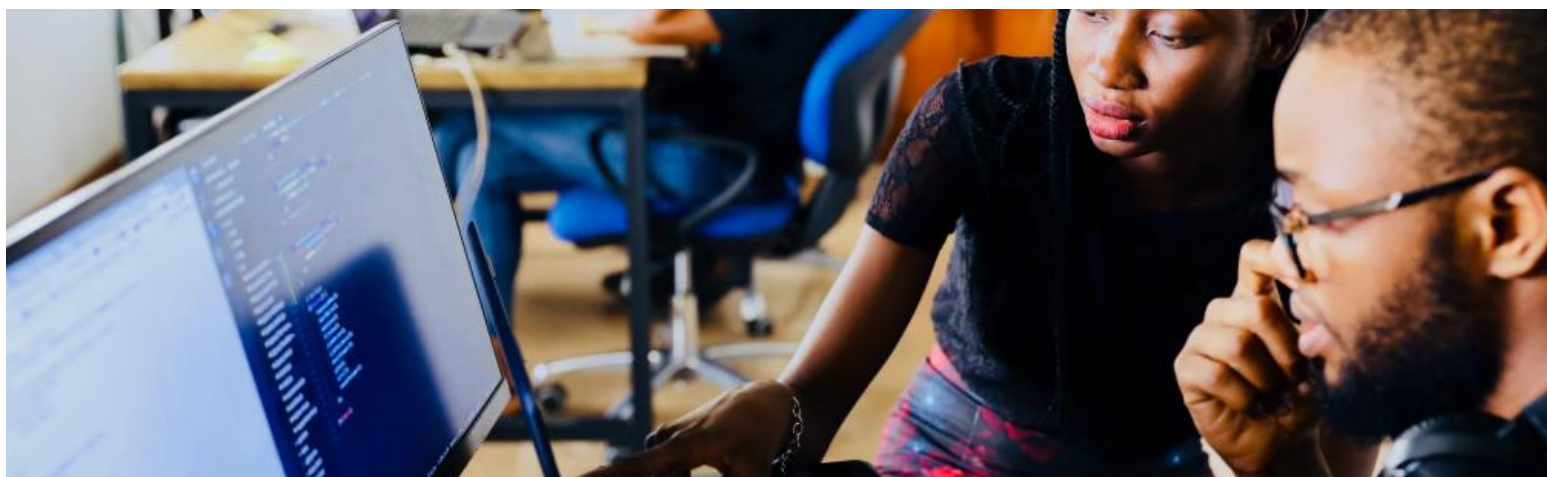


SynPath diabetes module

Specification for an intelligence layer



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Introduction

1.1 Context

Synthetic records techniques could give us the ability to create realistic patient records which hold the same properties and characteristics as sensitive patient data but are not identical to it. This would allow us to answer analytical questions without using individual patient data. Agent-based modelling is one way of creating longitudinal patient records. SynPath is a modelling framework for creating synthetic patient records in a simulated patient pathway (NHSX 2021j). This project is based on building the intelligence layer for the first module within the SynPath framework.

1.2 Aims and objectives

The main aim of the project was to generate a specification of what is needed to build an intelligence layer that works with SynPath and outputs realistic synthetic records. We used the example of the NHS England type 2 diabetes pathway as an example to try and do this.

1.3 Literature review

We used a range of literature for this project. There were key learnings to take from models in health economics, transport, and evacuation simulations.

Table 1: Literature review summary

| Model type | Examples | Learnings |
|---|--|---|
| Health economics simulation models in diabetes | UKPDS (2020) NIHR SPHR Diabetes prevention model (Squires et al., 2016) Day model of Diabetic retinopathy (2013) | Key stages of model building Key elements to include in the pathway Best practice for conceptualising a pathway |
| Simulation models in transport | Bus networks (Xie, Ma et al., 2014) Developments in the field (review)(Kagho, Balac et al., 2020) | Good modelling of ‘timing’, e.g., whether agents optimise their time leaving the house on a commute (Bottleneck and corridor modelling) |
| Evacuation models | Modelling evacuation using a neural network (Tkachuk, Song et al., 2018) | Adapting agents that respond to their environment in a model using a neural network |

In health economics, the Mount Hood Network holds an annual challenge for economic simulation models for diabetes, for example (Mount Hood Diabetes Challenge 2020). These models can often use a discrete event simulation (Delli Gatti 2018), showing the status of patients moving through a model in ‘cycles’ with limited interaction with their environment (HERC Oxford 2020; Thomas et al. 2017; Hayes et

al. 2013). This gave us a good idea of how to develop the conceptual model (Squires et al. 2016) of the diabetes pathway and to conceptualise clinical processes.

Models from the computer science discipline on type 2 diabetes pathways offer more of an agent-based approach but less focus on the resource impacts of complex behaviours and interactions (Paranjape, Wang, and Gill 2018). They also, however, offer approaches to incorporate models of the disease itself (Ackerman et al. 1965; Wu 2005), learning of positive behaviours to learn self-management within the patient-agent (Paranjape, Wang, and Gill 2018), and improvements in service provision within the clinical pathway itself (hash.ai 2021c). It was also helpful to look at the modelling of movement through environments from transport (Kagho, Balac, and Axhausen 2020) and evacuation modelling as they show how to portray bottlenecks and 'corridor problems' (Xie et al. 2014). These approaches may be helpful for the modelling of patient movement between services due to the way they look at the effects of limited capacity.

This use of SynPath for the diabetes module includes key elements from both approaches. The economics examples contribute to conceptual and structural approaches, and the computer science models more knowledge on modelling individual and system behaviour to portray learning and change over time. After this project, we hope the learning can then be adapted to pathways in other diseases to model capacity and resource impacts across the NHS. The hope is that this is done both within the NHS and by other researchers. The first module aimed to build in a digital transformation element to the diabetes pathways, using data from clinical trials and observational studies (Whaley et al. 2019; Murray et al. 2019).

1.4 Model summary

This model is meant to show a simulation of patients in the NHS through the type 2 diabetes pathway. The model was developed using Python 3.8.10 in VSCode.

The model takes place in a fictional local area with hospitals providing outpatient and inpatient services, GP practices and community healthcare services. The focus will be the interactions and costs provided in the primary, community and secondary care settings of the diabetes pathway. The model was planned to run for ten years with ten thousand patients with an element of pathway optimisation. The final model was run with over 800 patients for one year, and patients who reached kidney and liver services were referred to the GP due to the complexity of those pathways and the time constraints of the project.

Rather than a decision being made by a patient-agent, the decision about the next care setting the patient will visit is made by the health care professional in the care setting the patient is currently at. This means, in practice, that the interaction occurring within a care setting (model environment) contains a set of probabilities for the possible next environments that we have allocated within this project while constructing the pathway. In future, any intelligence algorithm would set the destinations (and possibly waiting times) for arriving at the next environment.

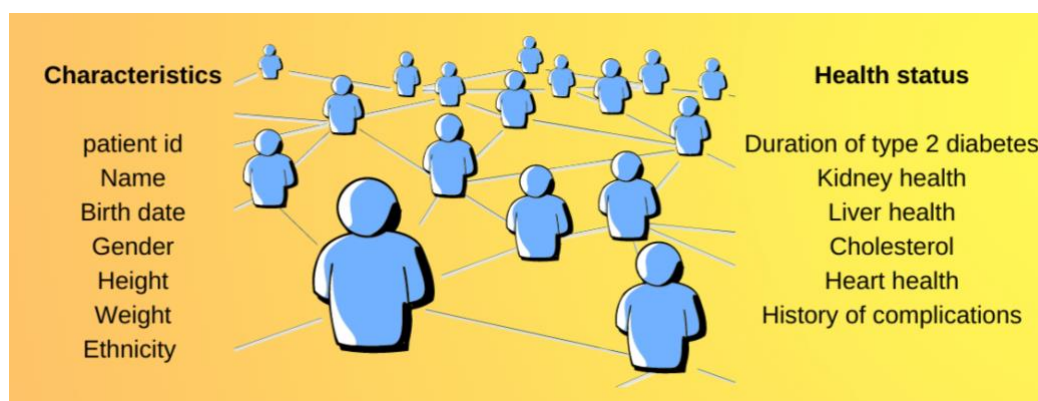
The rest of the report will describe how the patients and environments were populated, but not in particular detail as the original SynPath report has this. The following section will discuss the structure and contents of the intelligence layer. We then will lay out a guide (in the Appendices) on how to consider using this work.

Pathway components

2.1 Patients

Patients were created from scratch, using a Bayesian network method in R (Tucker et al. 2020; Kaur et al. 2021). To do this, we used the 'bnlearn' package (Scutari 2020; Scutari and Denis 2021). Ideally, if the model were to be completed and validated, patients would be synthesised (not using patient data directly) from a real patient dataset such as the Clinical Practice Research Datalink (CPRD) (CPRD 2021). This would mean the starting point for patient characteristics would be more accurate. The patients were then added to the model using a JSON format (Appendix 1). Further details that could improve the patients include the prevalence of diabetes and further details from the Health Survey for England (NHS Digital 2019). Relevant health status characteristics for the population of people with type 2 diabetes were adapted from UKPDS (HERC Oxford 2020), model requirements and components that were key to the interaction with certain services (e.g. smoking status).

Figure 1: Patient agent components



For the key changes that occur within the patient, this needs to be set up as part of the intelligence layer. We included pregnancy, smoking and glucose updates in draft form to reflect how these might be included in the intelligence layer. To complete the module data on mental and health conditions and learning disabilities need to be added to synthetic patient records in the model. This will be to allow the model to respond to these pre-existing conditions while optimising for the three key outcomes.

2.2 Environments

Services provided in the NHS to type 2 diabetes patients were added as model environments. The diabetes pathway that will be used in the model was adapted from several sources: the Diabetes RightCare pathway (NHS England 2018); the conceptual modelling paper for the NIHR SPHR Diabetes model (Squires et al. 2016); the NICE type 2 diabetes pathway (NICE 2020). Once the service diagram was prepared it was completed with help from expert opinion on services used by type 2 diabetes patients.

Table 2: Environments and interactions included in the pathway

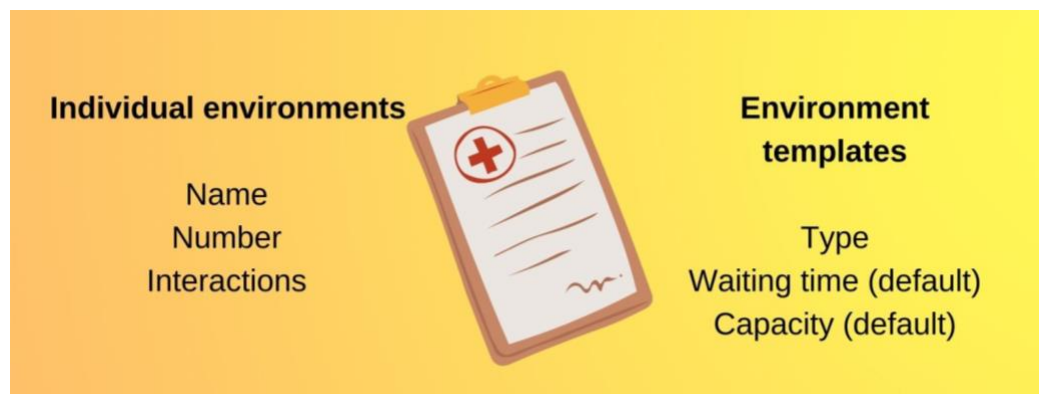
| Type of service | Interactions |
|---------------------------------------|--|
| GP | Blood test, Metformin prescription, The second line of therapy prescription, The third line of therapy prescription, Insulin prescription, Management of high risk of diabetes, Exercise prescription, Prediabetes diagnosis Type 2 diabetes diagnosis Glucose management Annual health check Hypertension management Complications management Glucose clinic |
| Structured education | Group education Online lifestyle education Digital Diabetes Prevention Programme (DDPP) |
| Learning disability service | Adjustments to care |
| Mental health services | Psychological assessment IAPT service Community mental health for SMI |
| Specialist antenatal diabetes service | Maternity specialist care |
| Maternity service | Maternity care |
| Smoking cessation service | Smoking cessation |
| Community footcare service | Preventative foot care Management of foot care |
| Eye care service | Retinopathy screening Aflibercept prescription |
| A&E | Initial diagnosis Acute event treatment |
| Inpatient services | Review and consultation Bed stay for hypoglycaemia Bed stay for hyperglycaemia Bed stay for lower limb episode Enhanced independence Retinal procedure Amputation |
| Outpatient services for diabetes | Outpatient consultation for type 2 diabetes |
| Outpatient urology services | Outpatient consultation for erectile dysfunction |
| Younger adults diabetes service | Intensive glucose control CVD risk reduction |
| Outpatient foot clinic | Preventative foot care Management of foot care |

| | |
|-------------------|------------------|
| Dietician | Nutrition advice |
| Kidney specialist | Refer to GP* |
| Liver specialist | Refer to GP* |

**Note: Kidney and liver pathways were not developed as part of this model.*

The primary output of the model is the service use of the patient agents.

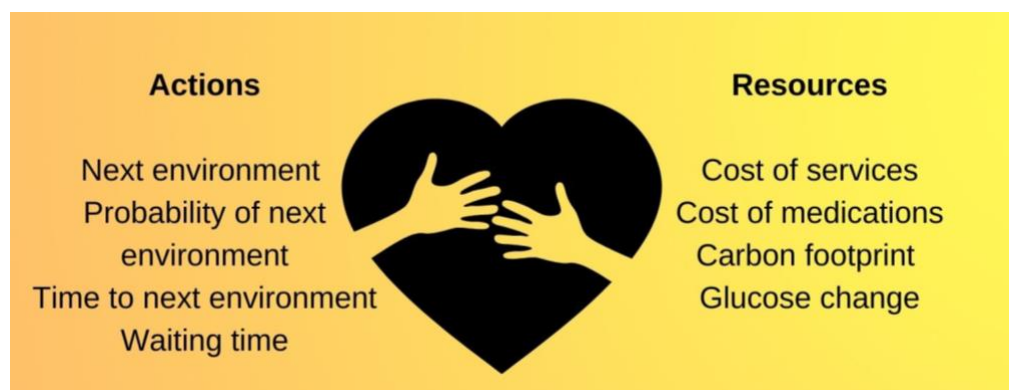
Figure 2: Environment components



2.3 Interactions

Interactions such as diabetes diagnosis and medication prescription were set up across the environments. Interactions were written with waiting times for the current environment, destinations of the next environment, and the cost, carbon and glucose impact of the current service being used. Environments were given a number, type, interactions. Environment types (source code) were given a dummy capacity and waiting time.

Figure 3: Interaction components



Each of the interactions was populated with details of the service supplied, its resource impact and the probability of moving to another service in the next simulation step. Data on types of medication used in the pathway was collected from NICE and Open Prescribing (National Institute for Health and Care Excellence (NICE) 2021, 2017; EBM DataLab 2021b, 2021a). Data on the services to be included in the diabetes pathway were collected from NICE, PHE, NHS England and expert opinion (National Institute for Health and Care Excellence (NICE) 2021; Public Health England (PHE) 2018/19; NHS England 2017). Data on resource impacts (cost and carbon) was collected from NHS England and academic sources (Personal

Social Services Research Unit (PSSRU) 2019; NHS England 2020a, 2020b; Grant 2015). Further details that could improve the accuracy of the inputs for the interactions include accurate waiting times (NHS England 2021), and replacing glucose impacts with EQ-5D impacts from the literature (Solli, Stavem, and Kristiansen 2010).

Intelligence

3.1 Capacity

In the SynPath model (version 1.0.0), one patient runs through at a time, with the plan for the simulation to check the capacity of the next environment after the simulation and learning have run to establish whether sending the patient agent on would mean that the next environment goes over its capacity. The value for the capacity of each environment type is set in the environment templates. The manager module runs the simulation, storing output for each step of the patient simulation in a directory. A planned update for SynPath will mean that more than one patient runs through at a time.

3.2 Outcomes

In our example, the relevant outcomes (inputs for learning) were:

- a) a patient health outcome - Hba1c (blood glucose test for type 2 diabetes)
- b) an efficiency outcome - cost (£s in 2018/19), and
- c) a system desire, reduction of carbon impacts (CO²kg)

Future intelligence layers could include different outcomes, more relevant to another disease area and might weigh them against each other.

3.3 Types of learning

The learning algorithm will be located within the intelligence module of the model alongside planned modules for capacity, calculation of cumulative outcomes, the logic for possible interactions, and a module that explains disease progression (see Appendix 4). The main function of the learning is to optimise the outcomes of the system, it does this by minimising cost, carbon emissions produced in services and reflecting improved levels of glucose control among patients.

We considered four types of learning. These were stochastic gradient descent, reinforcement learning, Monte Carlo tree search and A* search. In the beginning, we considered stochastic gradient descent (Ciaburro 2020; Geron 2019) with a cost function of cost, carbon and glucose. Then we also explored the potential of using a q-learning approach (hash.ai 2021b), which is where a quality score is assigned to each move along with the model and the model learns to move in a way that ensures that it is rewarded not penalised (hash.ai 2021b). Monte Carlo tree search was considered due to the complexity of the pathway but was difficult to adapt due to the adversarial, multidimensional approach of many examples (hash.ai 2021a). Finally, we considered A* search, an algorithm that picks the shortest route to a winning goal (Hart, Nilsson, and Raphael 1968), but it was difficult to define the goal of the SynPath model in this way.

Table 3: Types of learning

| | Description | Advantages | Disadvantages |
|---|--|---|--|
| Stochastic gradient descent | Minimising a cost function and picking random (stochastic) paths for building the graph search | Simpler implementation using some coding approaches | If there are multiple outcomes, they might not all be minimised at the same point, and the graph might find a local minimum instead of a global one. |
| Reinforcement learning (q-learning, or PPO) | Assign values to each interaction along a pathway – rewarding better actions and penalising worse ones | Simpler implementation | Multidimensional and adversarial. |
| Monte Carlo tree search | Tree search (assigns different values to different routes around the pathway) | Transparency if certain coding approaches are used which could make interpretation of outputs easier. | No transparency in PyTorch/ Keras Python implementation and slow in simpler implementations Multidimensional (taking place on a board) and adversarial (one agent playing against each other) |
| A* search | Graph search algorithm to find the shortest path to an end goal. | Stores all generated nodes in memory. Not multidimensional or adversarial. | Can be slow with an inefficient heuristic (ranking alternatives) algorithm. |

Data requirements

The data needs to capture what the resource impacts in terms of time and economic resources as well as carbon impacts, and health status improvements among patients. This needs to be done for patients, environments and interactions as shown above. Another useful addition to the model will be an average referral to treatment times so that the model is more realistic.

Optimisation

Eventually, the model needs to optimise on the outcomes, by making sure that patients are treated in time and in a way that helps them maintain their condition over time, and to ensure that relevant negative impacts can be minimised for patients and the health system uses resources more effectively as a result.

Discussion

The project showed how to develop a set of environments, interactions and patients from academic literature, policy, and clinical resources. The model currently runs a simulation that prints outputs of patient records into the console. It showed that it is possible to gain most of the inputs for a model that model's outcomes from the academic literature and NHS data. It will be important to make sure that these are up to date and captured for every service in the improvements to the model. When the project is extended it will have the ability to show system effects in healthcare pathways, and the diabetes pathway proof of concept is a crucial step towards this. The implication for clinicians is that they will be able to see the cumulative effects of healthcare interventions (potentially when a novel approach is added). For policymakers, there may be an opportunity to see what the impact of an intervention is pre-implementation on key outcomes when this type of model reaches its full potential.

The project has an innovative approach in terms of trying to develop an approach to optimise outcomes in a model of a patient pathway in the context of the NHS in England. The model shows the way that we might model system-level outcomes using simulation modelling to produce longitudinal synthetic data. As indicated at the beginning of the report, synthetic data is an interesting way of approaching this because we would not need to access individual patient data under the SynPath framework.

The model does not currently have a section of the module showing the progression of the disease itself like Synthea (Gregorowicz 2020). This is important as the progression of the disease is complex. We began to conceptualise the impact of this using patient updates within the intelligence layer, but it might be necessary to build an entire module that modifies patients along the pathway. This is especially important because it might be the case that the changes to patients might affect the convergence of an algorithm that is applied to the model to optimise outcomes.

This project set out a list of criteria for key elements of the intelligence layer to be used in different treatment pathway that builds upon Synthea, a framework for research using simulation in the NHS. It can be adapted for different interventions in future in the diabetes pathway and other pathways and interventions.

Next steps

The diabetes example for the model needs to have the comorbidity elements (e.g. mental health, learning disability and pregnancy) completed. Also, further patient updates outside those already included could be added. It would be useful to build a

model of disease and patient comorbidity progression that fits into the model in a comparable way to the Synthea approach. An improvement that could be made to the model would be setting up the environments and environment templates so that they could be read from a CSV.

Adding to the digital health intervention elements of the pathway to show the use of digital health in secondary care and its' impacts will be important as the model is developed. Interventions used primarily by healthcare professionals and the impact that they have on resources should also be added.

The project would benefit from further exploration of the right type of intelligence approach to use, this can be done using more intelligence literature and expert opinion.

Further examples of medical treatment pathway use cases could be shown using the SynPath approach. For example, it might be interesting to explore a mental health pathway and have a key output of self-reported mental wellbeing or a cancer pathway and have a cancer-specific quality of life measure. These are just examples of two disease areas that could be used in the completed SynPath framework.

Appendix

Set up

We used Anaconda and VSCode to run the model in Python version 3.8.10. We set up a virtual environment using conda install (Anaconda.com 2017). When you have set up the environment, activate your environment, go to the SynPath folder, and export the model as in the instructions from the original SynPath README. The commands for setting up the model initially are in the 't2dm' folder in a file called 'workbook.py'. If you run these commands, you can then run the model. When you open the terminal again, you can type the following commands in the terminal in VSCode or on your computer to run the type 2 diabetes module.

```
conda activate [name of your environment]
cd SynPath
export PATIENT_ABM_DIR="$(pwd)"
patient_abm simulation run --config_path template/t2dm/config.json
```

File locations for key elements of the model

The original mapping of the pathway (NHSX 2021a) is on GitHub, with a list of the procedures included and the resource impacts assigned to them (NHSX 2021e). The list of synthetic patient records to begin the model, including medical history and characteristics (NHSX 2021f), the converted JSON inputs (NHSX 2021g) and the list of commands to convert the CSV to JSON is in the create patients python notebook (NHSX 2021h) are also on the GitHub.

All files relating to the diabetes pathway are in the template folder under 't2dm'. The only edits to the source folder ('src') were to create different types of environments for the pathway (adding outpatient, community and inpatient) (NHSX 2021b). The list of environments and the interactions which occur in each are in the template folder (NHSX 2021c). When adding interactions, make sure you assign the environment name as a prefix to the interaction so that the model calls the relevant interaction for each environment.

The medical procedures or consultations are called interactions in the model. These carry out certain functions, such as choosing the service from the pathway, assigning probabilities for the next environment, and assigning values for the three impact outcomes. The full list of interactions is in the interactions folder (NHSX 2021d). An example of the interactions that relate to diabetes education for patients (NHSX 2021i) shows a simple setup of the decisions made within a service for patient care.

Intelligence

The intelligence layer has not been completed, but we know that it must carry out five main functions beyond the simulation. These are:

- allocating patients to an environment at a certain time conditional on the environment's capacity;
- updating patient characteristics for changing health states (e.g. pregnancy, smoking etc.);

- calculating the total impact of patients accessing services in the model, such as in the hash diabetes models' manager module (hash.ai 2021c);
- optimising the outcomes by choosing the best path for a patient in the list of patients created dependent on their characteristics (using an option from table 3);
- restricting the health systems' choice of the next environment for a patient by rewarding and penalising good and illogical next steps respectively as in the q-learning value table in the hash q-learning example (hash.ai 2021b)

References

- Ackerman, Eugene, Laël C. Gatewood, John W. Rosevear, and George D. Molnar. 1965. 'Model studies of blood-glucose regulation', *The bulletin of mathematical biophysics*, 27: 21-37.
- Anaconda.com. 2017. 'Conda cheat sheet', Accessed 25th August.
<https://docs.conda.io/projects/conda/en/4.6.0/downloads/52a95608c49671267e40c689e0bc00ca/conda-cheatsheet.pdf>.
- Ciaburro, G. 2020. *Hands On Simulation Modelling with Python* (Packt Publishing).
- CPRD. 2021. 'Clinical Practice Research Datalink (CPRD)', Accessed 9th August.
<https://www.cprd.com>.
- Delli Gatti, Domenico. 2018. *Agent-Based Models in Economics, a Toolkit*, (Cambridge University Press).
- EBM DataLab, University of Oxford. 2021a. '6.1 Drugs used in diabetes, OpenPrescribing'. <https://openprescribing.net/bnf/0601/>.
- . 2021b. 'OpenPrescribing.net', Accessed 9th August.
<https://openprescribing.net>.
- Geron, A. 2019. *Hands-on Machine Learning with Scikit-Learn, Keras and TensorFlow* (O'Reilly).
- Grant, P. 2015. 'How much does a diabetes out-patient appointment actually cost? An argument for PLICS', *Journal of Health Organization and Management*.
- Gregorowicz, A. 2020. 'Metabolic Syndrome Disease (2020)', Accessed 16th August.
https://github.com/synthetichealth/synthea/blob/master/src/main/resources/mondules/metabolic_syndrome_disease.json.
- Hart, P. E., N. J. Nilsson, and B. Raphael. 1968. 'A Formal basis for the Heuristic Determination of Minimum Cost Paths', *IEEE Transactions on Systems Science and Cybernetics*, 4: 100-07.
- hash.ai. 2021a. 'Monte Carlo Tree Search'. <https://core.hash.ai/@b/mcts/main>.
- . 2021b. 'Q-learning', Accessed 9th August.
<https://core.hash.ai/@hash/ql/1.0.0>.
- . 2021c. 'Risk of Diabetes model'. <https://core.hash.ai/@hash/risk-of-diabetes/2.1.0>.
- Hayes, A. J., J. Leal, A. M. Gray, R. R. Holman, and P. M. Clarke. 2013. 'UKPDS Outcomes Model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82', *Diabetologia*, 56: 1925-33.
- HERC Oxford. 2020. 'UKPDS model v.2'. <https://www.dtu.ox.ac.uk/outcomesmodel/>.
- Kagho, Grace O., Milos Balac, and Kay W. Axhausen. 2020. 'Agent-Based Models in Transport Planning: Current State, Issues, and Expectations', *Procedia Computer Science*, 170: 726-32.
- Kaur, D., M. Sobiesk, S. Patil, J. Liu, P. Bhagat, A. Gupta, and N. Markuzon. 2021. 'Application of Bayesian networks to generate synthetic health data', *J Am Med Inform Assoc*, 28: 801-11.
- Mount Hood Diabetes Challenge. 2020. 'Overview'.
<https://www.mthooddiabeteschallenge.com>.
- Murray, Elizabeth, Kerry Daff, Anthi Lavidia, William Henley, Jenny Irwin, and Jonathan Valabhji. 2019. 'Evaluation of the digital diabetes prevention

- programme pilot: uncontrolled mixed-methods study protocol', *BMJ Open*, 9: e025903.
- National Institute for Health and Care Excellence (NICE). 2017. 'Algorithm for blood glucose lowering therapy in adults with type 2 diabetes', Accessed 9th August 2021. <https://www.nice.org.uk/guidance/ng28/resources/algorithm-for-blood-glucose-lowering-therapy-in-adults-with-type-2-diabetes-2185604173>.
- . 2021. 'Type 2 diabetes treatment summary', Accessed 9th August. <https://bnf.nice.org.uk/treatment-summary/type-2-diabetes.html>.
- NHS Digital. 2019. 'Health Survey for England 2019'.
- NHS England. 2017. "RightCare pathway - reasonable adjustments for learning disability." In.
- . 2018. 'NHS RightCare Pathway: Diabetes'. <https://www.england.nhs.uk/rightcare/products/pathways/diabetes-pathway/>.
- . 2020a. "Delivering a 'Net Zero' National Health Service." In.
- . 2020b. "National Cost Collection 2019." In.
- . 2021. 'Consultant-led Referral to Treatment Waiting Times', Accessed 9th August. <https://www.england.nhs.uk/statistics/statistical-work-areas/rtt-waiting-times/>.
- NHSX. 2021a. 'Diabetes pathway diagram'. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/Resources/Diabetes_pathway_v2.pdf
- . 2021b. 'Environment types', Accessed 29th September. https://github.com/nhsx/SynPath/blob/master/src/patient_abm/agent/environment.py.
- . 2021c. 'Environments for SynPath Diabetes ', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/env_infos.json.
- . 2021d. 'Interactions list', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/tree/main/t2dm/manager/intelligence/interactions.
- . 2021e. 'List of procedures (SynPath Diabetes)', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/Resources/list_of_procedures.xlsx
- . 2021f. 'Patient list (SynPath Diabetes)', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/patients.csv
- . 2021g. 'Patient list JSON', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/patient_infos.json.
- . 2021h. 'Python notebook (create patients)', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/create_patients.ipynb.
- . 2021i. 'Structured education interactions', Accessed 29th September. https://github.com/nhsx/SynPath_Diabetes/blob/main/t2dm/manager/intelligence/interactions/se0.py.
- . 2021j. 'SynPath', Accessed 16th August. https://github.com/nhsx/SynPath_Diabetes.
- NICE. 2020. 'Type 2 diabetes in adults: management', Accessed 1st June 2021. <https://www.nice.org.uk/guidance/ng28>.
- Paranjape, R., Z. (G). Wang, and S. Gill. 2018. *The Diabetic Patient Agent: Modelling Disease in Humans and the Healthcare System Response* (Springer: Berlin, Germany).
- Personal Social Services Research Unit (PSSRU). 2019. "Unit costs 2018/19." In.

- Public Health England (PHE). 2018/19. 'Diabetes (Fingertips data profile)', Accessed 9th August. <https://fingertips.phe.org.uk/profile/diabetes-ft/data#page/0/gid/1938133136/pat/44/par/E40000003/ati/154/are/E38000004/cid/4/tbm/1>.
- Scutari, M. 2020. 'bnlearn - an R package for Bayesian network learning and inference'. <https://www.bnlearn.com/examples/custom/>.
- Scutari, M., and J.-B. Denis. 2021. *Bayesian Networks with Examples in R* (Chapman & Hall/ CRC).
- Solli, Oddvar, Knut Stavem, and I. S. Kristiansen. 2010. 'Health-related quality of life in diabetes: The associations of complications with EQ-5D scores', *Health and quality of life outcomes*, 8: 18-18.
- Squires, Hazel, James Chilcott, Ronald Akehurst, Jennifer Burr, and Michael P. Kelly. 2016. 'A Framework for Developing the Structure of Public Health Economic Models', *Value in Health*, 19: 588-601.
- Thomas, Chloe, Susi Sadler, Penny Breeze, Hazel Squires, Michael Gillett, and Alan Brennan. 2017. 'Assessing the potential return on investment of the proposed UK NHS diabetes prevention programme in different population subgroups: an economic evaluation', *BMJ Open*, 7: e014953.
- Tucker, Allan, Zhenchen Wang, Ylenia Rotalinti, and Puja Myles. 2020. 'Generating high-fidelity synthetic patient data for assessing machine learning healthcare software', *npj Digital Medicine*, 3: 147.
- Whaley, Christopher M., Jennifer B. Bollyky, Wei Lu, Stefanie Painter, Jennifer Schneider, Zhenxiang Zhao, Xuanyao He, Jennal Johnson, and Eric S. Meadows. 2019. 'Reduced medical spending associated with increased use of a remote diabetes management program and lower mean blood glucose values', *Journal of Medical Economics*, 22: 869-77.
- Wu, H. 2005. 'A case study of type 2 diabetes self-management ', *Biomed. Eng. Online*, 4.
- Xie, Qinmu, Shoufeng Ma, Ning Jia, and Yang Gao. 2014. 'Agent-Based Modeling and Simulation for the Bus-Corridor Problem in a Many-to-One Mass Transit System', *Discrete Dynamics in Nature and Society*, 2014: 652869.