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# Computer simulation of dementia care demand heterogeneity using hybrid simulation methods: improving population-level modelling with individual patient decline trajectories

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ABSTRACT

*Objectives:* The aim of the study was to model dementia prevalence and outcomes within an ageing population using a novel hybrid simulation model that simultaneously takes population-level and patient-level perspectives to better inform dementia care service planning, taking into account severity progression variability.
*Study design:* This is a simulation study.
*Methods:* We developed a hybrid computer simulation combining different methods to best represent population and individual dementia dynamics. Individual patient outcomes are aggregated into three progression rate types to report the effects of severity progression variability and intervention benefits.
*Results:* Fast progression of dementia severity is associated with higher annual care cost and short overall survival duration. Those patients are more likely to develop moderate to severe symptoms more quickly, highlighting a need for more urgent provision of appropriate care services. Slower severity progression is associated with lower annual care costs, but longer survival requires higher overall financial provision. Although lifestyle interventions reduce overall care costs, treatment and lifestyle intervention benefits are modest at the population level.
*Conclusions:* Individual variation of dementia decline is an important factor to include in planning adequate levels of care services and to ensure timely and appropriate service availability. Hybrid simulation models provide useful insights at the population and individual level, supporting effective decision-making.


## Introduction

In the healthcare domain, operational research (OR) methods are used to support service commissioners, health planners and service provider organisations. OR often uses computer simulation to better understand the behaviours of complex systems and the interactions between system elements, allowing exploration of the impact of different policy options and service scenarios. OR has been used to understand, evaluate and plan interventions and service delivery in a number of healthcare domains.[1] This article describes the application of OR simulation methods to support planning of care services for people with dementia, by informing decision makers about the variability of severity of dementia progression.

In ageing populations, healthcare policymakers and provider organisations face many challenges to meet the increasing need for care services for older people with dementia; increasing dementia prevalence will be an important driver for demand for care services.

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Care needs are complex, individualised and progressively more intensive depending on the age of onset, comorbidities, different pathologies and risk factors underlying dementia,[2,3] eventually resulting in considerable and profound dependence on care providers.

Currently available medical and clinical interventions for dementia rely on symptomatic treatments. These are licensed only for Alzheimer and Parkinson disease,[4] and there is currently no known dementia cure or preventative treatment.[5] Nevertheless, clinical benefits are widely regarded as modest, inconsistent and short-term.[6–9] In comparison, a healthy lifestyle is reported to improve outcomes, with delayed onset and fewer years with dementia (YWD).[10–13] The computer simulation model reported here allows benefit comparisons to be explored over time, capturing the interplay of competing risks and benefits.

### *Review of modelling studies*

Previous modelling work has addressed various aspects of dementia care service planning. This includes modelling treatment effects in a simulated randomised controlled trial (RCT),[14–18] strategic planning based on dementia prevalence,[19,20] diagnosis,[21] risk factors[22] and impact on long-term care provision.[23–25] State-based models stratify care needs based on severity 'compartments', but this approach assumes homogeneity within health states and cannot address individual variability in progression. More recently, microsimulation models[26–30] have attempted to overcome these issues; however, this approach can be computationally intensive and do not include potential interventions.

We therefore modelled individualised decline trajectories for people with dementia in our computer simulation and assessed intervention benefits in the presence of individual decline variability. We describe the results from a computer simulation model using population-level ageing, incidence and mortality in a hypothetical age cohort, hybridised with individual-level variability in onset, progressive decline, lifestyle and treatment effects. The results were used to assess the likely impacts on survival and total costs (health, social and unpaid care) at the population level over a 45-year cohort lifetime.

## Methods

### *Model architecture and outputs*

Our hybrid computer model was developed in AnyLogic[31] (a multimethod simulation software tool) using two different and complementary modelling methods. Fig. 1 shows how a deterministic population-level system dynamics (SD) model simulates ageing, dementia onset and mortality, whereas an agent-based (AB) model simulates individual survival, dementia severity progression and outcomes stochastically.

Population dynamics are modelled through cognitively normal (CN) deaths (removed progressively from the CN cohort), incident dementia (removed progressively from the CN cohort) and deaths with dementia (removed progressively from the 'dementia' cohort). Within a 5-year age group, this process is modelled using the stock-flow SD model shown in Fig. 1, wherein stocks are numbers of individuals in each state over time. These stock-flow models are cascaded to cover the 60–105 age range. To simulate ageing, every 5 years of model time, survivors are transferred to the next age group.

The SD part of the model links with the AB part, wherein agents (as a technical modelling term), can be equated to individual patients or people with dementia. The AB part creates and removes agents from the stocks within the SD component of the model, equivalent to individual dementia onset and death. The AB part also

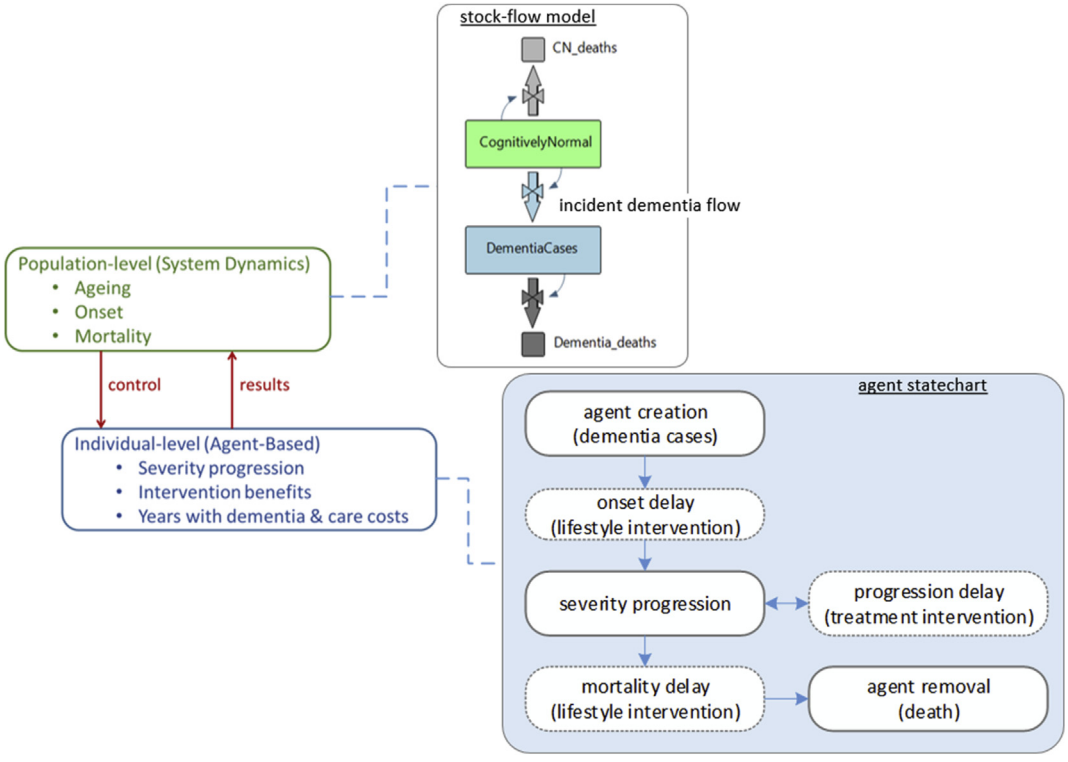


**Fig. 1.** Simulation overview showing hybrid SD and AB model functional partitioning. SD, system dynamics; AB, agent-based; CN, cognitively normal.

simulates dementia severity progression, updates individual attributes of age and YWD and calculates monthly and accumulated care costs for each individual agent.

These calculations are carried out in the agent's statechart, also shown in Fig. 1. An agent is created when the SD model simulates an onset case. In addition to an age group attribute, agents are assigned a progression rate type (slow, intermediate or fast) and positive or neutral responses to interventions. These are drawn from probability distribution models in the simulation. Further details of the model construction, parameterisation and validation are published in the study by Evenden et al.[32] and given in the supplement to this article.

### *Simulation scenarios and analysis methods*

As our focus was on late-onset dementia, a 'predementia' CN age cohort starts at the age of 60 years. We assume no dementia onset in the starting 60- to 65-year-old age group stock; only CN mortality rates were assumed. Dementia onset is modelled from the 65- to 70-year-age age group up to the 100- to 105-year-old age group.

The model starts with a hypothetical cohort of 35,000 CN people. This is typical of the number of 60- to 65-year-old people in a large geographic health service commissioning area in the UK. The simulation then calculates the projected number of dementia cases for those aged 65 years and older, over a 45-year follow-up.

Individual results were collected for YWD and care costs. Mean and median results were calculated for YWD and also reported for 90th and 95th percentiles to account for the positive skew.

In the baseline simulation, agents move directly to the 'severity progression' state, wherein severity, age, duration with dementia and care costs are calculated. When the SD model simulates a death, an agent is selected and removed based on age group and dementia severity. Individual outcomes generated in the AB part are aggregated for summary reporting for YWD and care cost outcomes.

We also conducted simulations to explore the impact of two intervention scenarios: medication and lifestyle. For the medication treatment intervention, agents with a positive intervention response move into the 'progression delay' state, after progression has started. This state temporarily pauses severity of dementia progression, while still accumulating care costs. In the case of the lifestyle intervention, agents reside initially in the 'onset delay' state and then later in the 'mortality delay' state. The results are summarised with and without treatment and lifestyle interventions within patient progression groups.

Patient-level interventions were modelled as two-year delayed onset and one-year delayed mortality resulting from the lifestyle intervention based on physical activity, exercise, diet, smoking cessation and moderate alcohol consumption[10–13] or one-year delayed progression as a result of acetylcholinesterase inhibitor medications (a range of symptomatic treatments).[7,33]

Interventions were compared with the baseline simulation using statistical tests for mean differences in nominal costs. Individual YWD data were combined and analysed using Cox proportional hazards, with survival differences tabulated as hazard ratios (HRs).

## Results

This section describes baseline simulation results for a population without interventions – and for comparison – the results for the two modelled intervention scenarios. Summaries of the graphical and tabulated results are shown.

Fig. 2 shows results from the SD part of the model; the vertical axis shows proportions of the starting cohort (the upper pane

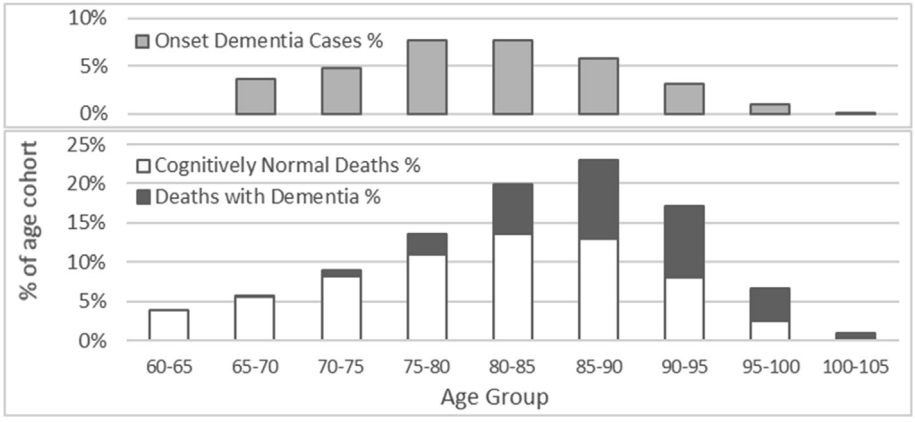


**Fig. 2.** Onset cases and deaths as percentages of the age cohort.

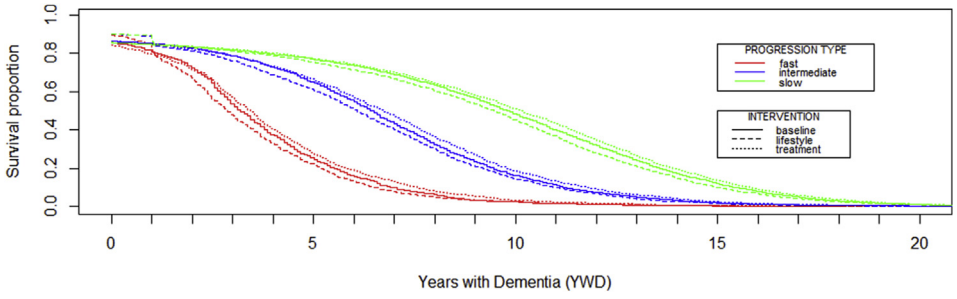


**Fig. 3.** Years with dementia (YWD) survival curves by progression type.

showing age-related prevalence). The results from the AB part of the model are presented as Kaplan-Meier survival curves in Fig. 3, showing YWD for the modelled agent survival. The agent population is treated in the same way as a real time-to-event survival analysis, comparing mean and median survival times.

Validation of the simulation outputs is an important consideration in developing computer simulation models. This is given in the supplementary material along with additional simulation results. Further details can be found in the study by Evenden et al.[32]

*Onset and mortality*

Up to the age of 85 years, the number of onset cases is higher than those dying with dementia (i.e., grey bar values larger than solid bars in Fig. 2), and it is only from the age of 90 to 95 years the number of deaths with dementia (solid bars) exceeds both onset (grey bars) and CN deaths (light bars). The simulation therefore illustrates the rising population prevalence and associated healthcare burden associated with dementia, despite higher death rates among people with dementia.

*Baseline costs*

Average accumulated care costs are £219k for slow progression types spread over 9 years or so. Fast progression types incur significantly lower overall costs, but owing to the shorter survival time of 3 years and 7 months, annual costs at £44.5k are nearly double the costs for slow progression types.

*Intervention results*

Delaying dementia onset improves incidence rates, whereas delayed progression reduces mortality rates. Successfully treated patients survive with dementia on an average of nearly 9 months longer than those not responding to treatment. This is somewhat less than the intervention benefit duration (12 months) as it is moderated by mortality at the population level.

Costs per progression type generally do not differ statistically (95% significance) or practically for this intervention. Generally, the cost benefits of this treatment intervention are lost owing to longer survival as reduced annual care costs are incurred over an increased duration. The results for the fast progression types are an exception as a temporarily paused fast progression prevents care costs accelerating over the short term.

The change in YWD for the lifestyle intervention suggests an overall reduction of 15 weeks at the population level. The YWD reductions are statistically significant in all cases, although the benefits are lower for fast progression types because of higher mortality (owing to becoming severe earlier).

*Survival with dementia*

Fig. 3 summarises these results as three Kaplan-Meier survival curve 'triples'. Each triple shows fast, intermediate and slow progression type survival time (from left to right). The time axis shows YWD. Within each triple, the middle trace is the baseline case. The left-hand traces show YWD under the lifestyle intervention, i.e., with shorter durations with dementia (reflecting a reduced duration of dementia care demand). The right-hand traces within each triple show the effect of the treatment intervention, which increases the duration with dementia. The features before one year are artefacts of the delayed onset in the lifestyle intervention.

The plotting artefacts in the first year result from the lifestyle intervention's one-year delayed mortality, following which survivors are subject to the higher mortality rates in older age groups owing to delayed onset. This combination realises compression of morbidity[34] and the associated lower care costs.

The simulation results in Fig. 3 show that median survival for people with dementia with slow progression is around 10 years, with 10% surviving beyond 15 years and 5% surviving beyond 17 years, whereas median survival for fast progressors is only three-and-a-half years after onset, with 5% of those surviving beyond 8 years.

Mean and median YWD survival durations are broadly similar within each progression type, except that the fast progression type has a positive skew. The results for the 95th percentiles reveal 1.74-fold median duration for the slow progression type, increasing to 2.58-fold median duration for the fast types. Despite the shorter mean and median survival durations with fast progression types, there is more fractional variation in survival duration.

*Overall outcomes*

Table 1 shows that the treatment intervention increases the duration that patients have dementia. This is because mortality rates are typically lower for those with the temporary pause in symptomatic decline associated with the intervention. Additional time with dementia between onset and death is equivalent to a reduced HR compared with the baseline simulation.

Table 2 shows the change in survival as negative values. There is a reduced duration between onset and death and thus shorter times with dementia, with an overall reduction of 15 weeks at the population level. The YWD reductions are statistically significant in all cases, but the benefits are smaller for the fast progression types. This is because of greater likelihood of mortality for those who become severe earlier.

Those who benefit from the lifestyle intervention have fewer YWD between onset and death, so in fact, they have an increased HR compared with the baseline case. As previously mentioned, these are population-level results, thus also include those not benefitting from the intervention.

Our analysis revealed higher annual costs for fast progression types albeit over a relatively short period. Although average accumulated care costs for a fast progression type are 73% of care costs (£158k versus £216k) for all people with dementia, the shorter accumulation period means that average annual care costs are 158% (£44·5k versus £28·2k). Similarly, average annual care costs for a slow progression type are 86% of the overall average annual care costs, but the longer accumulation period and the large proportion of slow progression types means that average total care costs are close to the overall accumulated care costs (£216k).

## Discussion

By highlighting the important differences between patient progression rate types, more appropriate consideration can be given to commissioning the variety of care services at the intensity level and duration needed to support people with dementia.

The originality of our study emerges from hybridising computer simulation methods to estimate key outcomes for older people with dementia including individual patient trajectories of cognitive and functional decline, driven by population-level dynamics of ageing, dementia incidence and mortality. The effect of symptomatic treatment and lifestyle interventions are also applied and modelled individually to better capture real-world heterogeneity.

Symptomatic medication treatment has the potential to increase care costs for those who survive longer in a poor health state. Lifestyle interventions have potential for greater benefit at the population level, but raise long-term adherence challenges. It is

**Table 1**
Comparison of medication intervention with baseline.

| Simulation result | Progression rate type | | | |
|---|---|---|---|---|
| | Slow | Intermediate | Fast | Overall |
| **Years with dementia—baseline** | | | | |
| Mean YWD ± CI | 9·050 ± 0·126 | 6·302 ± 0·131 | 3·550 ± 0·155 | 7·660 ± 0·092 |
| **Years with dementia—medication intervention** | | | | |
| Mean YWD ± CI | 9·299 ± 0·129 | 6·550 ± 0·136 | 3·748 ± 0·168 | 7·887 ± 0·094 |
| **Years with dementia—mean difference vs intervention** | | | | |
| YWD increase | 0·249 | 0·248 | 0·198 | 0·227 |
| YWD increase | 13 weeks longer | 13 weeks longer | 10 weeks longer | 11 weeks longer |
| *P*-value | 0·0034 | 0·0051 | 0·0450 | 0·0006 |
| **Years with dementia—Cox proportional hazards** | | | | |
| YWD hazard ratio | 0·9399 | 0·9269 | 0·9160 | 0.9440 |
| *P*-value | 0·0003 | 0·0013 | 0·0343 | <0.0001 |
| **Dementia care cost—change** | | | | |
| Mean cost increase | £1k | £4k less | £14k | £3k |
| *P*-value | 0·3635 ns | 0·1505 ns | 0·0052 | 0·0815 ns |

YWD, years with dementia; CI, confidence interval.

**Table 2**
Comparison of lifestyle benefit with baseline.

| Simulation result | Progression rate type | | | |
|---|---|---|---|---|
| | Slow | Intermediate | Fast | Overall |
| **Years with dementia—baseline** | | | | |
| Mean YWD ± CI | 9·050 ± 0·126 | 6·302 ± 0·131 | 3·550 ± 0·155 | 7·660 ± 0·092 |
| **Years with dementia—lifestyle intervention** | | | | |
| Mean YWD ± CI | 8·740 ± 0·121 | 6·027 ± 0·128 | 3·318 ± 0·149 | 7·378 ± 0·089 |
| **Years with dementia—mean difference vs intervention** | | | | |
| YWD change | −0·310 | −0·275 | −0·232 | −0·282 |
| YWD reduction | 16 weeks | 14 weeks | 12 weeks | 15 weeks |
| *P*-value | 0·0003 | 0·0022 | 0·0186 | <0·0001 |
| **Years with dementia—Cox proportional hazards** | | | | |
| YWD hazard ratio | 1·0796 | 1·0711 | 1·0945 | 1·0656 |
| *P*-value | <0·0001 | 0·0039 | 0·0296 | <0·0001 |
| **Dementia care cost—change** | | | | |
| Cost reduction | £14k | £16k | £13k | £15k |
| *P*-value | <0·0001 | <0·0001 | 0.0059 | <0·0001 |

YWD, years with dementia; CI, confidence interval.

evident that the need for adequate long-term service planning with considerable resources is not 'managed away' by the putative intervention benefits.

We report survival duration—between onset and death—as YWD with total care costs accumulated over that period. Individual results are aggregated and reported as per slow, intermediate and fast progression type groups. Categorising patients by progression groups has been suggested[35–37] to support *inter alia* better informed patient prognosis and family counselling support, and these results demonstrate their potential for long-term service planning. While our overall survival duration results compare well with previous results, partitioning by progression type provides better information to service providers.

Intervention benefits are compared with the baseline case to reveal worthwhile but relatively modest effects for each progression type at the population level. Interventions can be worthwhile individually for people with dementia—or for those likely to develop it—however, the results here suggest they are unlikely to make large reductions in population-level demand for care services.

Perhaps counterintuitively, symptomatic treatment increases the duration of YWD as survival is improved owing to lower mortality associated with lower severity. Any care cost reductions as a result of this are generally lost with increased survival. As lifestyle interventions delay onset, before care costs are incurred, the beneficial effects are larger. Although mortality is also delayed with this intervention, overall compression of morbidity means fewer YWD and saving in care costs.

### *Context and other studies*

Previous simulation studies have demonstrated the major challenges to be met in care service provision for people with dementia.[29,38] This study is consistent with prior simulation models in highlighting the need to consider the variability and complexity of heath conditions in old age to inform policy and resource allocation decisions. This article specifically highlights the importance of considering heterogeneity of severity progression for those with dementia—thus complementing and extending the recommendations from previous work.

### *Limitations*

Higher dementia incidence rates have been reported[39–41] than those used here, but different methods for cohort retention, underdetection adjustment and assumptions about dementia among decedents make direct comparison difficult. These differences are greater for the incidence rates among the oldest old,[42,43] but relatively few people are affected. This moderating assumption may become invalid in the future, however, as longevity increases. Nevertheless, prevalence estimates can be used to provide validation against empirical data.

Progression characteristics are based on a data set from the Alzheimer's Disease Neuroimaging Initiative clinical trial, so some caution is needed in generalising the trajectory characteristics. However, the purpose is to characterise the variability of progression, rather than to characterise a specific group. Progression types were identified using cognitive, functional and global metrics (in this case, Mini-Mental State Exam (MMSE), Clinical Dementia Rating Sum of Boxes (CDRSB), Alzheimer's Disease Assessment Scale (ADAS13) and Functional Assessment Questionnaire (FAQ)) to cluster the patient trajectories. Different cluster allocations could emerge using different metrics, and therefore, different mixed-effects regression coefficients could be obtained. Reassuringly, model validation for a range of results shows good consistency with a number of sources and published studies, particularly with average MMSE decline and survival.

Despite clustering using multiple domains, the need to map decline to care costs necessitated the use of an MMSE-based regression model. There are many published sources that allow the MMSE score to be mapped to care costs, so although it would have been possible to produce a variety of severity progression models, there would have been less scope for mapping this to care costs. This cost modelling approach could be a source of uncertainty, but overall results compare well with independent research.[44]

*Reflections on computer simulation in health care*

Computer simulation is a flexible approach that can be used in a wide range of healthcare applications to develop better intuition of cause-and-effect relationships. Not only the results can be useful to evaluate and compare interventions and service models on a consistent basis but also the effect of underlying assumptions can be explored without the considerable investment required for 'real-world' reorganisation.

Evidence may be incorporated and evaluated from a wide range of sources and is not limited by survey methods. Simulation results nevertheless require validation, and this can be supported using results from published studies. Where there is uncertainty or unclear trends, for example, about incidence rate variation,[45,46] this can be explored in 'what-if' computer simulation scenarios.

While summary results are reported here by the patient's progression type, the underlying simulation captures individuals with their inherent severity progression variability, and this is important when dementia severity has dependent effects such as differing risks of mortality. This is one of the benefits of hybrid AB modelling: one is potentially closer to real people than perhaps other, more abstracted simulation methods. Nevertheless, onset and death of the individual agents themselves are ultimately controlled by the more familiar population-level epidemiological model.

Although long-term trials to investigate lifestyle effects would be prohibitively difficult and expensive, as well as raising ethical issues, these can be readily explored in simulation modelling. An advantage of simulation is that model inputs and outputs can be tailored for specific contexts. Initial conditions and population characteristics such as starting age distributions, longevity and incidence rates can be easily modified to be generalisable to non-UK population address and adapted to additional research questions.

## Author statements

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*Ethical approval*

Not required. This article describes the results of a computer simulation modelling study. Model parameters were derived from anonymised public domain data sources and the published literature.

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None.

*Competing interests*

None declared.

*Author contributions*

The research was conceived by S.B., B.W., P.R. and D.E. D.E. conducted the research and data analysis and developed the simulation model. All others contributed to data interpretation and writing of the article. The project supervisors were S.B., P.R. and B.W. Expert clinical knowledge was provided by C.K.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2020.07.018.

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