80	2	40	8	16 staff members per unit
80	2	40	32	64 staff members per unit
Staff pool system				
80	2	40	16/15	The pool of 65 staff members are shared between the two units
80	2	40	16/15	Unlimited

Table E.7: Outputs from PRCC analyses

Parameter	Inter1		Inter6	
	PRCC	p-value	PRCC	p-value
	Outcome: Cumulative number of infected residents after 90 days			
Test sensitivity	-0.05	3.50E-01	-0.66	2.80E-39
Resident leaving rate	-0.05	3.50E-01	-0.09	1.15E-01
Staff turnover	-0.05	3.50E-01	-0.09	1.15E-01
SD Compliance	-0.20	4.12E-04	-0.35	6.18E-10
Probability of symptomatic among infected staff	-0.55	5.78E-25	-0.38	1.26E-11
Probability of symptomatic among infected residents	-0.10	8.98E-02	-0.08	1.93E-01
Infection probability	0.99	7.08E-267	0.99	2.47E-234
Infection prevalence in the community	0.70	3.81E-45	0.88	4.43E-77
Infection prevalence in hospitals	0.17	6.46E-02	0.00	9.38E-01
Contact across units	-0.03	5.57E-01	-0.01	8.39E-01
Average staff-visitor contact rate	0.24	2.61E-05	0.10	6.20E-02
Average staff-staff contact rate	-0.12	3.06E-02	-0.13	2.52E-02
Average staff-resident contact rate	0.85	5.25E-83	0.76	1.12E-58
Average resident-resident contact rate	0.22	1.57E-04	0.23	7.89E-05
Average number of visitors per resident per day	0.09	1.15E-01	0.09	1.03E-01
	Outcome: Cumulative number of infected residents after 180 days			
Test sensitivity	-0.08	1.44E-01	-0.65	2.84E-37
Resident leaving rate	-0.05	3.50E-01	-0.08	1.15E-01
Staff turnover	-0.05	4.11E-01	-0.10	8.02E-02
SD Compliance	-0.08	1.55E-01	-0.32	7.12E-09
Probability of symptomatic among infected staff	-0.36	1.55E-10	-0.34	2.03E-09
Probability of symptomatic among infected residents	-0.08	1.89E-01	-0.10	7.66E-02
Infection probability	0.99	1.79E-241	0.99	1.54E-240
Infection prevalence in the community	0.77	8.58E-60	0.87	1.94E-94
Infection prevalence in hospitals	0.09	1.25E-01	0.03	5.90E-01
Contact across units	-0.07	2.53E-01	-0.01	8.24E-01
Average staff-visitor contact rate	0.38	6.35E-12	0.08	1.50E-01

Average staff-staff contact rate	-0.21	3.44E-04	-0.17	3.50E-03
Average staff-resident contact rate	0.77	4.54E-60	0.77	6.74E-61
Average resident-resident contact rate	0.20	4.74E-04	0.23	4.56E-05
Average number of visitors per resident per day	0.19	8.88E-04	0.21	2.61E-04

A negative value indicates a negative correlation – increasing the parameter decreases the outcome. A positive value indicates a positive correlation – increasing the parameter increases the outcome. In PRCC analysis in general, the parameters with large PRCC values (>0.5 or <– 0.5) and corresponding small p-values (<0.05) are deemed the most influential in the model (Taylor, 1990).

Table E.8: Outputs from PRCC analyses

Parameter	Reference intervention		Weekly staff testing	
	PRCC	p-value	PRCC	p-value
	Outcome 1: Cumulative number of infected residents after 180 days			
Infection prevalence in hospitals	0·00	2·8E-01	0·01	7·4E-05
Infection prevalence in the community	0·51	0·0E+00	0·68	0·0E+00
Relative infection prevalence	0·00	2·2E-01	0·30	0·0E+00
Average resident-resident contact rate	0·06	2·0E-89	0·21	0·0E+00
Average staff-staff contact rate	-0·01	6·0E-02	0·01	4·1E-02
Average staff-resident contact rate	0·21	0·0E+00	0·38	0·0E+00
Average staff-visitor contact rate	0·37	0·0E+00	0·22	0·0E+00
Contact across units	0·00	7·6E-01	0·01	3·9E-02
Average number of visitors per reisdent per day	0·41	0·0E+00	0·36	0·0E+00
Leaving rate	0·29	0·0E+00	0·17	0·0E+00
Staff turnover	0·05	4·1E-58	0·11	8·7E-257
Probability of symptomatic among infected residents	-0·01	4·8E-03	0·01	2·0E-02
Probability of symptomatic among infected staff	0·04	4·5E-37	-0·09	7·4E-191
Infection probability	0·82	0·0E+00	0·93	0·0E+00
Infection probability per resident-visitor contact	0·06	6·2E-89	0·24	0·0E+00
Social distancing compliance	-0·07	2·3E-110	-0·27	0·0E+00
Isolation effectiveness	0·01	3·8E-03	0·06	7·0E-78
Test sensitivity	-0·01	2·8E-04	-0·28	0·0E+00
	Outcome 2: Time until the first resident is infected			
Infection prevalence in hospitals	0·00	7·2E-01	0·00	1·5E-01
Infection prevalence in the community	-0·52	0·0E+00	-0·52	0·0E+00
Relative infection prevalence	-0·15	0·0E+00	-0·15	0·0E+00

Average resident-resident contact rate	0·00	6·7E-01	0·00	5·6E-01
Average staff-staff contact rate	-0·01	1·0E-01	0·00	6·0E-01
Average staff-resident contact rate	-0·03	4·9E-22	-0·04	5·2E-31
Average staff-visitor contact rate	-0·01	1·5E-03	-0·01	4·3E-06
Contact across units	0·01	1·5E-02	0·00	8·5E-01
Average number of visitors per reisdent per day	-0·19	0·0E+00	-0·20	0·0E+00
Leaving rate	0·00	8·1E-01	0·00	2·3E-01
Staff turnover	0·00	8·5E-01	0·00	7·5E-01
Probability of symptomatic among infected residents	0·00	8·0E-01	0·00	8·3E-01
Probability of symptomatic among infected staff	0·00	8·1E-01	0·00	4·2E-01
Infection probability	-0·17	0·0E+00	-0·17	0·0E+00
Infection probability per resident-visitor contact	-0·23	0·0E+00	-0·24	0·0E+00
Social distancing compliance	0·00	3·3E-01	0·00	3·8E-01
Isolation effectiveness	0·01	6·1E-02	0·01	2·2E-02
Test sensitivity	0·00	3·4E-01	0·00	2·1E-01
	Outcome 3: The risk of outbreak occurrence within 90 days			
Infection prevalence in hospitals	0·00	7·6E-01	0·00	4·5E-01
Infection prevalence in the community	-0·51	0·0E+00	-0·52	0·0E+00
Relative infection prevalence	-0·25	0·0E+00	-0·24	0·0E+00
Average resident-resident contact rate	0·00	3·2E-01	0·00	7·3E-01
Average staff-staff contact rate	-0·01	5·2E-03	0·00	5·1E-01
Average staff-resident contact rate	-0·07	6·1E-112	-0·07	9·0E-118
Average staff-visitor contact rate	-0·03	4·0E-24	-0·04	3·1E-29
Contact across units	0·01	1·9E-02	0·00	9·4E-01
Average number of visitors per reisdent per day	-0·19	0·0E+00	-0·20	0·0E+00
Leaving rate	0·00	4·0E-01	0·01	1·3E-02
Staff turnover	0·00	8·0E-01	0·00	9·1E-01
Probability of symptomatic among infected residents	0·00	6·3E-01	0·00	6·6E-01
Probability of symptomatic among infected staff	0·00	9·0E-01	0·00	4·1E-01
Infection probability	-0·35	0·0E+00	-0·35	0·0E+00
Infection probability per resident-visitor contact	-0·21	0·0E+00	-0·22	0·0E+00
Social distancing compliance	0·01	7·9E-02	0·00	2·5E-01
Isolation effectiveness	0·01	8·9E-02	0·00	7·3E-01
Test sensitivity	0·00	4·1E-01	0·01	1·9E-04

A negative value indicates a negative correlation – increasing the parameter decreases the outcome. A positive value indicates a positive correlation – increasing the parameter increases the outcome. In PRCC analysis in general, the parameters with large PRCC values (> 0·5 or < – 0·5) and corresponding small p-values (< 0·05) are deemed the most influential in the model (Taylor, 1990).

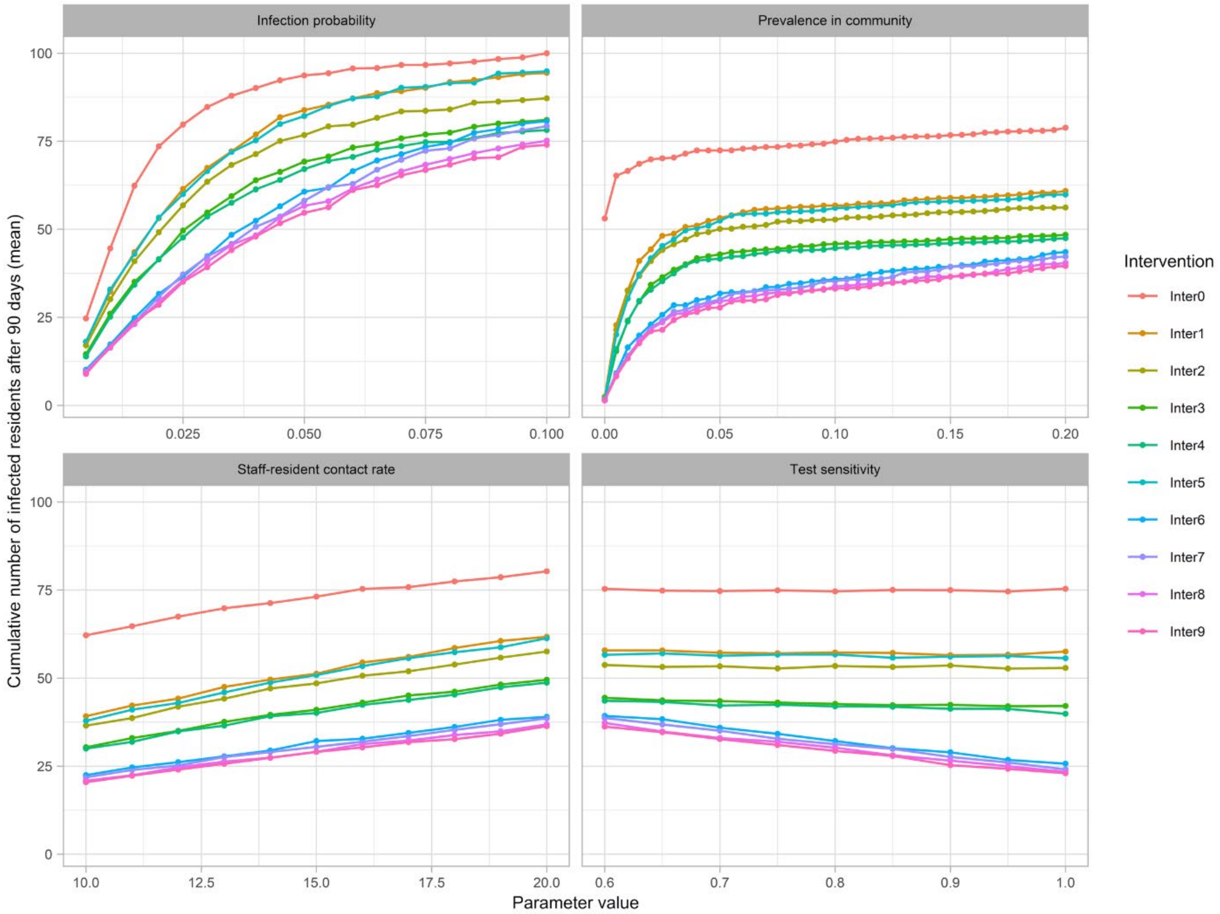

Figure E.7: Univariate sensitivity analysis

The impact of infection probability, infection prevalence in the community, staff-resident contact rate, and test sensitivity on the mean cumulative numbers of infected residents after 90 days in different intervention strategies over 300 simulations using the base case parameters

Appendix F. Supplementary Materials for the Hybrid Model

ODD Protocol

Purpose and Patterns

The purpose of the model is to investigate the impacts of staff working across different care homes as well as interventions to mitigate these impacts. The examined interventions include reducing or halting the use of bank/agency staff, weekly PCR testing of bank/agency staff, and creating bubbles of care homes. Care home bubbles restrict bank/agency staff to work only within a specific group of care homes that are designated as one bubble. We build confidence in our model by its ability to reproduce the following patterns observed in care homes in the UK:

- Pattern i: The higher risk of infection for residents and staff in care homes using bank/agency staff frequently compared with those care homes not using bank/agency staff (Shallcross et al., 2021)
- Pattern ii: The higher risk of infection for bank/agency staff compared with permanent staff in care homes using bank/agency staff frequently (Shallcross et al., 2021; Ladhani et al., 2020)
- Pattern iii: The risk of outbreaks in care homes using bank/agency staff frequently compared with those care homes not using bank/agency staff (Green et al., 2021)
- Pattern iv: The risk of outbreak occurrence in care homes specified by their resident population size and staff-to-resident ratio (Gatto et al., 2020; Scottish-Government, 2020a)

Pattern i, ii, and iii which reflect the impact of agency/bank staff use upon the spread of COVID-19 across care homes within a network, are important to clarify that our model is useful for its purposes. Pattern i, ii, and iii help validate the behaviours of the overall system. Pattern iv addresses the validity of the sub-systems' behaviour (care homes) when accounting for their interactions via bank/agency staff.

Entities, State Variables, and Scales

See section 9.4.2

Process Overview and Scheduling

In the warm-up period of 90 days (time step 1 to 90) without infections, the model only executes the process *Temporary_Staff_Schedule,* excluding the sub-model *Staff_Resident_Contact_Rate,* to establish the frequency distribution for bank/agency staff's work history (i.e., *WorkRecord*). From day 91, the model executes six actions in the following order at each time step (Figure F.1).

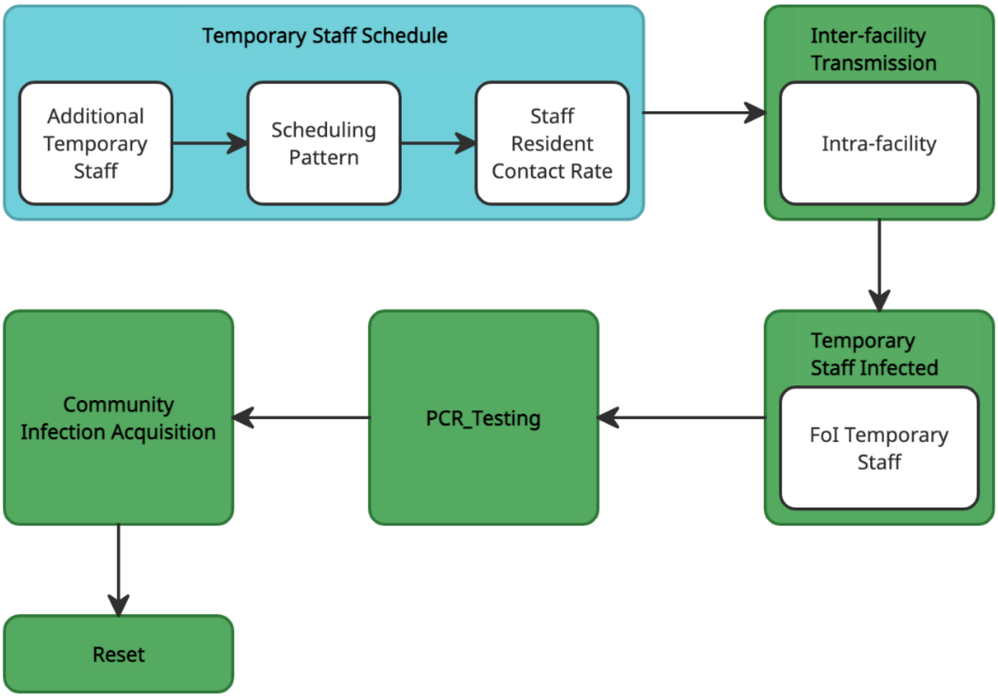

Figure F.1: The process overview and scheduling of the model at each time step

(White box: sub-model; sky-blue box: starting at time step 1; green box: starting at time step 91)

Note: FoI – Force of infection

Temporary_Staff_Schedule

This process is executed for every care home agent in random order. Care home *i* seeks to recruit $N_{B,i}$ bank/agency staff each day calculated as in the sub-model *Temporary_Staff_Requirement.*

The daily required bank/agency staff members are chosen based on one of the patterns described in the sub-model *Scheduling_Pattern.* Their *WorkID* changes to the *ID* of the care home. Among these daily bank/agency staff members, the number of susceptible and infectious ones are respectively used to update the state variables S_B and I_B of the care home agent.

The number of unfilled staff positions determines the state variable N_U of the care home. The daily number of contacts with residents per on-duty staff member (c_{SR}) are recalculated as described in the sub-model *Staff-Resident_Contact_Rate* due to changes in the daily staff-per-resident ratio.

Intra-facility_Transmission

The transmission of COVID-19 occurring within each care home is described in the sub-model *Intra-facility*.

Temporary_Staff_Infected

The daily rate at which susceptible bank/agency staff agents at work (*WorkID* ≠ 0) acquire the infection is calculated as described in the sub-model *FoI_Temporary_Staff*. The bank/agency staff members who are infected have their state variable *InfectionState* changed from 'susceptible' to 'exposed'.

Temporary_Staff_Disease_Progression

Exposed → Infectious (Pre/Asymptomatic): Exposed staff agents transit to either the pre-symptomatic state at the probability δ_S or the asymptomatic state at the end of the exposure period τ_e.

Within Infectious (Presymptomatic → Symptomatic): Pre-symptomatic staff agents transit to the symptomatic state when they develop symptoms at the end of their pre-symptomatic period τ_p. Symptomatic staff have to self-isolate at home (*Isolation* = 'true') in the next time step until they recover.

Infectious → Recovered: Infectious staff agents (*InfectionState* = 2,3, or 4) recover at the probability $(1 - d_S)$ at the end of their infectiousness period (τ_i). Their infection state changes to 'recovered' and the variable *Isolation* is set to 'false'. Staff that do not recover are deceased, and they are replaced by new susceptible bank/agency staff agents.

PCR_Testing

Bank/agency staff have RT-PCR testing at the interval τ_{pcr}, starting from the time step 95. Those staff members who are tested at the probability determined by their adherence to testing $\rho_{B,pcr}$ have their state variable *Tested* set to 'true'. After the time delay from testing to test result determined by the parameter τ_{trt}, the infected staff members whose *Tested* is 'true' are detected at the probability θ_{pcr} and have to self-isolate. Their state variable *Tested* is reset to 'false'.

Community_Infection_Acquisition

Bank/agency staff members can also acquire COVID-19 from interactions with other infectious people in the community at the probability β_C.

Reset

The variable *WorkID of a*ll bank/agency staff agents is reset to zero, indicating that they leave the workplace at the end of the day. Staff agents who leave the workforce at the turnover rate μ_S will have all of their state variables except *ID* reset as in *Initialization*.

Design Concepts

See section 9.4.3

Initialization

See section 9.5.1

Table F.1: Initial values of entities' state variables and parameters

Variable/ Parameter	**Initial value**	**Source**
Care-home-agent-specific state variables		
ID	1, 2, …, 12	
GroupID	0	
N_R	See Table S1-2	Provided by Health and Social Care Partnership Lanarkshire

Variable/ Parameter	**Initial value**	**Source**
N_S	See Table S1-2	Provided by Health and Social Care Partnership Lanarkshire
N_W	$0.4^* N_S$	Assumption based on discussions with care homes in Lanarkshire
N_U	0	
N_B	0	
I_B	0	
S_B	0	
Intra-facility	$S_R(0) = N_R$; $E_R(0) = I_R(0) = R_R(0) = Q_R(0) = 0$ $Ss = N_S$; $E_S(0) = I_S(0) = R_S(0) = Q_S(0) = E_{SD}(0) = I_{SD}(0) = 0$	See the sub-model *Intra-facility* for more details
Shared-staff-agent-specific state variables		
ID	1, 2, 3, …	
GroupID	0	
WorkID	0	
WorkRecord	[0, 0, …, 0]	
InfectionState	0 (susceptible)	
Tested	False	
Isolation	False	

Input Data

The daily incidence of COVID-19 in the community in the UK during the second wave is used to determine the time series input of the parameter β_C (GOV.UK, 2021a). The model assumes that the undetected cases represent 50% of the total cases in the community (Perez-Reche and Strachan, 2021). The adjusted incidence is, therefore, calculated by doubling the reported incidence.

Sub-models

Parameters used in the model are described in Table 9.1.

Temporary Staff Requirement

Care home i seeks to recruit $N_{B,i}$ bank/agency staff each day:

$$N_{B,i} = N_{BN,i} + \frac{Q_{S,i}\left(N_{W,i} - N_{NB,i}\right)}{N_{S,i}}$$

$$N_{BN,i} \sim Poisson\ \left(\alpha N_{W,i}\right)$$

$N_{NB,i}$ describes the number of bank/agency staff required in normal circumstances prior to the COVID-19 pandemic due to ongoing staff shortage and absence of staff for reasons such as holidays, unfilled vacancies, and sickness.

The component $\frac{Q_{S,i}\left(N_{W,i} - N_{NB,i}\right)}{N_{S,i}}$ represents the number of bank/agency staff agents required to cover for permanent staff members self-isolating due to COVID-19 (Q_S).
The parameter α is the average percentage usage level of bank/agency staff in all care homes in the network.

Scheduling Pattern

Bank/agency staff are chosen from those from those who have not been allocated to any other care home (*WorkID* = 0), are not self-isolating (*Isolation* = false*)*, and belong to the same sub-group of the care home (the same *GroupID*) where they are allocated following two rules one by one until the demand of this care home is fulfilled.

- Rule 1 with probability η: A randomly chosen bank/agency staff agent is allocated.
- Rule 2 with probability $(1 - \eta)$: For a care home with the identity number *i* in the network, the bank/agency staff agent with the largest value of *WorkRecord[i]* is allocated.

Staff Resident Contact Rate

The daily number of contacts with residents per staff member at work: $c_{SR} = \frac{c_{RS}N_R}{N_W - N_U}$

Intra-facility

See section 9.4.1

FoI Temporary Staff

Susceptible bank/agency staff can acquire the infection via contacts with infectious residents and staff members at the care homes where they work at the rate calculated as follow:

$$vc_{SR}\frac{I_R}{N_R} + vc_{SS}\left(1-\rho_{sd}\right)\frac{I_W}{N_W-N_U} \quad (1)$$

$$I_W = I_{SW} + I_B \quad (2)$$

$$I_{SW} = \frac{(I_S+I_{SD})(N_W-N_B)}{N_S} \quad (3)$$

In which,

$I_W - N_U$: The daily number of staff members at work (permanent and bank/agency staff)

$N_W - N_B$: The daily number of permanent staff members at work

I_W: The number of infectious staff members at work

I_{SW}: The number of infectious permanent staff members at work

Replace (2) & (3) into (1), the rate becomes:

$$vc_{SR}\frac{I_R}{N_R} + vc_{SS}\left(1-\rho_{sd}\right)\frac{\frac{(I_S+I_{SD})(N_W-N_B)}{N_S}+I_B}{N_W-N_U}$$

Verification

In code verification, we conducted unit testing – all processes and functions were tested individually before incorporating them into the main simulation code. For example, we tested creating bubbles of care homes in a simple ABM in which care home agents only had one state variable that defined the identity number of the bubble to which the care homes belonged. This test confirmed the number of care homes per bubble was as intended in the conceptual model before implementing the code in the full simulation. We also performed tracing of randomly chosen agents of each type via the simulation output and used the built-in debugger, bottom-up testing, stress testing, and regression testing for verification.

White-box Validation

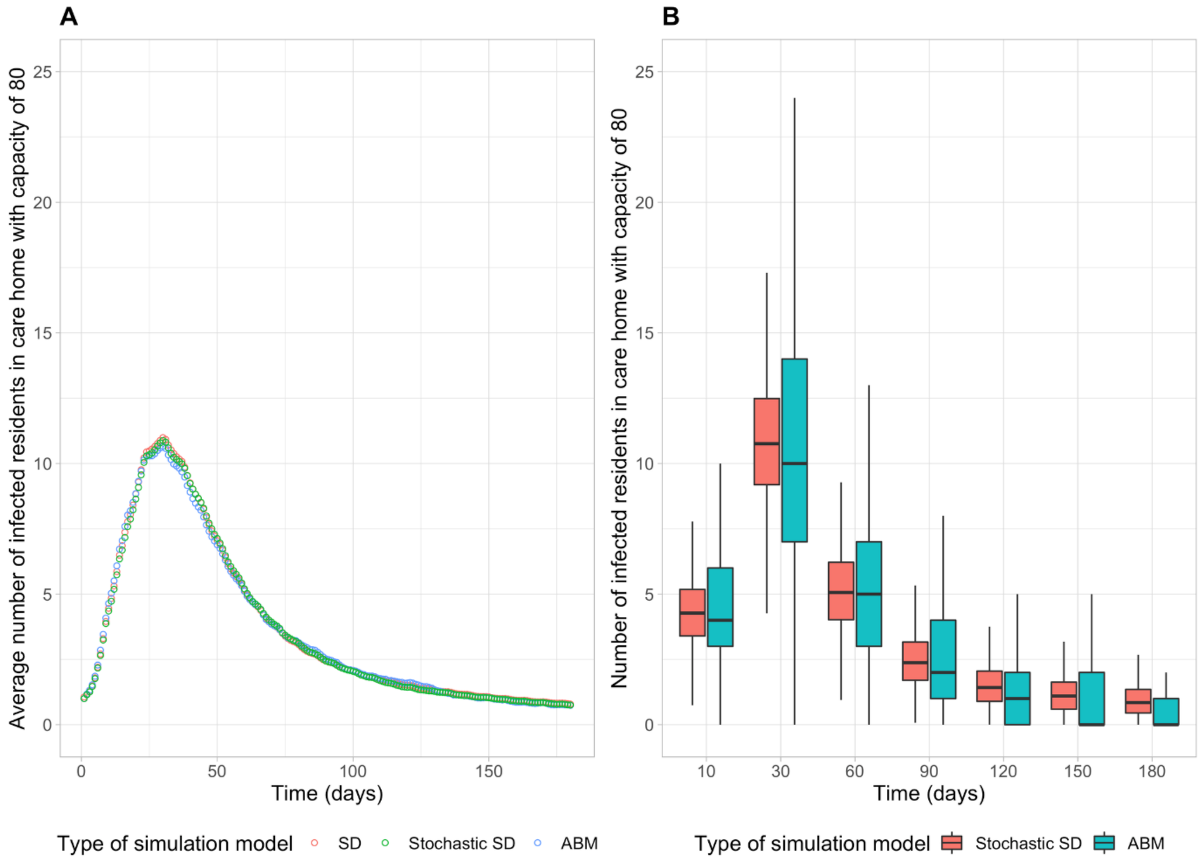

Figure F.2: Comparisons of results generated from parallel SD, stochastic SD, and ABM models

The figure describes the time series of COVID-19 prevalence among residents in care home with capacity of 80 residents (1,000 simulations per scenario). Base-case parameters are used. Interventions implemented in the care home include testing upon admission of residents, no visitation, hand hygiene and using PPE, social distancing, isolation of symptomatic/confirmed residents, and weekly testing of staff. Simulations are seeded with one infected resident.

Box-plot: lower hinge: 25% quantile; lower whisker: smallest observation greater than or equal to lower hinge − 1.5×IQR; middle: median; upper hinge: 75% quantile; upper whisker: largest observation less than or equal to upper hinge + 1.5×IQR). Note: IQR – interquartile range.

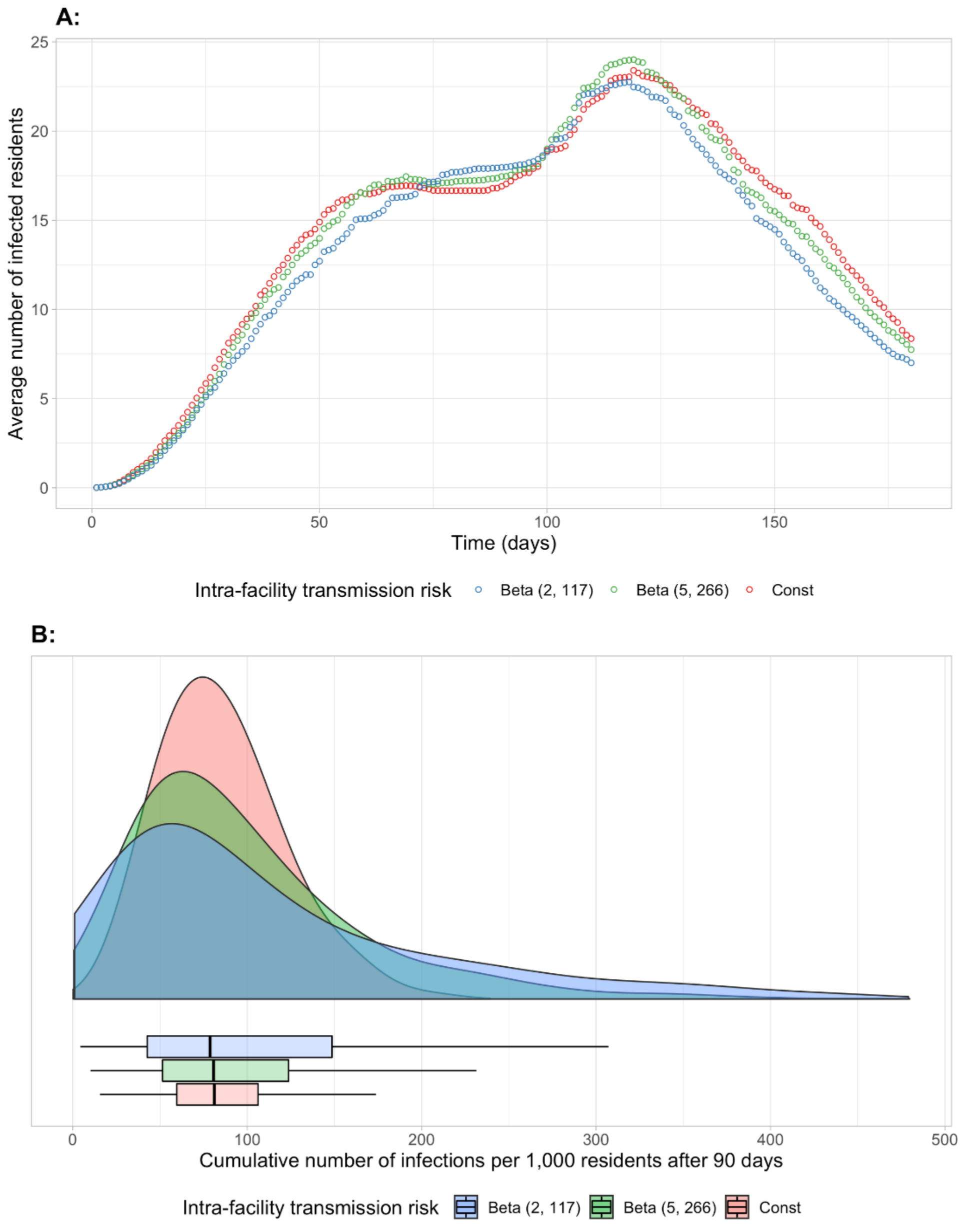

Figure F.3: Calibration – Different scenarios of intra-facility transmission risk

Time series of COVID-19 prevalence among residents(A) and cumulative number of infected residents after 90 days (B) with different values of intra-facility transmission risk. The figure describes the model outcomes for network B in three scenarios: The intra-facility per-contact transmission risk is

i) "Const": homogeneous across care homes (0.02);

ii) heterogeneous across care homes and drawn from Beta distribution (5, 266);

iii) heterogeneous and drawn from Beta distribution (2, 117).

*No intervention in bank/agency staff is implemented. Bank/agency staff comprises 10% of total staff. Other parameters have the base-case values. Boxplot: middle – median; lower hinge – 25% quantile; upper hinge – 75% quantile; lower whisker = smallest observation greater than or equal to lower hinge - 1.5 * IQR; upper whisker = largest observation less than or equal to upper hinge + 1.5 * IQR.*

Black-box Validation

We searched PubMed, the WHO COVID-19 database, and medRxiv on the 25th June 2021, with the search terms (“COVID-19” OR “SARS-CoV-2” OR “coronavirus”) AND (“care home*” OR “LTCF*” OR “long term care” OR “nursing home*”) AND (“staff*” OR “healthcare worker*” OR “HCW*” OR “outbreak*”). These searches returned 306 studies, of which five examined the impact of staff working across multiple care homes on the inter-facility transmission or the impact of care home characteristics, including resident population size and staff-to-resident ratio on the risk of outbreak occurrence. In addition to these searches, we identified relevant information from daily COVID-19 data for Scottish and English care homes. Table F.1 below lists the studies to which we compared our modelling results.

Table F.2: Relevant studies for black-box validation identified from a systematic search

Baister M, McTaggart E, McMenemy P, Megiddo I, Kleczkowski A. COVID-19 in Scottish care homes: A metapopulation model of spread among residents and staff. *medRxiv.* 2021:2021.2008.2024.21262524. (Added on the 30th August)
Burton JK, Bayne G, Evans C, et al. Evolution and impact of COVID-19 outbreaks in care homes: population analysis in 189 care homes in one geographic region. *medRxiv.* 2020:2020.2007.2009.20149583.
Green R, Tulloch JSP, Tunnah C, et al. COVID-19 testing in outbreak free care homes: What are the public health benefits? *The Journal of hospital infection.* 2021.
Ladhani SN, Chow JY, Janarthanan R, et al. Increased risk of SARS-CoV-2 infection in staff working across different care homes: enhanced CoVID-19 outbreak investigations in London care Homes. *Journal of Infection.* 2020.
Scottish Government. Coronavirus (COVID-19): daily data for Scotland. https://www.gov.scot/publications/coronavirus-covid-19-daily-data-for-scotland/ Published 2020. Accessed 25 June, 2021.
Shallcross L, Burke D, Abbott O, et al. Factors associated with SARS-CoV-2 infection and outbreaks in long-term care facilities in England: a national cross-sectional survey. *The Lancet Healthy Longevity.* 2021;2(3):e129-e142.

Additional Modelling Results

Table F.3: Risk of infection in residents and staff in various usage levels of bank/agency staff

Experiment scenario	Average usage level of bank/agency staff	Compliance to weekly PCR testing among bank/agency staff	
		0%	**80%**
Different networks			
		RR of infection for residents in care homes using bank/agency staff to care homes not using bank/agency staff	
A (Heterogeneous size & staff-to-resident ratio)	5%	1.68 (1.64 – 1.73)	1.14 (1.12 – 1.17)
	10%	2.65 (2.57 – 2.72)	1.28 (1.25 -1.31)
	15%	3.73 (3.63 – 3.84)	1.43 (1.39 – 1.47)
	20%	5.17 (5.03 – 5.30)	1.64 (1.60 – 1.68)
B (Homogeneous size & staff-to-resident ratio)	5%	1.65 (1.61 – 1.69)	1.14 (1.12 – 1.16)
	10%	2.54 (2.45 – 2.61)	1.28 (1.25 – 1.31)
	15%	3.72 (3.62 – 3.82)	1.49 (1.45 – 1.53)
	20%	5.07 (4.94 – 5.21)	1.66 (1.57 – 1.69)
		RR of infection in bank/agency staff to permanent staff	
A (Heterogeneous size & staff-to-resident ratio)	5%	1.34 (1.29 – 1.38)	1.28 (1.24 – 1.32)
	10%	1.55 (1.52 – 1.58)	1.35 (1.32 – 1.38)
	15%	1.72 (1.69 – 1.75)	1.42 (1.39 – 1.45)
	20%	1.98 (1.95 – 2.01)	1.48 (1.46 – 1.51)
B (Homogeneous size & staff-to-resident ratio)	5%	1.33 (1.29 – 1.37)	1.29 (1.25 – 1.33)
	10%	1.52 (1.49 – 1.55)	1.33 (1.30 – 1.36)
	15%	1.72 (1.69 – 1.75)	1.45 (1.42 – 1.48)
	20%	1.98 (1.95 – 2.01)	1.48 (1.45 – 1.50)
		RR of outbreaks in care homes using bank/agency staff to care homes not using bank/agency staff	
A (Heterogeneous size & staff-to-resident ratio)	5%	2.43 (2.30 – 2.56)	1.64 (1.54 – 1.73)
	10%	3.76 (3.58 – 3.96)	1.83 (1.73 – 1.94)
	15%	4.71 (4.48 – 4.95)	2.19 (2.08 – 2.32)
	20%	5.64 (5.37 – 5.92)	2.48 (2.35 – 2.61)
B (Homogeneous size & staff-to-resident ratio)	5%	2.62 (2.48 – 2.76)	1.25 (1.17 – 1.33)
	10%	4.36 (4.14 – 4.59)	1.82 (1.72 -1.93)
	15%	5.84 (5.56 – 6.13)	2.38 (2.25 – 2.52)
	20%	6.87 (6.55 – 7.21)	2.83 (2.68 – 2.98)
Heterogeneous intra-facility transmission risk drawn from a distribution (Network A)			

		RR of infection for residents in care homes using bank/agency staff to care homes not using bank/agency staff	
Beta (5, 266)	5%	1.75 (1.66 – 1.85)	1.17 (1.12 – 1.23)
	10%	2.64 (2.51 – 2.78)	1.28 (1.22 – 1.35)
	15%	3.80 (3.62 – 4.00)	1.56 (1.48 -1.64)
	20%	5.02 (4.79 – 5.27)	1.69 (1.60 -1.78)
Beta (2, 117)	5%	1.65 (1.53 – 1.78)	1.15 (1.06 – 1.24)
	10%	2.34 (2.17 – 2.52)	1.21 (1.13 – 1.29)
	15%	3.12 (2.90 – 3.35)	1.37 (1.27 – 1.49)
	20%	3.99 (3.73 – 4.28)	1.71 (1.57 – 1.85)
		RR of infection in bank/agency staff to permanent staff	
Beta (5, 266)	5%	1.43 (1.39 – 1.48)	1.32 (1.29 – 1.36)
	10%	1.62 (1.58 – 1.65)	1.38 (1.35 – 1.41)
	15%	1.84 (1.80 – 1.87)	1.56 (1.52 – 1.59)
	20%	2.06 (2.02 – 2.10)	1.59 (1.56 – 1.62)
Beta (2, 117)	5%	1.64 (1.58 – 1.69)	1.53 (1.49 – 1.57)
	10%	1.76 (1.71 – 1.80)	1.60 (1.56 – 1.64)
	15%	1.91 (1.87 – 1.95)	1.61 (1.56 – 1.66)
	20%	2.12 (2.08 – 2.16)	1.75 (1.71 – 1.79)
		RR of outbreaks in care homes using bank/agency staff to care homes not using bank/agency staff	
Beta (5, 266)	5%	2.03 (1.92 – 2.13)	1.34 (1.27 – 1.42)
	10%	3.00 (2.85 – 3.14)	1.50 (1.42 – 1.59)
	15%	3.80 (3.63 – 3.98)	1.95 (1.85 – 2.06)
	20%	4.51 (4.31 – 4.72)	2.11 (2.00 – 2.22)
Beta (2, 117)	5%	1.90 (1.80 – 2.00)	1.35 (1.27 – 1.43)
	10%	2.61 (2.48 – 2.74)	1.48 (1.40 – 1.56)
	15%	3.21 (3.06 – 3.36)	1.68 (1.59 – 1.77)
	20%	3.85 (3.67 – 4.03)	2.02 (1.92 – 2.13)

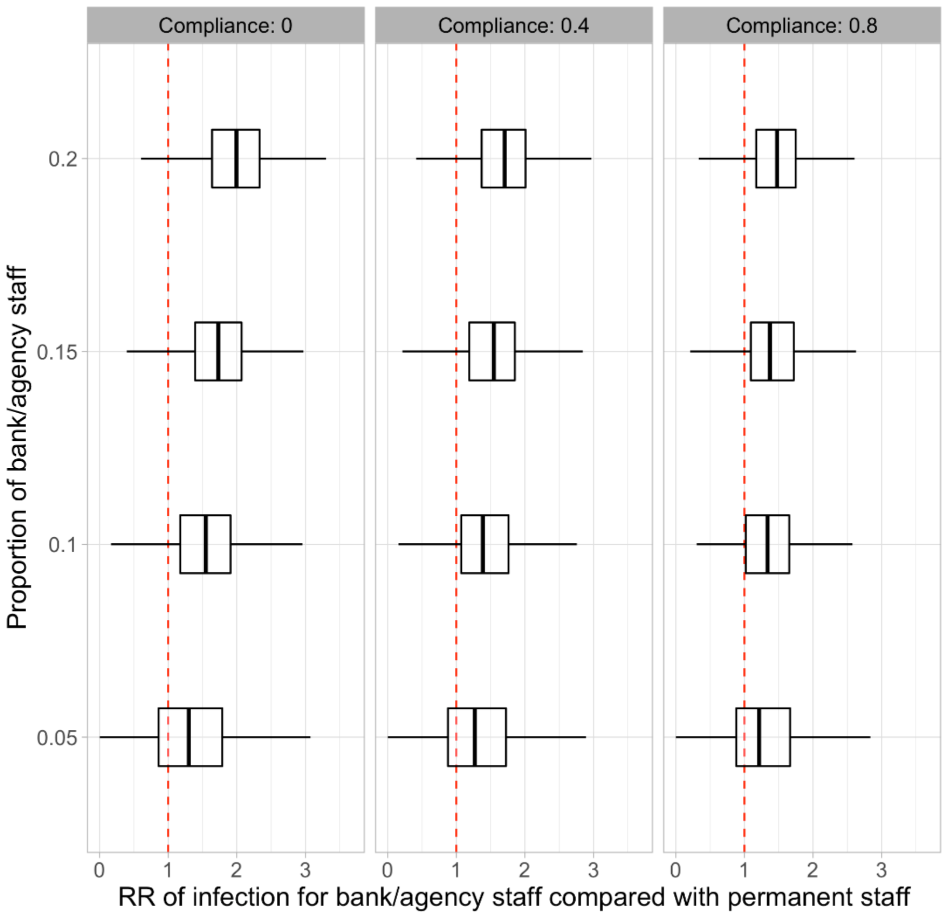

*Figure F.4: RR of infection for bank/agency staff to permanent staff in care homes using bank/agency staff Bank/Agency staff have different compliance rates to weekly PCR testing. Compliance to weekly testing among permanent staff is 80%. Results are for 1,000 simulations in each scenario. Boxplot: middle – median; lower hinge – 25% quantile; upper hinge – 75% quantile; lower whisker = smallest observation greater than or equal to lower hinge - 1.5 * IQR; upper whisker = largest observation less than or equal to upper hinge + 1.5 * IQR*

Results of Sensitivity and Uncertainty Analyses

Table F.4: Output from PRCC analyses

Parameter	Cumulative number of infected residents		Relative risk of infection in bank/agency staff to permanent staff	
	PRCC	**p-value**	**PRCC**	**p-value**
Community incidence	0.68	3.81E-45	0.17	6.06E-316
IFR for residents	-0.01	2.77E-02	0.01	1.75E-01
IFR for staff	0.00	7.18E-01	0.00	9.04E-01
Average resident- resident contact rate	0.12	1.21E-165	0.05	1.43E-26
Average staff-staff contact rate	0.07	9.16E-51	0.05	6.76E-31
Average staff-resident contact rate	0.69	5.25E-83	0.47	1.12E-58
Staff turnover	0.00	6.66E-01	0.00	3.65E-01
Resident leaving rate	0.00	4.12E-01	0.00	3.21E-01
Probability of symptomatic in infected residents	-0.14	3.32E-231	-0.12	3.60E-149
Probability of symptomatic in infected staff	-0.30	1.55E-10	-0.12	1.13E-149
Per-contact transmission probability	0.91	1.79E-241	0.77	1.50E-47
Pre-symptomatic time	0.58	7.96E-102	0.43	2.57E-104
Infectious time	0.06	1.50E-47	0.05	4.62E-27
Social distancing compliance rate	-0.10	2.57E-104	-0.10	1.75E-114
PCR sensitivity	0.00	8.68E-01	0.00	7.43E-01
Test turnaround time	0.07	3.45E-52	0.03	1.03E-11

A negative value indicates a negative correlation – increasing the parameter decreases the outcome. A positive value indicates a positive correlation – increasing the parameter increases the outcome. In PRCC analysis in general, the parameters with large PRCC values (>0.5 or <– 0.5) and corresponding small p-values (<0.05) are deemed the most influential in the model.

The effect of the heterogeneity of resident population sizes was more significant than staff-to-resident ratios, whilst the latter had no impact on the risk of outbreaks across care homes. Decreasing staff-to-resident ratios increased the number of contacts with residents per staff member as the average number of contacts with staff per resident remained the same. This is based on our model assumption that the number of contacts with staff per resident per day was maintained regardless of the staffing level as the overall care home workload does not change. Increasing the number of per-staff-member contacts with residents increased the force of infection in staff which in turn increased the force of infection in residents. However, decreasing staff-to-resident ratios reduced the risk of COVID-19 ingress as fewer staff members enter the care home each day. Overall, staff-to-resident ratios had no impact on the risk of outbreaks in care homes (Figure F.4A). Our model assumption that staff-to-resident ratios did not affect the per-contact transmission risk or staff's compliance to other infection control measures may underestimate the impact of this parameter on the risk of outbreaks in care homes. Larger care homes had an increased risk of COVID-19 ingress compared with smaller care homes (Figure F.4B).

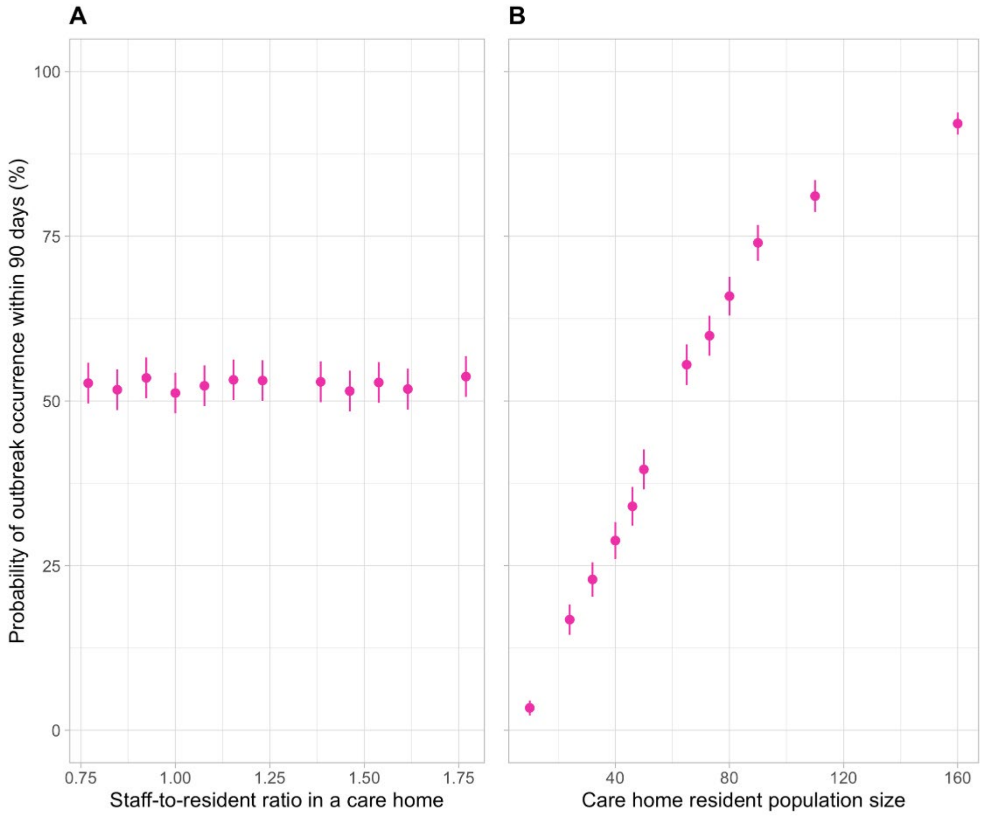

Figure F.5: Impact of staff-to-resident ratio and resident population size on the risk of outbreak

The plot describes the risk of outbreak occurrence within 90 days in individual care homes with

A: the same population size of 65 residents but different staff-to-resident ratios (network C).

B: different resident population size (network D).

The average intra-facility transmission risk in care homes is homogeneous. The average usage level of bank/agency staff is 10% of total staff. No intervention on bank/agency staff is implemented. The risk of outbreak occurrence (point) is the probability of simulations where outbreaks occur in 1,000 simulation for each scenario. Line range denotes the 95% CI of this outcome.

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