Impactibility Modelling

Background motivation and proof of concept using multi-state modelling

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Title

Impactibility modelling: Background motivation and proof of concept using multi-state modelling

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Abstract

The sustainability pressures faced by health systems today will not be the same in the future. To ensure the long-term viability of Universal Health Care provision, agile solutions are being designed to navigate the dynamic problem of optimising health under constraints. Within the UK, population health management is being researched and applied. Impactibility modelling is a new development in this area which seeks to achieve the greatest increase in population health, patient experience, and reduction in health inequalities for the cost incurred.

This paper details the background motivation for Impactibility modelling and provides a proof of concept model. Through a case study of Type 2 Diabetes Mellitus, the usefulness of multi-state modelling for the purpose of impactibility modelling is explored.

Keywords

Population health management, Impactibility modelling, Multi-state modelling, Type 2 Diabetes Mellitus

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1 Introduction

To ensure people are protected against the financial hardships of poor health and to ensure long-term economic development, Universal Healthcare Coverage ('UHC') is established or is being established in many countries (WHO, 2010). The health systems that deliver UHC take many forms globally (WHO, 2010). In the UK, the National Health System ('NHS') was established in 1948 to deliver society-wide affordable medical treatment and has continued to be predominately publicly funded (NHS England, 2014).

Shortly after the creation of the NHS there were sustainability pressures which saw adaptations to how the health system operated including the privatisation of dental and optical services (The Kings' Fund, 2018). Today sustainability pressures to systems that contribute to health are present in varying nature across the world. Western health and social care systems, including the NHS in the United Kingdom ('UK'), face demand-side pressures from demographic and epidemiological causes, including an ageing population, obesity trends and increased prevalence of chronic disease (Ham et al., 2012, NHS England, 2014, Corbett-Nolan et al., 2018). In addition, supply-side political and financial pressures occur, including increasing public and patient expectations, medical advances, human resource skills shortages and reduced budgets (Ham et al., 2012, NHS England, 2014, Corbett-Nolan et al., 2018). These pressures creates sustainability concerns for health systems and without change the problem is expected to worsen (Ham et al., 2012, NHS England, 2014).

This has motivated efforts to reimagine health systems by adopting an 'Integrated Care' approach that aims to deliver health services more holistically; increasing the ability of the health system to supply care more efficiently (NHS England, 2014, NHS England, n.d., Sansoni et al., 2015, Stokes et al., 2018). Now attention has turned to Population Health Management ('PHM') to deliver further improvements in health system sustainability by reducing the demand for care. PHM seeks improvement in population health status and patient experience, while reducing health inequalities and the associated costs. This approach shifts attention from simply delivering care to preventing the requirement for care in the first place. It does so by targeting intervention on those at risk of adverse health events.

It may be possible to improve the results of targeted interventions further by using Impactibility Modelling ('IM'). This requires identifying those in a population most likely to be impacted positively by a particular intervention. This approach has the potential to further improve health system sustainability.

2 Methodology

As part of a Masters in Public Health, research was undertaken to explore IM as a new development to PHM and make steps forward in that development through a literature review and proof of concept, at a time when it is just being created[1]. This paper provides a summary of the literature review conducted to provide an appreciation of the objective and current state of IM development[2]. An overview of the proof of concept model using multi-state modelling for people with Type 2 Diabetes Mellitus ('T2DM') is provided herein.

3 Background motivation for Impactibility modelling

The pressures described in the introduction are those faced now but these may be different in the future. In general, the problem is one of optimisation; to optimise health under constraints. To match the dynamic nature of the problem, an agile solution is required. The wider system that IM sits within must be appreciated as it influences its design, objectives and implementation.

[1] This research was conducted concurrently but independently to membership of the PHM Working Party.
[2] This is a substantial part of the research but is beyond the scope of a Hot Topics paper. Further information can be provided upon request.

3.1 A dynamic problem: To optimise health under constraints

The struggle faced internationally to optimise health under constraints can be viewed within the health and social care system and within a wider system that determines health. Before individuals need health or social care, multiple systems work to maintain and improve health. This wider system that determines health, referred to here as a wider health system, is also where causes of ill-health mostly lie (Institute for Healthcare Improvement, 2012). An example of a wider system that determine health is the food production system that delivers healthy food at affordable prices to the population, as shown in Dhalgren and Whitehead's rainbow model in Figure 1 (Public Health England, 2017b).

Figure 1: Dhalgren and Whitehead rainbow model

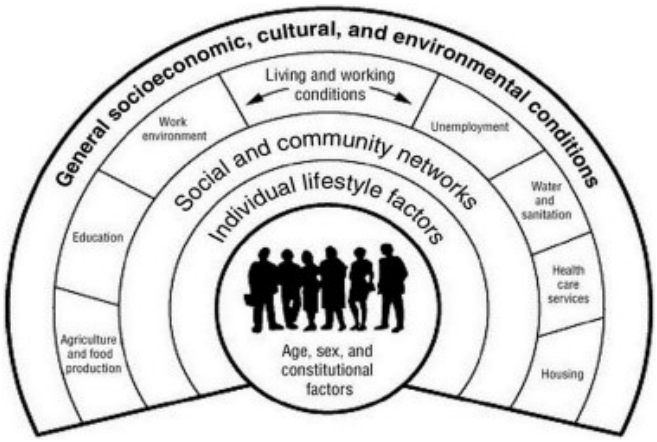
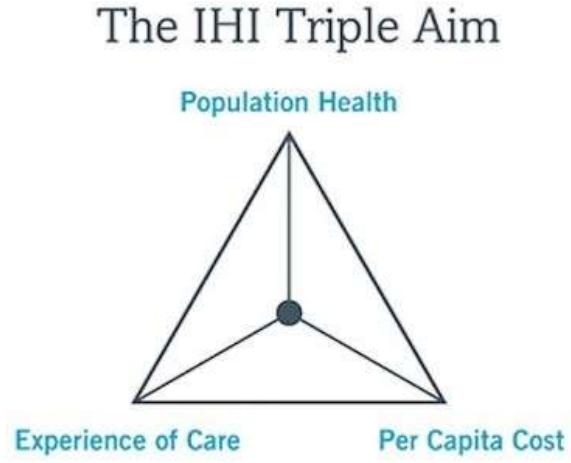


Image sourced from Public Health England (Public Health England, 2017b)

The Institute for Healthcare Improvement's Triple Aim refers to the simultaneous objective of "improving patient experience (including quality and satisfaction)[,] improving the health of populations[,] ..and reducing the per capita cost of achieving health" (Institute for Healthcare Improvement, 2012), as shown in Figure 2. This framework describes "an approach to optimi[se] [the wider] health system performance" (Institute for Healthcare Improvement, 2012) and can therefore be used to view the optimisation problem across both the health and social care system and the wider health system (Nash et al., 2016, Goodwin and Alonso, 2014).

Figure 2: The IHI Triple Aim



Visual representation of the IHI Triple Aim (Norman, 2019)

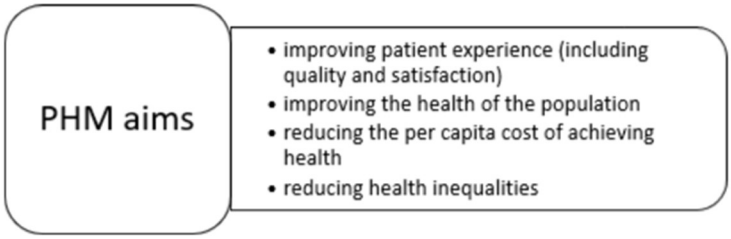
These aims have been used as optimisation criteria when designing solutions to optimise population health under constraints (Nash et al., 2016, Lewis et al., 2013, Corbett-Nolan et al., 2018, NHS England, 2014, Wharam and Weiner, 2012, Lewis, 2015). In the UK, a fourth aim of reducing health inequalities has been adopted (Corbett-Nolan et al., 2018).

3.2 An agile solution: a control cycle

The nature of the optimisation problem varies by local context, over time and with the population. The solution must therefore adapt, requiring ongoing tailoring to suit both the local health and care system and the wider health system. A control cycle is a generic systematic framework to develop an agile solution within (Moen and Norman, 2011). A control cycle is well suited to dynamic problems such as optimising health under constraints. It is also well suited where a solution is not yet known but can be established through iterative development based on learning from the process.

Population Health Management ('PHM') is a growing area of research and practice that seeks better health outcomes and distribution of outcomes using a control cycle (Buck et al., 2018). PHM seeks to "estimate[e] .. the cross-sectoral cost-effectiveness of different types and combinations of investments for producing health" (Kindig and Stoddart, 2003, p.381). It seeks to optimise health as delivered in both the health and social care system and the wider health system (Nash et al., 2016). The triple aim has therefore been adopted as the optimisation criteria of PHM (Lewis, 2010, Stokes et al., 2018, Nash et al., 2016, Lewis et al., 2013, Corbett-Nolan et al., 2018, NHS England, 2014, Wharam and Weiner, 2012, Lewis, 2015, Curry et al., 2005, Huckel Schneider et al., 2017). Herein, the UK quadruple aim will be referred to as the PHM aims (see Key Term 1).

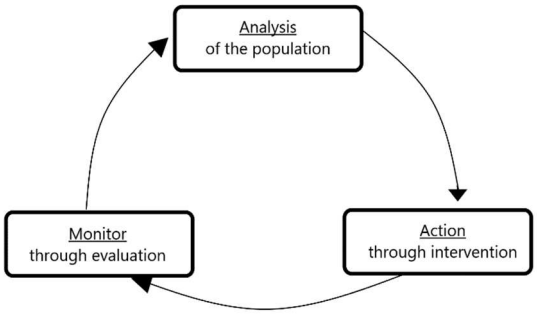
Key Term 1: Population health management aims



Sourced from dissertation (Robertson, 2019)

Fundamental to PHM is data analysis which aims to better understand individual and population need in order to better meet those needs (Corbett-Nolan et al., 2018, Nash et al., 2016). This understanding allows for a targeted approach to the delivery of downstream and upstream[3] interventions (Corbett-Nolan et al., 2018, Nash et al., 2016). PHM systems seek to analyse population need and intervene accordingly, with the combination monitored for effectiveness in achieving the PHM aims (Nash et al., 2016), as shown in Figure 3.

Figure 3: Analysis, action and monitor stages of a PHM system



Sourced from dissertation (Robertson, 2019)

When a control cycle is applied in a health system context it is known as a Learning Health System ('LHS'). The population analysis undertaken in PHM is an example of the analysis undertaken in an

[3] Downstream and upstream are used in this context to describe interventions to treat disease and interventions to treat the causes of disease.

LHS (Foley and Vale, 2017), however, an LHS is not just analysis. An LHS describes a way of working that strives for continuous improvement (The Learning Healthcare Project, n.d., Foley and Vale, 2017) where health systems develop iteratively and are responsive to the dynamic nature of the optimisation problem. With each complete cycle, the health system learns and improves to better optimise health under constraints (Foley and Fairmichael, 2015, Foley and Vale, 2017).

In many countries, including the UK, the emphasis is moving away from "health systems designed to better manage chronic disease care towards systems designed to enhance population health" (Corbett-Nolan et al., 2018, p.8). That is, moving away from solutions designed for today's problems to agile solutions that can adapt to the changing nature of the optimisation problem including PHM and LHS (Lewis, 2015, Goodwin and Alonso, 2014).

3.3 UK application

The NHS model of acute episode healthcare delivery is seen as unsustainable by policymakers (Corbett-Nolan et al., 2018). A new model of integrated care allows for "locally appropriate proposals to improve health and care for residents"(NHS England, n.d.) providing a more seamless service to patients and investment in downstream and upstream prevention (NHS England, 2014). The NHS's journey toward this integrated model is progressing with Sustainability and Transformation Partnerships due to be replaced by Integrated Care Systems by April 2021 (NHS England, n.d.). These collaborations between local NHS organisations and councils, to improve population health, plan the long-term needs of the local community and take "collective responsibility for managing resources" (NHS England, n.d.). That is, optimising health under constraints across the health and social care system and the wider health system.

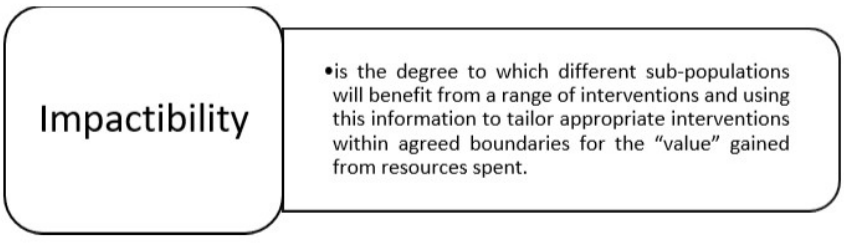
To further this journey, PHM is being researched and applied in the UK (Lewis, 2015, Stokes et al., 2018, Foley, 2016, Lewis et al., 2012, Steventon et al., 2011, Woodhams et al., 2012). An interest in progressing PHM in the UK, and in applying the actuarial skillset, has led to the creation of an IFoA PHM Working Party (Institute & Faculty of Actuaries, 2018). The working party's initial focus is on the next development in PHM, namely Impactibility modelling ('IM').

3.4 Impactibility modelling

3.4.1 What is it?

'Impactibility[4] model' was coined by Geraint Lewis (Lewis, 2010), Chief Data Officer at NHS England (NHS England, n.d). The working definition of IM reflects the desire to optimise health under constraints (see Key Term 2).

Key Term 2: Impactibility



Sourced from PHM Working Party (Population Health Management Working Party, 2019)

3.4.2 Why consider it?

In a PHM system, data analytics are leveraged in population analysis (Goodwin and Alonso, 2014) to understand and predict population need (Corbett-Nolan et al., 2018). This predictive modelling

[4] The term should be spelt 'impactibility' or 'impactability' however, following Lewis' publication in 2010, 'impactibility' appears to have been adopted in the proceeding literature.

provides insights that allow lives at risk of adverse health outcomes and lives that can benefit from an intervention, or not, to be considered by clinical practitioners before the event occurs (Corbett-Nolan et al., 2018, Lewis, 2010, Goodwin and Alonso, 2014). It facilitates the proactive provision of interventions and is therefore intended to better manage the risk of adverse health outcomes and better achieve the PHM aims (Curry et al., 2005, Lewis, 2015, Goodwin and Alonso, 2014, Lewis et al., 2012, Lewis, 2010, Huckel Schneider et al., 2017).

Currently the predictive modelling involves risk stratification which highlights the people at risk of an adverse health outcome such that an appropriate intervention can be allocated (Jean-Baptiste et al., 2017, Lewis et al., 2011, Curry et al., 2005, Sansoni et al., 2015, Lewis, 2015, Lewis, 2010). IM goes beyond predicting who is at-risk, to provide insight on 'impactibility' (Lewis, 2010). It highligths "who will and who will not respond to preventive interventions"(Corbett-Nolan et al., 2018, p.13).

Steventon and Billings provides a strong argument and clear rationale for IM; the objective of preventing the outcome of interest is to achieve the PHM aims and risk stratification alone, without consideration for impactibility, will not meet this objective (2017). Interventions use limited resources therefore there is a need to increase the 'value' gained from resources spent.

The problem of optimising health under constraints is one of seeking a higher return on investment; for the cost incurred the greatest improvement to population health, patient experience and reduction to health inequalities is sought, i.e. the PHM aims. The objective of IM is to contribute to the return on investment through population analysis to better target the allocation of resources to population need or target the allocation of patients to interventions (Lewis et al., 2013, Lewis, 2015, Lewis, 2010, Goodwin and Alonso, 2014).

3.4.3 What exists so far?

The literature related to IM primarily concerns the rationale and theoretical approaches with few worked examples. Impactibility criteria can be derived based on clinical judgement, rules or be data-driven including the use of thresholds (Shadmi and Freund, 2013, Lewis et al., 2011). Criteria can be inclusive or exclusive (Freund et al., 2012). The effectiveness of criteria varies therefore using criteria in combination may improve accuracy in predicting risk and impactibility (Shadmi and Freund, 2013, Freund et al., 2012).

IM can be used for population analysis for the purpose of patient selection, resource tailoring or resource allocation. Three examples of IM were found in the literature for patient selection with impactibility criteria based on disease and/or patient characteristics (Cohen et al., 2015, Buja et al., 2019, Stokes et al., 2017). Resource tailoring or resource allocation require an understanding of the drivers of risk and impactibility rather than just an assessment. One example of IM was found in the literature that sought to understand the drivers of impactibility by patient characteristics (DuBard and Jackson, 2018). Given the varied nature of these examples, meaningful meta-analysis or consolidation is not possible. The model used varies which may indicate that IM will develop as a selection of models in lieu of a single 'best' model type. The models have developed in different locations showing the commonality of the problem, to optimise health under constraints, but the variation in explanatory variables and outcomes of interests show its dynamic nature. In most cases the link to the PHM aims is weakly established or indirect.

The literature provides a cautious yet optimistic view of IM in the achievement of the PHM aims and navigating health system sustainability. A potential pitfall of IM comes from linking the impact (health outcomes) to the provision of an intervention (the access) which may deepen health inequalities. This requires PHM to be designed, and the control cycle managed, to actively reduce or monitor inequalities (Lewis et al., 2013, Lewis, 2010, Shadmi and Freund, 2013). It is recommended that these concerns be actively addressed to maximise the potential of IM (Lewis et al., 2013, Foley and Vale, 2017, Wharam and Weiner, 2012, Roland and Abel, 2012).

IM is part of population analysis, but it interacts with the intervention and the achievement of PHM aims, assessed in the evaluation. The literature does not adequately reflect this or the need for IM to be developed as an agile solution in order to successfully contribute to PHM.

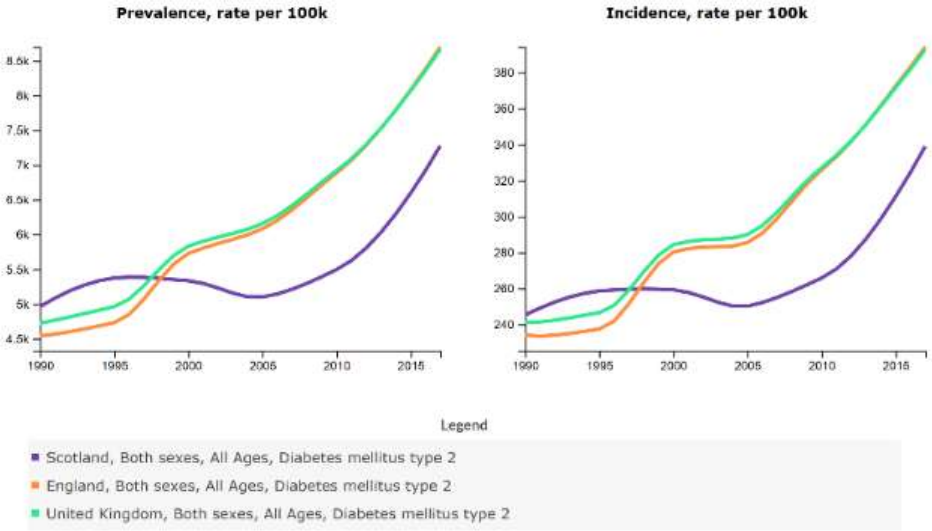
4 Proof of concept

The objective of the proof of concept was to explore the usefulness of Multi-state modelling ('MSM') for the purpose of IM. In addition, its purpose was to show how health inequalities could be actively monitored using MSM.

4.1 Case study

Type 2 Diabetes Mellitus ('T2DM') is used as a case study for the proof of concept. Chronic diseases are long-term conditions that cannot currently be cured but are controlled with a range of interventions and therefore contribute to demand-side pressures on a health system (Curry et al., 2005). T2DM "is a chronic metabolic condition characterised by insulin resistance .. and insufficient pancreatic insulin production, resulting in high blood glucose levels" (NICE, 2015, p.6). The incidence and prevalence of the disease has been increasing in the UK (IHME, 2017), as shown in Figure 4, and the disease burden is anticipated to increase in the future (Gatineau et al., 2014).

Figure 4: Prevalence and Incidence of T2DM in England, Scotland and UK 1990-2017



Images sourced from The Institute for Health Metrics and Evaluation (IHME, 2017)

4.2 Rationale for model choice

Multi-state modelling ('MSM') is useful for the purpose of IM as it "provides a natural and powerful framework" for describing and analysing life history processes (Cook and Lawless, 2018, p.xiii). The outputs contain insights to "the probability of moving from one state to another, and the duration of spells spent in specific states"(Cook and Lawless, 2018, p.2) which are useful for interpreting impactibility when related to a cost or health state. MSM is suitable for routine health data as it can accommodate common issues like intermittent observation and uninformative truncation or censoring.

Importantly MSM can be used for many objectives, as shown in Table 1. The nature of these objectives aligns, not only with the data-driven derivation of impactibility criteria for patient selection or resource tailoring, but also it can be used for resource allocation and intervention evaluation.

Table 1: MSM model objectives

1	increasing the understanding of the modelled process and of variation across individuals, groups or populations;
2	identifying and characterizing relationships between processes and covariates, or between two or more processes;
3	identifying risk factors associated with adverse outcomes;
4	assessing the effectiveness of individual or population level interventions; and
5	developing predictive models that can be used for activities such as resource allocation, policy formulation and patient management

Sourced from Cook & Lawless (Cook and Lawless, 2018, p.12)

4.3 Applying the model

An individual's life history is considered as "represented by time spent in states and movement between states" (Macdonald et al., 2018, p.256). An individual can occupy one of the possible "'states' at any given time and moves between states at random times governed by the probabilistic model" (Macdonald et al., 2018, p.xv). To apply MSM, a state space and transition intensity matrix must be defined, explanatory variables chosen, and life history data sourced to populate the matrix[5].

4.3.1 State space

In this proof of concept, the management of the outcome of interest is related directly to the management of the disease and therefore the PHM aim of improving health status. Two models are defined based on measures used in the T2DM care guidelines (NICE, 2015, Healthcare Improvement Scotland, n.d.). Haemoglobin A1c ('HbA1C') is a clinical measure used for diagnosis and ongoing disease management; it is a measurement of blood glucose levels in the last 3 months (NICE, 2015, Diabetes.co.uk, 2019). Body Mass Index ('BMI') is a modifiable risk factor for T2DM before diagnosis and a target of lifestyle interventions after (WHO, n.d., NICE, 2015). To overcome issues of short-term variation when using raw biomarker values, states are defined in terms of ranges (Cook and Lawless, 2018) included in Appendix 1. A deceased state is added to both models, as an absorbing state, to account for mortality risk during the period, as shown in Figure 5 and 6.

Figure 5: BMI model state space

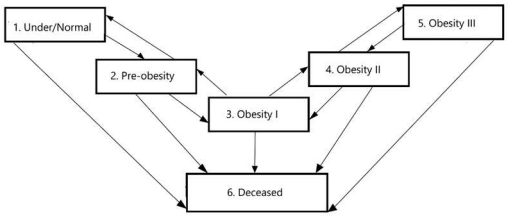
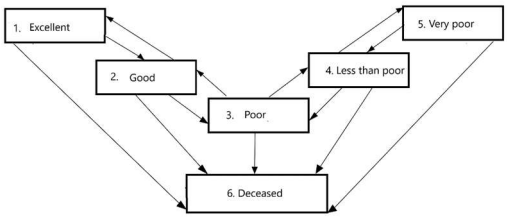


Figure 6: HbA1c model state space



4.3.2 Transition intensity matrix

Transition intensities, μ_x^{jk}, are the forces to which an individual is subject; keeping the individual in the current state or transitioning to another state[6]. Data is analysed to populate the transition intensity matrix, Q[7]. Transitions that are not possible in the process are set to zero, as shown in Equation 1. The structure of the matrices is the same for both models as there is the same number of states and allowable movements between states.

Equation 1: Transition intensity matrix

$$Q(t) = \begin{bmatrix} \mu_x^{11} & \mu_x^{12} & 0 & 0 & 0 & \mu_x^{16} \\ \mu_x^{21} & \mu_x^{22} & \mu_x^{23} & 0 & 0 & \mu_x^{26} \\ 0 & \mu_x^{32} & \mu_x^{33} & \mu_x^{34} & 0 & \mu_x^{36} \\ 0 & 0 & \mu_x^{43} & \mu_x^{44} & \mu_x^{45} & \mu_x^{46} \\ 0 & 0 & 0 & \mu_x^{54} & \mu_x^{55} & \mu_x^{56} \\ 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

[5] A summary is provided here. Further information can be sourced from the original research ROBERTSON, J. 2019. *Impactibility modelling: A literature review and proof of concept using multi-state modelling.* Master of Public Health Dissertation, University of Edinburgh.

[6] The transition intensity is the instantaneous force, μ_x^{jk}, at age x from state j to state k.

[7] The *msm* package in R is used for computation JACKSON, C. 2007. Multi-state modelling with R: the msm package. *Cambridge, UK*.

4.3.3 Explanatory variables

Testing for an explanatory variable is the first step in deriving impactibility criteria. In a MSM, an explanatory variable can be added to the model to test if transition rates vary significantly by that factor.

The PHM aim of reducing health inequalities is built directly into this proof of concept by testing the socio-economic indicator, Scottish Index of Multiple Deprivation ('IMD'), as an explanatory variable for impactibility. IMD is known to be correlated with health inequalities (Public Health England, 2017a, Scottish Government, 2018). Two IMD groups are created, most deprived including IMD deciles 1 to 5 and least deprived including deciles 6 to 10.

If transition rates toward unhealthier ranges of BMI and HbA1c (progression through states) are higher or if transition rates toward healthier ranges of BMI and HbA1c (regression through states) are lower – then a patient would have lower impactibility. By testing if transition rates vary by IMD, an awareness is brought to the implications of IM for health inequalities. The use of IM for patient selection has the potential to deepen health inequalities by reducing access where there is a disparity in health outcomes (Lewis et al., 2013, Lewis, 2010, Lewis, 2015, Foley and Vale, 2017, Stokes et al., 2018, Wharam and Weiner, 2012, Shadmi and Freund, 2013, Fleming et al., 2017). However, resource tailoring and allocation could reduce inequalities by more effectively matching interventions to individual.

4.3.4 Data

Individual life history data is required to populate the transition intensity matrix. There are a number of BMI or HbA1c observations recorded in a patients' data and these are considered as events in MSM.

A longitudinal retrospective cohort was extracted from the Scottish Diabetes Epidemiology database ('SCI'). Access to SCI was agreed for research purposes through the University of Edinburgh. The SCI database is a population disease register for diabetes in Scotland sourced from linked routine primary and secondary care health data with good coverage (SCI-DC, n.d). The 2016 SCI database is the most recent available cleaned version which contains anonymised individual medical event and demographic life history data for lives with T2DM[8].

To account for confounding variables, that may cause spurious association, the model would need to be more complex than is within scope. In the spirit of a proof of concept and for model parsimony, simplifying criteria were applied to create a more homogeneous test cohort. In summary, a multi-state model was applied to model transition rates under 'current practice' for T2DM interventions in the first 5-years of diagnosis for ages diagnosed from 40 to 49 inclusive between 2011 and 2016.

Variation in the ability to control HbA1c or keep a healthy BMI following diagnosis may vary by gender, age, duration, morbidity. There was little variation in the distribution of these factors by IMD group that would confound the explanatory variable test (Robertson, 2019). There is likely to be smoking prevalence bias by IMD group however, the evidence for the impact is mixed so it is assumed for the purpose of the proof of concept that there is no impact on BMI or Hba1C[9] (McCulloch et al., 2002, Kar et al., 2016). It is assumed that there is no bias in medical adherence by IMD group under free healthcare and affordable prescriptions. It is not possible to check due to poor data coverage, but there may be bias in the distribution of ethnicity by IMD.

The full dataset is split into a training (75%) and validation (25%) dataset using uniform distribution random numbers.

[8] The cleaned data is considered to be high quality with good coverage. No further adjustments were considered necessary for the purpose of a proof of concept.

[9] This assumption would require further development to expand the model beyond a proof of concept.

5 Results and analysis

5.1 Data Summary

In the full dataset, a total of 11,240 patients were included in the BMI model and 13,364 in the HbA1c model. Approximately 60% of the lives in each dataset are in the most deprived IMD group. The median number of observations per patient is 4 for BMI and 6 for HbA1c in a 5-year period. The number of observations recorded is similarly distributed by IMD group. This implies that one group is not contributing more transitions to the model than the other.

5.1.1 Observed transition

Table 2 and Table 3 shows the observed transitions in the training dataset. This can be read as 25 lives transitioned from a state of Under/Normal weight to Deceased. There were 7,996 observations recorded as Obesity 1 at one observation and recorded as Obesity 1 at the following observation.

Table 2: BMI observed transitions

State	To					
From	Under/ Normal	Pre-obesity	Obesity 1	Obesity 2	Obesity 3	Deceased
Under/Normal	2,000	187	2	0	0	25
Pre-obesity	225	4,931	510	1	0	35
Obesity 1	2	614	7,996	517	1	31
Obesity 2	1	2	700	6,314	403	23
Obesity 3	0	0	8	560	7,259	29

When most of the observations lie on the diagonal of the matrix, i.e. not changing state, the process is said to be more stationary. The BMI process is more stationary than HbA1c, as seen in Table 3.

Table 3: HbA1c observed transitions

State	To					
From	Excellent	Good	Poor	Less than poor	Very poor	Deceased
Excellent	10,580	2,232	653	493	374	57
Good	2,233	3,261	1,456	1,217	762	20
Poor	715	1,308	1,433	1,389	831	12
Less than poor	761	1,308	1,471	3,166	2,191	19
Very poor	794	935	969	2,905	10,123	50

5.2 Output rates

From the defined state space, transition intensities, μ_{x+t}^{jk}, are inferred from the observed data and are the basis for all other output rates[10].

5.2.1 Transition intensities

Without consideration for covariates, the estimates of transition rates, μ_x^{ij}, are shown in Table 4 and Table 5 on page 13, along with the a 95% confidence interval. The final column indicates the force of mortality from each state; however, these are under-estimated by the model when compared to the Scotland Life tables, especially for the HbA1c model (Office of National Statistics, 2018).

[10] High level checks have been performed on these results however, a full independent check was not permissible as part of the Masters research.

An individual who is Pre-obesity is 2.5 (0.015/0.06) times more likely to move to Obesity 1 than Under/Normal BMI. Those in Obesity 1 and 2 are only a little more likely to lose weight than gain weight.

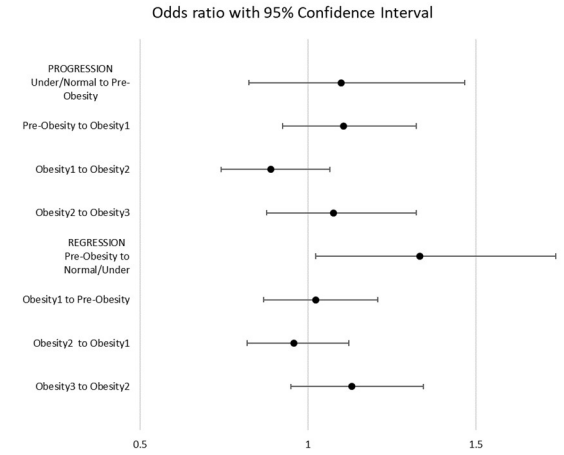
An individual who has Good HbA1c is 2.5 (0.409/0.165) times more likely to move to Poor than Excellent HbA1c. Those with Poor control are almost equally likely to progress or regress. Those with Less than poor HbA1c are twice as likely to improve HbA1c control to Poor than progress to Very Poor.

5.2.2 Transition intensities by IMD group

Neither model resulted in a statistically significant difference in transition rates by IMD. The odds ratio, with 95% confidence interval, represents a comparison of the transition rates of the least deprived group to the baseline most deprived group. These are grouped into progression (worsening) or regression (improving) BMI and HbA1c states for interpretation for impactibility.

The confidence interval for the odds ratio generally cross 1 for BMI, as shown in Figure 7: Odds ratio on transition rates for IMD covariate – BMI ModelFigure 7. For regression from Pre-Obesity to Normal/Under the least deprived group have a higher transition intensity (greater impactibility) than the most deprived, however the confidence interval is wide.

Figure 7: Odds ratio on transition rates for IMD covariate – BMI Model



The odds ratios significantly different to 1, shown in Figure 8, provide a mixed message in the HbA1c model; the least deprived group has lower transition intensities from Poor to Less than poor (higher impactibility), and lower transitions from Good to Excellent and Less than poor to Poor (lower impactibility) but higher transition from Very poor to Less than poor (high impactibility).

Figure 8: Odds ratio on transition rates for IMD covariate – HbA1c Model

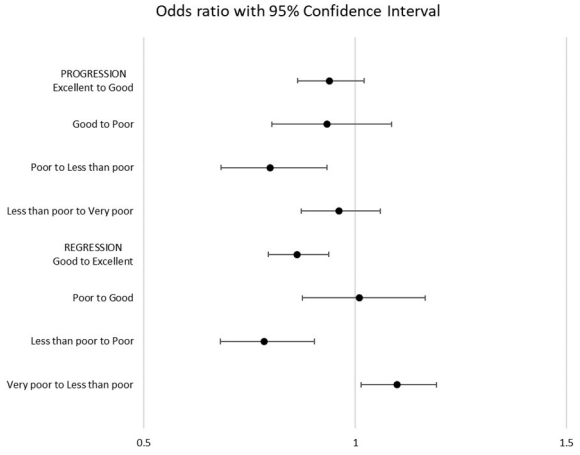


Table 4: BMI model transition intensities

State	**To**					
From	Under/ Normal	Pre-obesity	Obesity 1	Obesity 2	Obesity 3	Deceased
Under/ Normal	-0.018 *(-0.021, -0.016)*	0.016 *(0.014, 0.019)*	-	-	-	0.002 *(0.001, 0.003)*
Pre-obesity	0.006 (0.006,0.007)	-0.022 (-0.024,-0.021)	0.015 *(0.014, 0.016)*	-	-	0.001 *(0.001, 0.001)*
Obesity 1	-	0.012 *(0.011, 0.012)*	-0.022 (-0.023,-0.021)	0.010 *(0.009, 0.011)*	-	0.000 *(0.000, 0.001)*
Obesity 2	-	-	0.018 *(0.017, 0.020)*	-0.030 (-0.031,-0.028)	0.011 *(0.010, 0.012)*	0.000 *(0.000, 0.001)*
Obesity 3	-	-	-	0.015 *(0.014, 0.016)*	-0.016 (-0.017,-0.015)	0.001 *(0.000, 0.001)*

Table 5: HbA1c model transition intensities

State	**To**					
From	Excellent	Good	Poor	Less than poor	Very poor	Deceased
Excellent	-0.080 *(-0.083, -0.076)*	0.079 *(0.076, 0.082)*	-	-	-	0.001 *(0.000, 0.001)*
Good	0.165 (0.158,0.171)	-0.574 (-0.605,-0.545)	0.409 *(0.381, 0.440)*	-	-	0.000 *(0.000, 0.002)*
Poor	-	0.672 *(0.627, 0.720)*	-1.402 (-1.463,-1.343)	0.729 *(0.675, 0.788)*	-	0.000 *(0.000, 0.003)*
Less than poor	-	-	0.521 *(0.486, 0.559)*	-0.755 (-0.793,-0.719)	0.233 *(0.223, 0.244)*	0.000 *(0.000, 0.001)*
Very poor	-	-	-	0.180 *(0.173, 0.187)*	-0.181 (-0.188,-0.174)	0.001 *(0.000, 0.001)*

5.2.3 Transition probabilities

Estimated transition probability for 12- and 60-months for BMI are provided in Table 6 and Over a 5-year period the probabilities of BMI changing states are higher, as shown in Table 7. For example, an individual with a BMI of Obesity 2 has a 32% chance of remaining in the same state over a 5-year period, compared to 20% of progressing to Obesity 3 and 44% chance of regressing to a lower BMI.

Table 7. An individual with a BMI of Obesity 2 has a 72% chance of remaining in the same state in a 1-year period, compared to 10% of progressing to Obesity 3 and 16% chance of regressing to Obesity 1.

Table 6: BMI model transition probabilities (%) - 12 months

State	To					
From	Under/ Normal	Pre-obesity	Obesity 1	Obesity 2	Obesity 3	Deceased
Under/Normal	80.8	15.5	1.4	0.1	0.0	2.3
Pre-obesity	6.1	78.1	13.9	0.8	0.0	1.0
Obesity 1	0.4	10.7	78.8	8.9	0.6	0.6
Obesity 2	0.0	1.1	16.3	72.0	9.9	0.6
Obesity 3	0.0	0.1	1.5	13.9	83.7	0.8

Over a 5-year period the probabilities of BMI changing states are higher, as shown in Table 7. For example, an individual with a BMI of Obesity 2 has a 32% chance of remaining in the same state over a 5-year period, compared to 20% of progressing to Obesity 3 and 44% chance of regressing to a lower BMI.

Table 7: BMI model transition probabilities (%) – 60 months

State	To					
From	Under/ Normal	Pre-obesity	Obesity 1	Obesity 2	Obesity 3	Deceased
Under/Normal	39.5	34.0	14.3	2.5	0.4	9.3
Pre-obesity	13.5	41.6	30.8	7.4	1.7	5.0
Obesity 1	4.4	23.7	45.2	17.5	5.9	3.3
Obesity 2	1.4	10.5	32.2	32.1	20.6	3.2
Obesity 3	0.3	3.4	15.2	28.9	48.5	3.7

Table 8 shows that an individual having an Hba1c of Less than poor has a 19% chance of remaining in the same state in a 1-year period, compared to 27% of progressing to a worse HbA1c and 52% chance of regressing to better HbA1c.

Table 8: HbA1c model transition probabilities (%) - 12 months

State	To					
From	Excellent	Good	Poor	Less than poor	Very poor	Deceased
Excellent	57.2	17.4	8.3	9.1	7.3	0.7
Good	36.3	18.9	11.3	15.3	17.6	0.6
Poor	28.5	18.6	12.1	17.5	22.7	0.6
Less than poor	22.4	18.0	12.5	19.1	27.4	0.6
Very poor	13.8	16.0	12.5	21.2	35.8	0.7

Over a 5-year period the probabilities of HbA1c improving, are higher as shown in Table 9. For example, an individual with a HbA1c of Less than poor has a 14% chance of remaining in the same state over a 5-year period, compared to 19% of progressing to worse HbA1c and 63% chance of regressing to better HbA1c. At this stage the results for the HbA1c model may not be as expected.

This is due to a lack of accuracy in accommodating a duration affect in the extreme HbA1c ranges of Excellent and Very poor. This inaccuracy is shown in the fit to historic data in Section 5.3.

Table 9: HbA1c model transition probabilities (%) - 60 months

State	To					
From	Excellent	Good	Poor	Less than poor	Very poor	Deceased
Excellent	36.2	17.2	10.4	14.5	18.6	3.2
Good	35.8	17.2	10.4	14.6	18.9	3.1
Poor	35.6	17.2	10.5	14.7	19.0	3.1
Less than poor	35.4	17.2	10.5	14.7	19.1	3.1
Very poor	35.1	17.1	10.5	14.8	19.3	3.2

5.2.4 Total length of time

The estimated total length of time spent in each state is forecast, for an individual starting in each state, over 60-months and shown in Table 10 and Table 11.

A life diagnosed with a Pre-obesity BMI is expected over a 5-year period to have roughly half a year in Under/Normal weight, 3 years in Pre-obesity and 1 year with a BMI in Obesity 1.

Table 10: BMI model - total length of time in state over 60-month period

State	To					
From	Under/ Normal	Pre-obesity	Obesity 1	Obesity 2	Obesity 3	Deceased
Under/Normal	38.0	14.6	3.8	0.5	0.1	3.1
Pre-obesity	5.8	37.3	13.1	2.1	0.3	1.5
Obesity 1	1.2	10.1	38.4	7.8	1.6	1.0
Obesity 2	0.3	2.9	14.4	32.5	9.1	0.9
Obesity 3	0.0	0.6	4.1	12.7	41.4	1.1

An individual with Poor HbA1c is expected over a 5-year period to have roughly 1.5 years in Excellent, under 1 year in Good, just over half a year in Poor and under 1 year in Less than poor and Very poor.

Table 11: HbA1c model - total length of time in state over 60-month period

State	To					
From	Excellent	Good	Poor	Less than poor	Very poor	Deceased
Excellent	28.7	10.0	5.4	6.9	7.9	1.0
Good	20.9	12.3	6.8	8.8	10.4	0.9
Poor	18.6	11.1	7.6	10.0	11.8	0.9
Less than poor	17.0	10.4	7.1	11.2	13.4	0.9
Very poor	15.0	9.4	6.5	10.3	17.8	1.0

5.3 Accuracy

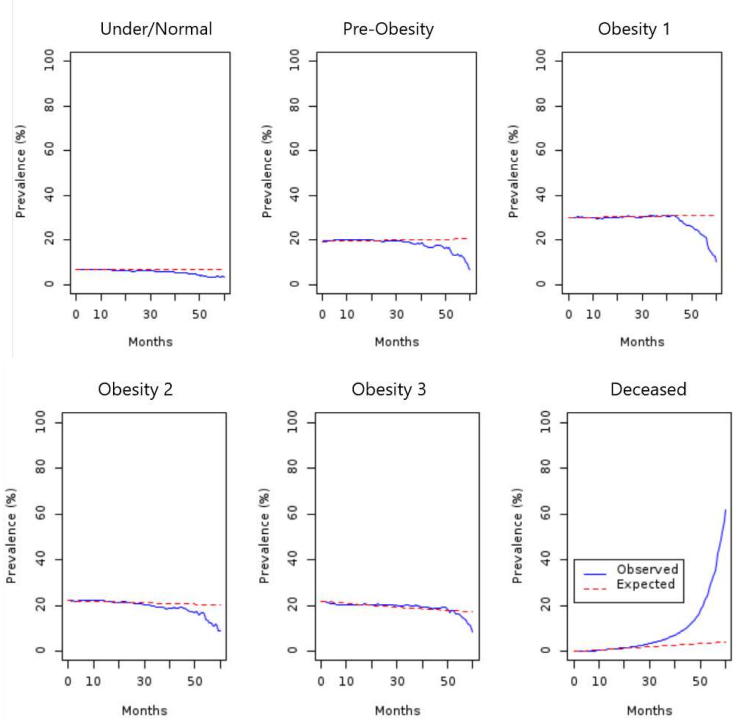
The model is tested for its fit to the historic data using the training dataset and predictive accuracy using the validation dataset in an Expected vs Observed analysis.

5.3.1 Fit to historic data

The transition rates are used to generate expected transitions which are compared to the observed transitions in the training dataset.

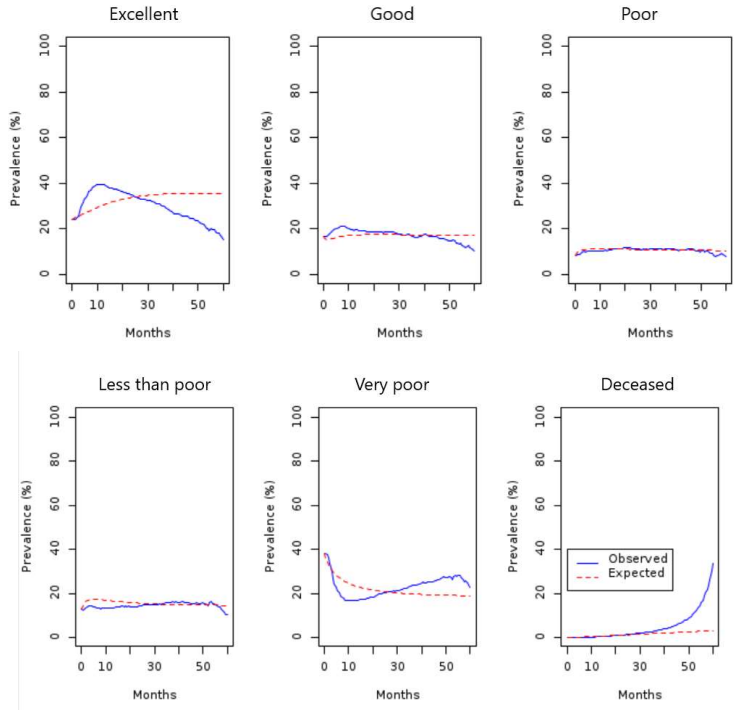
The BMI model fit to the historic data is fair until 50-months, as shown in Figure 9. The model is greatly underestimating the number of deaths which is causing an overestimation in other states. The effect of the inaccuracy accumulates with time as seen after 50-months.

Figure 9: BMI model Observed vs Expected - historic fit



Similarly, the HbA1c model is greatly underestimating the number of deaths, as shown in Figure 10 under the Deceased state. However, the model is also overestimating Excellent and underestimating Very poor at longer time periods. This is due to a short-lived effect, i.e. durational, seen in Excellent and Very poor states at around 10 months which is not being captured by the model.

Figure 10: HbA1c model Observed vs Expected - historic fit



5.3.2 Predictive accuracy

The transition rates are used to generate expected transition based on the validation dataset and compared to the observed transitions. The areas of weakness are similar to those shown in the historic fit.

6 Conclusions

Impactibility criteria have not been established as part of this proof of concept. The results are not considered generalisable, nor do they provide medical insight. However, this proof of concept does explore the usefulness of Multi-state modelling ('MSM') for the purpose of Impactibility modelling ('IM').

MSM may be a useful tool for the purpose of IM for several reasons: it is suitable for the analysis routine health data; it can be used for multiple objectives which align to IM use, and; it provides insight into the time spent in different states from which impactibility can be inferred when related to cost or health status.

The model design has been directly related to the PHM aims by linking the outcome of interest to BMI and HbA1c. Control of HbA1c is considered to reduce the impact of diabetes and the risk of its complications, i.e. sequalae (NICE, 2015, Weber and Neeser, 2006). Control of BMI is considered to reduce the risk of diabetes before and is a target of lifestyle interventions after diagnosis (NICE, 2015). Therefore, impactable lives could be considered as those who: regress through states by either decreasing BMI or HbA1c; or lives who spend longer in healthier states such as lower BMI states or controlled HbA1c state.

Creating an impact on these measures would directly improve health status and, is indirectly assumed to reduce costs. The many sequalae of T2DM require high health service utilisation (NICE, 2015, Weber and Neeser, 2006, NHS England, 2014). The risk of sequalae is assumed to decrease with improved HbA1c and BMI (NICE, 2015, NHS Highland, 2010, Diabetes.co.uk, n.d.) and therefore the utilisation and costs would reduce in proportion. This assumption is made explicitly and would need to be evaluated.

Patient experience would require separate evaluation.

A barrier to successful IM implementation is the concern regarding inequalities (Huckel Schneider et al., 2017). This simplified model was not able to show that transition rates vary by IMD, a variable associated with health inequalities. However, it is not proposed that this is taken in evidence against these concerns but shows how a model can be created to directly assess if impactibility varies by variables associated with health inequalities during its design and ongoing evaluation. Ongoing monitoring and evaluation of the ramification of IM is promoted in the literature.

Testing an explanatory variable is a step in deriving impactibility criteria. In this proof of concept, impactibility criteria were not derived however odds ratios produced by MSM can test the significance of explanatory variables for that purpose.

Impactibility assessed in terms of BMI, a modifiable risk factor, highlights the importance of earlier stages of prevention; as at an individual level the drivers of impactibility may be "highly resistant to change"(Stokes et al., 2018, p.249) as evidenced by the relative stationarity in the BMI process. For chronic diseases like T2DM there is a "need to look beyond simply providing medical care, toward services which address patients' broader social and behavioural health needs" (Sterling et al., 2018, p.2018). The results of IM analysis could be used to promote and target earlier stages of prevention and work across the wider health system. For example, the age of screening could be brought forward where there is a lack of impactibility.

Research will be progressed in this area, including improvements to this MSM model for T2DM.

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Appendix 1: Further model information

BMI state space

For BMI, the well-established ranges shown in Table 12, are adopted for the model states (WHO, n.d.).

Table 12: BMI categorisation by nutritional status

BMI	Nutritional Status
Below 18.5	Underweight
18.5 – 24.9	Normal weight
25.0 – 29.9	Pre-obesity
30.0 – 34.9	Obesity Class I
35.0 – 39.9	Obesity Class II
40 and above	Obesity Class III

Categorisation as provided by World Health Organisation(WHO, n.d.)

The underweight category was grouped with normal weight due to a lack of data, as represented in Figure 5, to create a state space.

HbA1c state space

Once diagnosed, ranges of HbA1c are used to categorise the management of the chronic condition, as shown in Table 13.

Table 13: HbA1c categorisation by diabetes control

HbA1c %	mmol/mol	Diabetes control
Below 5.9	31 - 49	Excellent
5.9 – 6.6	50 - 55	Good
6.7 – 7.2	56 – 60	Poor
7.3 – 8.6	61 – 70	Less than poor
8.7 and above	71 +	Very poor

Categorisation from Southend NHS (Southend University Hospital, 2011)

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