**Can Agent Based Simulation be used as a tool to support polypharmacy prescribing practice?**

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**Abstract**

*Objective*

We sought to develop a simulation modelling method to help better understand the complex interplay of factors that lead to people with Type 2 diabetes and asthma not taking all of their medication as prescribed when faced with multiple medications (polypharmacy).

*Research Design and Methods*

In collaboration with polypharmacy patients, GPs, pharmacists and polypharmacy researchers, we developed a map of factors that directly and indirectly affect somebody's decision to take their medication as prescribed when faced with multiple Type 2 diabetes and asthma medications. We then translated these behavioural influences into logical rules using data from the literature and developed a proof-of-concept Agent Based Simulation model that captures the medicine taking behaviours of those with Type 2 diabetes and asthma taking multiple medications, and which predicts both the clinical effectiveness and rates of adherence for different combinations of medications.

*Conclusions*

The model we have developed could be used as a prescription support tool or a way of estimating medicine taking behaviour in cost-effectiveness analyses.

**What this paper adds**

*What is already known on this subject*

- A significant number of people who are prescribed multiple medications do not take all of their medications as prescribed.
- Prescribed medication not being taken can lead to risks for patients as well as wasted costs for the NHS, and increased access to health services as people fall ill.
- The reasons why people do not take their medication as prescribed are numerous and complex.

*What this study adds*

- We have developed a proof-of-concept simulation tool to capture the complex behavioural dynamics leading to people with both type 2 diabetes and asthma not taking their medication as prescribed.
- The tool can be used to predict the likely medication adherence, clinical wellbeing and treatment burden of different prescription combinations for these conditions.
- The tool could be easily extended to incorporate other combinations of conditions that lead to multiple medications being prescribed.

## Introduction

Polypharmacy, in which people are prescribed multiple medications (commonly for multiple comorbidities) [1] is growing [2-4], particularly as we face an ageing population developing multiple conditions [5]. Polypharmacy can be problematic because of the consequent treatment burden, safety issues and because a significant number of people who are prescribed multiple medications do not take all of their medication [6]. This can lead to wasted costs from unused medication [7] and the resource and cost burden of patients accessing health services that might result from sub-optimal control of their conditions [8]. However in some situations, non-adherence can lead to fewer adverse drug reactions [9].

For many years, there has been a focus on increasing "adherence" (formerly termed "compliance") within such populations [10]. Many studies have examined the potential factors that might lead to people not adhering to their prescription [11], although often such studies have focused on single factors or small subsets. Other studies have been concerned with understanding how people manage their medicines in the context of their everyday lives [12]. In a synthesis of qualitative research, Pound et al [13] found considerable reluctance to take medicine and a preference to take as little as possible. Recognising the problem of treatment burden, May and colleagues [14] have coined the term 'minimally disruptive medicine' to guide the search for less burdensome clinical practice.

Agent Based Simulation (ABS) is a simulation modelling method that allows for the modelling of behavioural and motivational aspects within a system, and uses such individual-level behaviours as the building blocks for the model, allowing population-level dynamics to emerge as properties of individual behaviours and interactions [15]. Agent Based Simulation has a rich heritage of being used in this way in ecology [16], but has less often been applied to human systems [17]. However, there is a developing interest in applying Agent Based

Simulation to model health and social care systems in which the behaviours of individuals within that system are the focus or an integral component [17-22].

In this paper, we present a novel and innovative proof-of-concept model, developed in collaboration with people experiencing polypharmacy, health professionals and polypharmacy researchers, to demonstrate the potential of Agent Based Modelling to better understand medicine taking behaviour in the context of polypharmacy for those with both type 2 diabetes and asthma. We describe the development of the model, how the model works, and its potential further development to be used as a tool for supporting polypharmacy prescribing policy.

## Research Design and Methods

### *The Software*

The model described in this paper was built using AnyLogic University 6.7.1 (© The Anylogic Company, http://www.anylogic.com/).

### *The Working Group*

The project working group included two operational researchers, two polypharmacy researchers, two patients taking multiple medications from the local patient involvement group (PenPIG), two pharmacists (one of whom is also a representative for the local Academic Health Science Network) and a General Practitioner.

### *Population of Interest*

People with both type 2 diabetes and asthma represent a growing sub-population [23], who have to manage two very different conditions where treatment burden may be high because of potential conflicts between medications [24]. Therefore, we selected our population of interest in this model as those with both (and only) type 2 diabetes and asthma, although the modelling approach used here could be applied to other sub-populations.

*Mapping the Behavioural System*

A key step when designing and developing any model is to gain an understanding of the system to be modelled [25]. In this project, we sought to understand the behavioural logic associated with the taking of prescribed medications. Therefore, we developed a map of potential factors that might directly or indirectly affect the medicine taking behaviour of someone with type 2 diabetes and asthma. This map was developed collaboratively within the working group, drawing on the expertise of people taking multiple medications, researchers and prescribers, and exploring the significant body of literature in this area. Literature search strategies were strategic, and looked for combinations of terms for the conditions of interest and literature concerning medication that included broad terms of “burden of treatment”, “patient experiences” and “adherence”. Specific searches were also undertaken that looked for special factors of interest, such as “needle anxiety”, “supply of medication” and “storage of medication”. We also included studies of multimorbidity that featured one or more of the conditions of interest, and included both qualitative and quantitative studies. A total of 164 relationships were identified using an iterative process.

*Identifying Relationships to Model*

We assume that our population of interest does not include pregnant women or children, as medicine taking amongst these sub-populations is more complex [26, 27]. For this initial prototype, we assume that the prescribed combination of medications represents the complete set of medications available to patients in that simulation, and therefore we did not need to consider the impact of someone’s willingness to try new medications, or how that might be affected by their desire to be in control of their condition, their personal goals or their desire to feel better. Also, we did not need to model the impact of the patient having conditions other than type 2 diabetes and asthma, as we assume our population has both and only these two conditions. As diabetes and asthma medications are not considered to be either addictive or analgesic in nature (local pharmacist opinion), we did not need to consider how the addictive properties of medication or whether or not the medication provides pain relief would impact medicine taking. Our pharmacists considered that such medications were less likely to lose effectiveness over time (although obviously the severity of the conditions could worsen over time). We also assumed that medication supply problems were unlikely for common conditions such as diabetes and asthma. Finally, in order to ensure we were modelling individual behaviours associated with medicine taking, we assumed that our population was able to make their own decisions about their medications, and therefore we did not consider the impact of cognitive impairment or the need for assistance taking medications. After eliminating these factors, we were left with 142 influencing relationships to model (Appendix A).

Once we had identified those influencing factors that were not relevant to our modelled population, we explored the literature to identify potential quantitative and qualitative data that could be used to represent the remaining factors within the model. Principally, we were looking for data that could be translated into behavioural 'rules of thumb', either via quantitative data from which probabilities of behaviour could be inferred, or qualitative data from which we could infer categorical data and relationships. As part of this process, for some relationships we found evidence that they were untrue, and for others we were unable to find usable data. In all, we were left with 70 relationships to be included in the model.

Due to the timeframe of the project, we were unable to include real medication data in the prototype model, and instead opted to develop the tool such that users could input such drug data by specifying the probability of condition progression and improvement for each medication. Consequently, some of the medication and condition severity related factors are not explicitly captured in the prototype. This left us with a final total of 59 relationships that were modelled. Full details of the relationships that were included and excluded, and the reasons for exclusion, are detailed in Appendix A.

*Translating the Behavioural System into Behavioural Rules*

For the 59 relationships to be included in the model, we needed to translate the quantitative and qualitative data found in the literature into behavioural rules that could be implemented in the model. Typically, these rules translated the data into "IF THEN" statements that would determine the 'state' of certain influencing factors. For example, we found evidence to show that if someone's perception of the severity of their condition is low, there is a 22% increased probability of non-adherence [28]. In the model, we translated this into a rule that states that if an agent's perception of their state of health is less than or equal to 50%, the "proposed action" from this influencing relationship would be to adhere only 78% of the time. Appendix B details the full set of behavioural rules for each influencing factor modelled.

Evidence shows that the impact of perceived state of health has twice the impact on adherence as any other factor that might influence medicine taking behaviour [29]. Therefore, in the model we split the behavioural influences into two categories – "Wellness Factors" which represent the influence of someone's state of health, how well they feel, and the effects of the drugs they are taking, and "General Factors" which represent everything else. We configured the model so that the "Wellness Factors" influenced behaviour twice as often as the "General Factors".

The influence of someone's state of health on their medicine taking can be thought to be comprised of two central components – how well they actually are / the effects of their medication and their perception of how well they are / the effects of their medication [28].

Such concepts can also be found in the Health Belief Model [30]. Perceptions of state of health will change over time. To capture these elements, we used a Linear Operator Learning Rule within a Reinforcement Learning framework [31], which is a commonly used approach to describe reinforcement behaviours in ecological modelling [32]. Reinforcement Learning describes a learning in which actions that are more rewarding are increasingly taken, whilst actions that offer less reward (or punishment) are gradually avoided. In the context of medicine taking, this represents the way in which people will tend to take medications based on their beliefs about the effects the medication is having and their experience taking the medication [33].

Specifically, each person in the model maintains a perception of how well each combination of drugs makes them feel. If they have yet to experience a drug combination, we assume that they perceive that combination of drugs to be no better or worse than any other combination they have yet to try. For each simulated day in the model, each person updates their perception of the combination of drugs they are currently taking using the following Linear Operator Learning Rule :

$$w^t = W^t s\alpha + (1-\alpha)w^{t-1}$$

where $w^t$ is the person's perception of their state of health at time $t$, $W^t$ is the person's actual state of health at time $t$, $s$ is their sensitivity to their true state of health (ranging from 0 representing complete insensitivity to 1 representing full awareness of true state of health), $\alpha$ represents how much their medicine taking is weighted in favour of how they currently feel compared to how they felt previously (ranging from 0 for people who do not update their perceptions based on new information to 1 for people who only consider new information), and $w^{t-1}$ is the person's previous perception of their state of health taking this drug combination.

After a person in the model has updated their perception of their health state, they will compare it to their perceptions about how well they felt taking the other drug combinations. A threshold $T$ is given by the "perceived wellness" value of previously sampled medication combinations. If the person's perception of their current health falls a given percentage below the threshold $T$, the proposed action from the "Wellness Factors" will be to not take their medication. The person may then switch to the combination of medications that they perceive to make them feel most "well". However, this may not be the action that is taken, as people are not just influenced by "Wellness Factors".

In addition, each "General Factor" resolves to a binary value of "Take" or "Don't Take" via the behavioural rules translated from the data, which represents the "proposed action" from that influencing factor. At the end of each simulated day, a proposed action will be selected at random from each person's set of factors (both "General Factors" and "Wellness Factors"). The probability of selecting any action is determined by its weighting. In the prototype model, the probability of choosing the proposed action from the "Wellness Factors" is 67%, compared to 33% for the "General Factors" [29]. In the absence of data, we assume that all "General Factors" have equal weighting.

If the selected proposed action is "Take", then no action will be taken. Otherwise, if the selected proposed action is from the "Wellness Factors", then the person in the model will switch to the proposed alternative drug combination that they perceive to make them feel most "well". If the selected proposed action is from a "General Factor", then the person will either switch to their perceived best alternative or select a drug combination at random if the influence from how well they feel says they should take their medication.

Figure 1 provides an overview of how the behaviour in the model works.

*States of health*

Each person in the model is in two states at any one time – one representing their type 2 diabetes state of health, and one representing their asthma state of health. These represent the true states of health for each person in the model. For simplicity, we use three states of health for each condition in the prototype model, emulating the three most common stages of treatment for each condition [34, 35]. The true state of health value is calculated as the sum of the health values assigned to each state from each condition, with a Stage 1 (least severe) state of health assigned a value of 50%, a Stage 2 state of health assigned a value of 25%, and a Stage 3 state of health (most severe) assigned a value of 0%. Therefore, the true overall state of health of any person in the model can range between 0% (most severe state of health for both conditions) to 100% (least severe state of health for both conditions).

*Medication Effects*

Medication effects are specified in the model for each possible combination of medication. In the prototype, there are four prescribed medications – two for asthma, and two for diabetes. People with both Type 2 diabetes and asthma may take up to three to four different medications, depending on the stages of their conditions [34, 35]. The effects of the drugs for each combination are specified by the user of the model in terms of the probability per day of a transition between health states for each condition. This allows users to specify the effectiveness of each combination of medications for each condition.

*Outputs*

Whilst running, the model reports adherence and wellness levels within the population over time. Users of the model are also able to access the details of any given person within the population. These details include their current state of health and perceived state of health, the severity of their conditions, the medicine taking decision they are currently making and the factors that influenced that decision, and parameter values relevant to the various factors that influence medicine taking.

## Conclusions

The intention of building this model was for it to serve as a proof-of-concept to demonstrate how the medicine taking behaviours of those taking multiple medications for both type 2 diabetes and asthma could be simulated, and how such a model could be used to provide evidence to inform prescribing practice. We have shown how such behaviours can be translated from qualitative and quantitative data in the literature into behavioural rules that can be used in an Agent Based Simulation, and how the effect of state of health and medication effectiveness on medicine taking decisions can be simulated using Reinforcement Learning and a Linear Operator Learning Rule. We have also shown how adherence rates and states of health across the simulated population can be calculated and reported, which, along with the level of treatment burden, are likely to be key outcome measures when comparing medication combinations to inform prescribing practice.

The principal way in which this model could be used is to compare combinations of medication prescribed for those with type 2 diabetes and asthma, not only in terms of their clinical effectiveness but also the likely treatment burden and adherence to this prescription within a given population. However, the modelling method could be applied to any combination of conditions where people are taking multiple and perhaps conflicting medications. The evidence generated by a model such as we've described would allow trade-off decisions to be made – for example, a particular combination of medications may have a slightly lower clinical effectiveness but result in fewer side effects or a much higher level of adherence, helping to inform a decision about whether to accept a trade-off in clinical effectiveness in return for more people taking more of their medication as prescribed. These decisions could be made by the prescriber (such as a General Practitioner) with individual patients using a simulation 'population' reflecting the patient in question, or on a larger scale in terms of informing prescribing policy locally or nationally. Comparisons in terms of treatment burden (how burdensome a treatment or combination of treatments is to follow) could be made externally to the model using expert judgement, or internally if the model were extended to incorporate influencing factors such as complexity, frequency and flexibility of the treatment regimen, adverse drug reactions, complexity and portability of the format of delivery of the medications, and total number of medications prescribed. We already include the influence of the level of interference with daily life, which is likely an important aspect of treatment burden [36], and this could be extended to reflect specific medication regimens.

There is also potential for this model to be used to enhance traditional cost-effectiveness analyses. Such analyses seek to determine the cost-effectiveness of an intervention (often a new treatment) in terms of its incremental benefits and costs compared with an existing intervention for a given sub-population [37]. Some cost-effectiveness studies have started to incorporate simple estimates of adherence [38], acknowledging the potential impact of adherence on the cost-effectiveness of an intervention [39]. However, such studies typically use poor or invalid methods to incorporate concepts of adherence [40]. Our model could be used as a means of better estimating adherence rates for the studied population, either directly if the population was those with type 2 diabetes and asthma, or with extension to the model for other sub-populations. Alternatively, the model could be extended to incorporate the cost-effectiveness elements, as we already allow the user to specify transition probabilities between health states with different drug combinations, and we assign quantifications of 'wellness' to each combination of drug states which could easily be used to represent Quality Adjusted Life Years (QALYs) [41]. If the model were extended to also assign costs to each combination of states, the cost-effectiveness analysis could be conducted solely using this simulation model, with the added benefit of a more sophisticated intrinsic means of considering medicine taking behaviours.

To our knowledge, the method of simulating medicine taking behaviours that we have outlined in this paper has not been developed before, and therefore presents an innovative and exciting opportunity to model systems in health and social care where the medicine taking behaviours of people within those systems is a non-trivial component. Furthermore, beyond medicine taking in polypharmacy, there is an increasing acknowledgement that many healthcare systems are significantly dependent upon the behaviour of the 'actors' within that system. Clearly, the model would need to be validated against relevant data sets before being applied in any of the ways we have proposed in this paper, but we feel strongly that the modelling approach we have outlined could be a vital tool to help to better understand the complex interplay of factors that lead to people who are prescribed multiple medications not taking all of their medication as prescribed.

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## Contributorship

Daniel Chalk led the project, designed and developed the simulation model, and led the authorship of the paper. Sean Manzi assisted with the design of the model and the translation of the research evidence into rules for the model, and contributed edits and feedback for the paper. Nicky Britten initially proposed the study, offered insight into polypharmacy behaviour and practice to inform the model, and contributed edits and feedback for the paper. Bettina Kluettgens, Ratidzai Magura and Jose Valderas offered insight into polypharmacy behaviour and practice to inform the model, and contributed edits and feedback for the paper.

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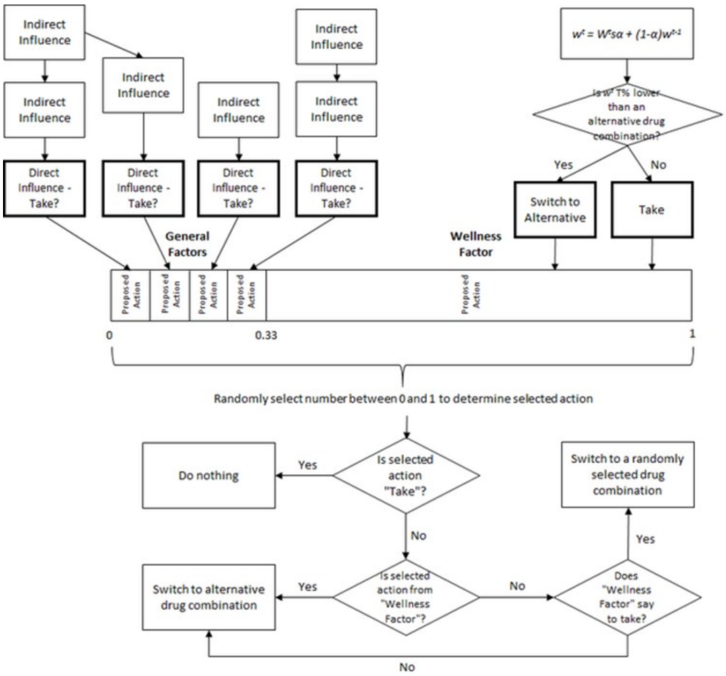


*Figure 1. Overview of the behavioural logic of the model for each person at each time step. Indirect general factors influence direct general factors, which resolve to a binary proposed action to take the medicine or not to take it. The wellness factor also resolves to a proposed action, depending on the person's perception of their state of health with their current drug combination. Proposed actions are selected at random according to the weighting attributed*

*to them, and the person will either switch their medication or continue as they are depending on the selected action.*

## Competing Interests

All authors declare no competing interests in respect of this research.

Appendix A

| Relationship # | Influencing Factor (FROM) | Factor Being Influenced (TO) | Included in Model? | Reason for Exclusion (if applicable) |
|---|---|---|---|---|
| 1 | Affordability of medications to patient | Adherence | YES | |
| 2 | Household income / financial status | Affordability of medications to patient | NO | Not needed as socio-economic status specified directly by the user when setting up model |
| 3 | Household income / financial status | Health literacy | NO | No data |
| 4 | Level of education | Health literacy | YES | |
| 5 | Ethnicity | Adherence | NO | (Osborn, Cavanaugh et al. 2011) found that it is health literacy that explains disparities in diabetes medication adherence, not ethnicity itself |
| 6 | Ethnicity | Health literacy | NO | Not needed as health literacy specified directly by user |
| 7 | Ethnicity | Language barriers | NO | Not needed as language barriers specified directly by user |
| 8 | Language barriers | Frequency of interaction with health professionals | YES | |
| 9 | Language barriers | Health literacy | YES | |
| 10 | Health literacy | Frequency of research of information on the internet | YES | |
| 11 | Frequency of research of information on the internet | Health literacy | NO | It is the opposite relationship that is true (health literacy influences frequency of research of information on the internet) (see relationship 10) (Neuberger 2000, Wald, Dube et al. 2007, Sarkar, Karter et al. 2010) |
| 12 | Health literacy | Awareness of severity and / or nature of condition | NO | Not needed as user directly specifies level of understanding of necessity of treatment |
| 13 | Health literacy | Awareness of why prescribed | NO | Not needed as user directly specifies level of |

| | | | | |
|---|---|---|---|---|
| | | medications | | understanding of necessity of treatment |
| 14 | Health literacy | Adherence to recommended lifestyle changes | NO | We don't use real progression data in the prototype, so unable to capture this |
| 15 | Preference to use non-drug alternatives (diet etc) | Adherence | YES | |
| 16 | Pregnancy | Adherence | NO | We assume our population does not contain pregnant women |
| 17 | Support in workplace / place of education to take medication | Adherence | YES | |
| 18 | Support in workplace / place of education to take medication | Openness about condition | YES | |
| 19 | Openness about condition | Adherence | YES | |
| 20 | Desire to feel "normal" by not having to take medication | Adherence | YES | |
| 21 | Desire to feel "normal" by not having to take medication | Openness about condition | YES | |
| 22 | Willingness to try new medications | Adherence | NO | We assume that the prescribed combination of drugs in the model represents the complete set of drugs available |
| 23 | Willingness to try new medications | Desire to be "in control" of self / condition | NO | We assume that the prescribed combination of drugs in the model represents the complete set of drugs available |
| 24 | Desperation to feel better | Willingness to try new medications | NO | We assume that the prescribed combination of drugs in the model represents the complete set of drugs available |
| 25 | Desire to be "in control" of self / condition | Adherence | YES | |
| 26 | Desire to be "in control" of self / condition | Willingness to try new medications | NO | We assume that the prescribed combination of drugs in the model represents the complete set of drugs available |
| 27 | Personal goals | Willingness to try new medications | NO | We assume that the prescribed combination of drugs in the model represents the complete set of drugs available |

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| 28 | Personal goals | Desire to be "in control" of self / condition | NO | No data |
| 29 | Life events | Adherence | YES | |
| 30 | Stress | Adherence | NO | Covered under Life Events |
| 31 | Needle anxiety | Adherence | YES | |
| 32 | Presence of other conditions that may affect ability to take medications | Adherence | NO | We assume our population has both and only Type 2 Diabetes and asthma |
| 33 | Gender | Adherence | YES | |
| 34 | Alcohol abuse, illicit drug use and smoking status | Adherence | YES | |
| 35 | Addictive properties of medication | Adherence | NO | Diabetes and asthma medications do not tend to be addictive in nature |
| 36 | Whether medication provides pain relief | Adherence | NO | Diabetes and asthma medications do not tend to be analgesic in nature |
| 37 | Severity of condition | Adherence | YES | |
| 38 | Severity of condition | Desperation to feel better | NO | Desperation to feel better only influences willingness to try new medications in our map, and is therefore not required because we are not modelling a willingness to try new medications |
| 39 | Time since onset | Severity of condition | YES | |
| 40 | Time since diagnosis | Acceptance of diagnosis | YES | |
| 41 | Acceptance of diagnosis | Adherence | YES | |
| 42 | Prioritisation of condition and treatment regimen | Adherence | NO | No data |
| 43 | Prioritisation of condition and treatment regimen | Adherence to recommended lifestyle changes | NO | No data |
| 44 | Severity of condition | Prioritisation of condition and treatment regimen | NO | No data |
| 45 | Adherence to recommended lifestyle changes | Severity of condition | NO | We don't use real disease progression data in the prototype, so unable to capture this |
| 46 | Reduced efficacy of drugs over | Adherence | NO | Diabetes and asthma medications unlikely to lose |

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| | time | | | effectiveness over time (although severity of condition could worsen over time) |
| 47 | Time since diagnosis | Adherence | YES | |
| 48 | Time since diagnosis | Reduced efficacy of drugs over time | NO | Diabetes and asthma medications unlikely to lose effectiveness over time (although severity of condition could worsen over time) |
| 49 | Time since diagnosis | Severity of condition | NO | It is the time since onset that would influence condition severity, not time since diagnosis (see relationship 39) |
| 50 | Severity of condition | Total number of drugs prescribed | NO | Total number of drugs prescribed fixed at four in prototype |
| 51 | Total number of drugs prescribed | Adherence | NO | Total number of drugs prescribed fixed at four in prototype |
| 52 | Severity of condition | Complexity and portability of format of delivery of drugs | NO | No real drug data used in prototype |
| 53 | Complexity and portability of format of delivery of drugs | Adherence | NO | No real drug data used in prototype |
| 54 | Severity of condition | Complexity and frequency of treatment regimen | NO | No real drug data used in prototype |
| 55 | Complexity and frequency of treatment regimen | Adherence | NO | No real drug data used in prototype |
| 56 | Severity of condition | Flexibility of treatment regimen | NO | No real drug data used in prototype |
| 57 | Flexibility of treatment regimen | Adherence | NO | No real drug data used in prototype |
| 58 | Severity of condition | Frequency of interaction with health professionals | NO | No data |
| 59 | Time since diagnosis | Level of interference with daily life | NO | No data |
| 60 | Level of interference with daily life | Adherence | YES | |
| 61 | Age | Adherence | YES | |
| 62 | Age | Level of interference with daily life | NO | No data |
| 63 | Age | Cognitive impairment | NO | We assume our population is able to make their own decisions about their medication |
| 64 | Cognitive impairment | Adherence | NO | We assume our population is able to make their |

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| | | | | own decisions about their medication |
| 65 | Age | Deference | YES | |
| 66 | Deference | Adherence | YES | |
| 67 | Relationship with / trust in health professionals | Awareness of severity and / or nature of condition | NO | Not needed as user directly specifies level of understanding of necessity of treatment |
| 68 | Awareness of severity and / or nature of condition | Adherence | YES | |
| 69 | Relationship with / trust in health professionals | Undertaking a Medicine Use Review (MUR) | NO | No data |
| 70 | Undertaking a Medicine Use Review (MUR) | Adherence | NO | No data |
| 71 | Relationship with / trust in health professionals | Deference | NO | No data |
| 72 | Relationship with / trust in health professionals | Awareness of why prescribed medications | NO | Not needed as user directly specifies level of understanding of necessity of treatment |
| 73 | Awareness of why prescribed medications | Adherence | NO | No data, and considered similar enough to "Awareness of severity and / or nature of condition" |
| 74 | Stigma of taking medication in public (e.g. injections) | Adherence | YES | |
| 75 | Influence of health professionals to promote adherence | Adherence | YES | |
| 76 | Concerns about potential long term effects | Adherence | YES | |
| 77 | Adverse interactions with other drugs (POM and OTC) | Adherence | NO | We assume no drugs other than those prescribed are available to the patient (and those interactions would be captured in the user-specified transition probabilities) |
| 78 | Difficulties obtaining timely repeat prescriptions | Adherence | YES | |
| 79 | Concerns about medication supplies | Adherence | NO | We assume there would not be supply problems for diabetes and asthma medication |

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| 80 | Lack of space to store medications at home | Adherence | NO | We did not feel this would be problematic for diabetes and asthma medications |
| 81 | Level of shared decision making about treatment | Adherence | NO | No data |
| 82 | Dislike of taking medications | Adherence | YES | |
| 83 | Need for assistance | Adherence | NO | We assume our population is able to make their own decisions about their medication |
| 84 | Level of patient agreement with treatment plan | Adherence | NO | No data |
| 85 | Perceived adverse effects | Adherence | YES | |
| 86 | Perceived benefits | Adherence | YES | |
| 87 | Perceived "wellness" | Adherence | YES | |
| 88 | Influence of information found on the internet | Adherence | YES | |
| 89 | Influence of the media | Adherence | NO | No data |
| 90 | Influence of family, friends and carers (social connectivity) | Adherence | YES | |
| 91 | Receiving shock / sudden degradation of health | Adherence | NO | No data |
| 92 | Frequency of interaction with health professionals | Awareness of why prescribed medications | NO | No data |
| 93 | Frequency of interaction with health professionals | Awareness of severity and / or nature of condition | NO | No data |
| 94 | Relationship with / trust in health professionals | Influence of health professionals to promote adherence | YES | |
| 95 | Relationship with / trust in health professionals | Frequency of research of information on the internet | YES | |
| 96 | Relationship with / trust in health professionals | Level of shared decision making about treatment | NO | No data |
| 97 | Frequency of interaction with health professionals | Relationship with / trust in health professionals | NO | No data |
| 98 | Frequency of research of | Influence of information found on | YES | |

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| | information on the internet | the internet | | |
| 99 | Influence of information found on the internet | Expectations of drug benefits | NO | No data |
| 100 | Influence of information found on the internet | Expectations of drug adverse effects | NO | No data |
| 101 | Need for assistance | Influence of family, friends and carers (social connectivity) | NO | We assume our population is able to make their own decisions about their medication |
| 102 | Living alone | Influence of family, friends and carers (social connectivity) | NO | Already captured in data used for relationship 90 |
| 103 | Level of shared decision making about treatment | Level of patient agreement with treatment plan | NO | No data |
| 104 | Frequency of interaction with health professionals | Level of shared decision making about treatment | NO | No data |
| 105 | Frequency of interaction with health professionals | Influence of health professionals to promote adherence | YES | |
| 106 | Reluctance to consult with professionals for fear of “wasting their time” | Frequency of interaction with health professionals | YES | |
| 107 | Time since diagnosis | Experience of taking similar / equivalent medication | NO | No data |
| 108 | Access to transport | Access to health professionals | NO | No data |
| 109 | Access to health professionals | Frequency of interaction with health professionals | NO | No data |
| 110 | Access to health professionals | Difficulties obtaining timely repeat prescriptions | NO | No data |
| 111 | Frequency of interaction with health professionals | Information received from health professionals | NO | No data |
| 112 | Medication supply problems | Concerns about medication supplies | NO | We assume there would not be supply problems for diabetes and asthma medication |
| 113 | Medication supply problems | Difficulties obtaining timely repeat prescriptions | NO | We assume there would not be supply problems for diabetes and asthma medication |
| 114 | Difficulties obtaining timely repeat | Concerns about medication | NO | We assume there would not be supply problems for |

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| | prescriptions | supplies | | diabetes and asthma medication |
| 115 | Availability of convenient prescription services | Difficulties obtaining timely repeat prescriptions | NO | No data |
| 116 | Level of prescription record sharing | Adverse interactions with other drugs (POM and OTC) | NO | We assume no drugs other than those prescribed are available to the patient (and those interactions would be captured in the user-specified transition probabilities) |
| 117 | Lifestyle / work patterns | Level of interference with daily life | NO | No data |
| 118 | Concerns about potential long term effects | Dislike of taking medications | NO | No data |
| 119 | Perceived adverse effects | Concerns about potential long term effects | YES | |
| 120 | Perceived adverse effects | Expectations of drug adverse effects | YES | |
| 121 | Perceived adverse effects | Perceived "wellness" | YES | |
| 122 | Sensitivity to drug adverse effects | Perceived adverse effects | YES | |
| 123 | True adverse effects | Perceived adverse effects | YES | |
| 124 | True adverse effects | Sensitivity to drug adverse effects | NO | We do not include real drug data, and therefore assume sensitivity to drug effects to be constant over the duration of the simulation |
| 125 | True adverse effects | True "wellness" | YES | |
| 126 | Expectations of drug adverse effects | Sensitivity to drug adverse effects | NO | We do not include real drug data, and therefore assume sensitivity to drug effects to be constant over the duration of the simulation |
| 127 | Perception of the adverse effects experienced by others taking medication | Sensitivity to drug adverse effects | NO | We do not include real drug data, and therefore assume sensitivity to drug effects to be constant over the duration of the simulation |
| 128 | True adverse effects experienced by others taking the medication | Perception of the adverse effects experienced by others taking medication | NO | No data |
| 129 | Level of contact with others with condition | Perception of the adverse effects experienced by others taking | NO | No data |

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| | | medication | | |
| 130 | Level of contact with others with condition | Perception of the benefits experienced by others taking medication | NO | No data |
| 131 | True clinical benefits experienced by others taking the medication | Perception of the benefits experienced by others taking medication | NO | No data |
| 132 | Perception of the benefits experienced by others taking medication | Sensitivity to drug benefits | NO | No data |
| 133 | True clinical benefits | True “wellness” | YES | |
| 134 | True clinical benefits | Perceived benefits | YES | |
| 135 | True clinical benefits | Sensitivity to drug benefits | NO | We do not include real drug data, and therefore assume sensitivity to drug effects to be constant over the duration of the simulation |
| 136 | Sensitivity to drug benefits | Perceived benefits | YES | |
| 137 | Expectations of drug benefits | Sensitivity to drug benefits | NO | We do not include real drug data, and therefore assume sensitivity to drug effects to be constant over the duration of the simulation |
| 138 | Perceived benefits | Expectations of drug benefits | YES | |
| 139 | Perceived benefits | Perceived “wellness” | YES | |
| 140 | True “wellness” | Perceived “wellness” | YES | |
| 141 | Information received from health professionals | Expectations of drug adverse effects | NO | No data |
| 142 | Information received from health professionals | Expectations of drug benefits | NO | No data |
| 143 | Experience of taking similar / equivalent medication | Expectations of drug adverse effects | YES | |
| 144 | Experience of taking similar / equivalent medication | Expectations of drug benefits | YES | |
| 145 | Use of blister packs and / or other aids to organise medication | Complexity and frequency of treatment regimen | NO | No data |

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| 146 | Complexity and frequency of treatment regimen | Use of blister packs and / or other aids to organise medication | NO | No real drug data (and therefore regimen data) used in prototype |
| 147 | Complexity and frequency of treatment regimen | Level of interference with daily life | NO | No real drug data (and therefore regimen data) used in prototype |
| 148 | Total number of drugs prescribed | Complexity and frequency of treatment regimen | NO | Total number of drugs prescribed fixed at four in prototype |
| 149 | Total number of drugs prescribed | Concerns about potential long term effects | NO | Total number of drugs prescribed fixed at four in prototype |
| 150 | Total number of drugs prescribed | Adverse interactions with other drugs (POM and OTC) | NO | We assume no drugs other than those prescribed are available to the patient (and those interactions would be captured in the user-specified transition probabilities) |
| 151 | Complexity and portability of format of delivery of drugs | Stigma of taking medication in public (e.g. injections) | NO | No real drug data used in prototype |
| 152 | Complexity and portability of format of delivery of drugs | Level of interference with daily life | NO | No real drug data used in prototype |
| 153 | Prioritisation of condition compared to comorbidities | Adherence | NO | No data |
| 154 | Seasonal and environmental factors | Severity of condition | NO | We don't use real condition progression data in the prototype, and so would be unable to translate this into the model |
| 155 | Level of forgetfulness | Adherence | YES | |
| 156 | Age | Level of forgetfulness | NO | No data – (Ardila, Ostrosky-Solis et al. 2000) looked at cognitive decline with age, but the nearest proxy they tested we could use would be "verbal memory", but this does not show a significant reduction with age (or one that we could translate into the model in this context) |
| 157 | Pattern of condition progression | Adherence | YES | |
| 158 | Time since onset | Pattern of condition progression | YES | |
| 159 | Desire to conceive | Adherence | NO | We assume our population does not contain pregnant women (and therefore choose not to model a desire to conceive) |

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| 160 | Desire to conceive | Pregnancy | NO | We assume our population does not contain pregnant women |
| 161 | Caring responsibilities | Adherence | YES | |
| 162 | Living alone | Caring responsibilities | NO | Not needed as user directly specifies caring responsibilities |
| 163 | Perceived addictive qualities of medication | Adherence | NO | Diabetes and asthma medications do not tend to be addictive in nature |
| 164 | Addictive properties of medication | Perceived addictive qualities of medication | NO | Diabetes and asthma medications do not tend to be addictive in nature |

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Appendix B

| Relationship # | Influencing Factor (FROM) | Factor Being Influenced (TO) | Relationship in Literature | Behavioural Rule Used in Model |
|---|---|---|---|---|
| 1 | Affordability of medications to patient | Adherence | (Bezie, Molina et al. 2006) – 12 out of 14 people in a higher socio-economic group were compliers, compared to 31 out of 80 in a lower socio-economic group | If socio-economic status = "low" then proposed action from affordability of medication is to adhere 39% of the time, else proposed action is to adhere 86% of the time |
| 4 | Level of education | Health literacy | (Schillinger, Barton et al. 2006) – health literacy increased moderately for those with up to A-Level education, and more significantly for those with up to university education | Health literacy set to "low", "medium" or "high" depending on whether level of education is "below A-Level", "A-Level" or "university" |
| 8 | Language barriers | Frequency of interaction with health professionals | (Derose and Baker 2000) – Latinos with fair and poor English proficiency reported around 22% fewer physician visits than non-Latinos whose native language was English, even after adjusting for other determinants of physician visits | If primary language is not English, the probability of frequent contact with a physician is 22% lower |
| 9 | Language barriers | Health literacy | (Schillinger, Barton et al. 2006) – health literacy moderately decreased for those for whom English is not primary language | Reduce health literacy by one classification if English is not primary language (remain at "low" if health literacy is already "low") |
| 10 | Health literacy | Frequency of research of | (Murray, Lo et al. 2003) – 30% | If health literacy = "low" then |

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| | | information on the internet | of those with GCSE or A-Level equivalent education reported searching for health-related information on the internet. 47% of those with an undergraduate degree reported searching for health-related information on the internet. 57% of those with an advanced degree reported searching for information on the internet. | 30% probability of being influenced by information found on the internet else if health literacy = “medium” then 47% probability of being influenced by information found on the internet else 57% probability of being influenced by information found on the internet |
| 15 | Preference to use non-drug alternatives (diet etc) | Adherence | (Chiu, Boonsawat et al. 2014) – around 12% of asthma patients agree or strongly agree that herbal medicines are safer than inhalers. 12.5% of those with low adherence agreed or strongly agreed with this. | 12% probability that person prefers alternative treatments. If they do, then the proposed action from this preference is to not adhere 12.5% of the time. |
| 17 | Support in workplace / place of education to take medication | Adherence | (Nebiker-Pedrotti, Keller et al. 2009) – discrimination in the workplace for those with diabetes ranges from 4% to 15% in Switzerland<br><br>John Marshall Law Review (McGrath 2004) – denial of access to medically needed treatment occurs in all types of employment. Employers have denied or significantly restricted access to food, blood glucose testing and insulin. | Probability of discrimination in the workplace is randomly true according to a uniform distribution with lower bound 4% and upper bound 15%. Probability of proposed action from support in workplace being to adhere = 1 – probability of discrimination. |

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| 18 | Support in workplace / place of education to take medication | Openness about condition | (Ruston, Smith et al. 2013) – Private sector : 5/19 forced to disclose diabetes due to hypoglycaemic attack / sickness (received poor support), 6/19 reported full disclosure (received good support), 8/19 reported partial disclosure (only 1 of whom received any support). Public / voluntary sector : 9/19 forced to disclose due to hypoglycaemic attack (received poor support), 4/19 reported full disclosure (3 of whom reported any support), 6/19 reported partial disclosure (1 of whom reported any support). | If person works in public sector, there is a 75% probability that they will be open about their condition. If person works in private sector then there is a 12.5% probability that they will be open about their condition. If neither apply, then openness about condition is not modified by this influence. |
| 19 | Openness about condition | Adherence | (Chiu, Boonsawat et al. 2014) – low adhering asthma patients more likely to report feeling uneasy about using inhaler in public (50.1%) compared to medium and high adhering patients (28.7%) | If person currently taking at least one third of their prescribed medication, there is a 71.3% probability that they will be open about their condition. If they are currently taking less than a third of their medication, there is a 49.9% that they will be open about their condition. This may be overridden by the support they receive in the workplace (relationship #19) or their desire to feel "normal" (relationship |

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| | | | | #21). If they are open about their condition, the proposed action from their openness will be to adhere, otherwise it will be to not adhere. |
| 20 | Desire to feel “normal” by not having to take medication | Adherence | (Baiardini, Braido et al. 2006) – avoidance strategies for coping had negative correlation with taking medications correctly (coeff = -0.40). Inability to accept illness in 34.9% of patients and inability to accept limitations of illness (49.2%) may both impact on medication adherence. | There is a 35% probability that the proposed action from a desire to feel “normal” is to not adhere. |
| 21 | Desire to feel “normal” by not having to take medication | Openness about condition | (Partridge, van der Molen et al. 2006) – 28% of asthma patients agreed that the thought of feeling different from other people was a negative aspect of asthma. | There is a 72% probability that a person’s desire to feel “normal” will lead to them being open about their condition. |
| 25 | Desire to be “in control” of self / condition | Adherence | (Polonsky, Fisher et al. 2005) – 50.6% of diabetes patients believed that insulin therapy would restrict their lives<br><br>(Mann, Ponieman et al. 2009) – 48% of those with diabetes are poorly adherent when they have little confidence in their ability to control their diabetes, compared to 18% when they do have confidence | There is a 49.4% probability that a person has confidence in their ability to control their condition. If they do have this confidence, then the proposed action from desire to be in control is to not adhere 18% of the time. If they don’t have this confidence, then the proposed action from desire to be in control is to not adhere 48% of the time. |

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| 29 | Life events | Adherence | (Helgeson, Escobar et al. 2010) –Adolescents with Type 1 diabetes followed for 5 years : stressful life events led to poorer self-care behaviour<br><br>(Bogner, Morales et al. 2012) – integrated care intervention to improve adherence to anti-glycaemics and anti-depressants for those suffering from depression was found after 12 weeks to have increased the % of good adherers from 35% to 65% (could view the "impact" of depression as 30% reduced adherence) | User specifies frequency and duration of stressful events. When the person is experiencing a stressful event, the proposed action from this influence is to not adhere 30% of the time. |
| 31 | Needle anxiety | Adherence | (Aronson 2012) – up to 94% of insulin users have symptoms of anxiety, stress or phobia - 33% dreaded injections, 22% had to mentally prepare themselves. Prescence of these symptoms strongly associated with less self-monitoring, fewer injections, poorer control | There is a 33% probability that the person will suffer needle anxiety. If they do, then the proposed action from this influence will be to not adhere. |
| 33 | Gender | Adherence | (Kirkman, Rowan-Martin et al. 2015) – males 14% more likely to adhere than females | If person is female, proposed action from gender influence is to not adhere 14% of the time. |
| 34 | Alcohol abuse, illicit drug use and smoking status | Adherence | (Baiardini, Braido et al. 2006) – use of alcohol has negative correlation with taking | If alcohol use is high, then proposed action from this influence is to not adhere. |

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| | | | medications correctly (coeff = -0.30) | |
| 37 | Severity of condition | Adherence | (DiMatteo, Haskard et al. 2007) – there is a 22% higher risk of nonadherence among those who do not believe their condition is a threat because of its severity | If person estimates their current combination of medication to provide them with above average (> 0.5) wellness, then the proposed action from the severity of condition is to not adhere 22% of the time. |
| 39 | Time since onset | Severity of condition | No real condition progression data used, but mechanism for disease progression included in prototype | User manually specifies daily probability of progression to different states of health |
| 40 | Time since diagnosis | Acceptance of diagnosis | (Richardson, Adner et al. 2001) – people with insulin-dependent diabetes with disease duration ranging from 1-43 years had high degree of acceptance of condition (high Acceptance of Disability Scale Modified (ADM) Score)<br>Grey et al (1997) – 1 year from diagnosis, children with diabetes tended to have stable psychosocial status and coping behaviours | If time since diagnosis is one year or less, then the person does not accept their diagnosis. If time since diagnosis is greater than one year, then the person does accept their diagnosis. |
| 41 | Acceptance of diagnosis | Adherence | (Gaude 2011) – 6% of asthma patients were non adherent due to anger about their condition | If person accepts their diagnosis, then the proposed action from this influence is to adhere, otherwise the proposed action is to not adhere. For those who do accept their diagnosis, there is a 6% |

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| | | | | probability that an anger about their condition will lead them to not accept their diagnosis. |
| 47 | Time since diagnosis | Adherence | (Khattab, Khader et al. 2010) – 80.7% of patients had poor glycemic control if they had diabetes for more than 7 years, compared to 50% for those with diabetes for 7 years or less | If time since diagnosis is more than 7 years, then the proposed action from this influence will be to not adhere 80.7% of the time. If time since diagnosis is 7 years or less, then the proposed action from this influence will be to not adhere 50% of the time. |
| 60 | Level of interference with daily life | Adherence | (Blaiss, Kaliner et al. 2009) – inconvenience was given as a reason for non adherence by 3.7% of asthma patients<br><br>(Mann, Ponieman et al. 2009) – 43% are poorly adherent when diabetes significantly interferes with their social life | 3.7% probability that conditions interfere with daily life. If conditions do interfere with daily life, the proposed action from this influence is to not adhere 43% of the time. |
| 61 | Age | Adherence | (SAJITH, PANKAJ et al. 2014) – 28.57% of 18-40 were low adherers, compared with 17.65% of 41-60 and 27.66% of over 60 | If person aged 18-40, proposed action from this influence is to not adhere 29% of the time. If person aged 41-60, proposed action from this influence is to not adhere 18% of the time. If person aged over 60, proposed action from this influence is to not adhere 28% of the time. |
| 65 | Age | Deference | (Kennelly and Bowling 2001) – patient group are all aged 56 and over and displayed high | If person aged 56 or over, deference increases by one classification (up to a maximum |

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| | | | deference. | of “high”). |
| 66 | Deference | Adherence | (Bezie, Molina et al. 2006) – estimates based on figure 2. Of those Type 2 Diabetes patients with no regular follow-up, around 66% were non-compliers. Of those with general practitioner follow-up around 44% were non-compliers. Of those with diabetologist follow-up around 28% were non-compliers. | User specifies level of deference to clinicians. If level of deference is “low”, the proposed action from this influence is to not adhere 66% of the time. If level of deference is “medium”, the proposed action from this influence is to not adhere 44% of the time. Otherwise, the proposed action from this influence is to not adhere 28% of the time. |
| 68 | Awareness of severity and / or nature of condition | Adherence | (Van Steenis, Driesenaar et al. 2014) – asthma patient attitudes to inhaled corticosteroids (ICS). 44% were “Accepting” (high belief in necessity of treatment, low level of concern), 17% were “Ambivalent” (high belief in necessity of treatment, high level of concern), 6% were “Skeptical” (low belief in necessity of treatment, high level of concern) and 33% were “Indifferent” (low belief in necessity of treatment, low level of concern). 63.2% of those who were “Accepting”, 40% of those who were “Ambivalent”, 80% of those | User specifies level of understanding of necessity of treatment, and level of concern about condition. Based on these choices, the person’s personality is determined as “Accepting” (high, low), “Ambivalent” (high, high), “Skeptical” (low, high) or “Indifferent” (low, low). If personality is “Accepting”, the proposed action from this influence is to adhere 63.2% of the time. If personality is “Ambivalent”, the proposed action from this influence is to adhere 40% of the time. If personality is “Skeptical”, proposed action from this |

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| | | | who were "Skeptical" and 55.2% of those who were "Indifferent" were adherent (according to refills). | influence is to adhere 80% of the time. If personality is "Indifferent", proposed action from this influence is to adhere 55.2% of the time. |
| 74 | Stigma of taking medication in public (e.g. injections) | Adherence | (Farsaei, Sabzghabaee et al. 2015) – 15% of Type 2 Diabetes patients did not take statins because they don't take medication when outside the home | 15% probability that the person doesn't take their medication outside of the home. If they don't, then the proposed action from this influence is to not adhere. |
| 75 | Influence of health professionals to promote adherence | Adherence | (Peláez, Lamontagne et al. 2015) – 21.74% of patients received education / advice from a physician.<br><br>(Meece 2014) – Type 2 diabetes patients receiving advice were twice as likely to adhere | 21.74% probability that person is influenced by their physician. If they are, then the proposed action from this influence is to adhere. If they don't then the proposed action is to not adhere. The physician's influence may be overridden by relationship #94 or #105. |
| 76 | Concerns about potential long term effects | Adherence | (Sundberg, Torén et al. 2010) – medication all the time was considered harmful by 48.2% of men with asthma and 35.3% of women with asthma (weighted average across population = 40.49%)<br><br>(Van Steenis, Driesenaar et al. 2014) – average probability of lower adherence for those with high concern ("Ambivalent" and "Skeptical" groups) was | 40.49% probability that person has concerns about the potential long term effects of medication. If they do, then the proposed action from this influence is to not adhere 63.3% of the time. |

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| | | | 63.3% | |
| 78 | Difficulties obtaining timely repeat prescriptions | Adherence | (Chiu, Boonsawat et al. 2014) – 25.8% of asthma patients felt it was inconvenient to get a new inhaler on time due to travel distance. 35.5% of such patients had low adherence. | 25.8% probability that person has difficulty getting timely repeat prescriptions. If they do, then the proposed action from this influence is to not adhere 35.5% of the time. |
| 82 | Dislike of taking medications | Adherence | (Osman, Russell et al. 1993) – 31% of patients reported disliking using daily medication<br><br>(Gaude 2011) – 6% of people reported not adhering to medication due to a dislike of taking it. | 31% probability that person dislikes taking medications on a daily basis. If they do, then proposed action from this influence is to not adhere 6% of the time. |
| 85 | Perceived adverse effects | Adherence | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 86 | Perceived benefits | Adherence | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 87 | Perceived “wellness” | Adherence | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 88 | Influence of information found on the internet | Adherence | (Weaver Iii, Thompson et al. 2009) – if a person searches for information on the internet they are 11.2% likely to not adhere | If a person is influenced by information found on the internet, then the proposed action from this influence will be to not adhere 11.2% of the time. |
| 90 | Influence of family, friends and carers (social connectivity) | Adherence | (SAJITH, PANKAJ et al. 2014) – family support was present with 35.24% of Type 2 Diabetes patients. Of those with family support, 45.94% had high adherence, 35.13% had | 35.24% probability that person has family support. If they do, then the proposed action from this influence is to not adhere 18.92% of the time. If they don’t, then the proposed action |

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| | | | medium adherence and 18.92% had low adherence. Of those with no family support, 35.29% had high adherence, 39.7% had medium adherence and 25% had low adherence. | from this influence is to not adhere 25% of the time. |
| 94 | Relationship with / trust in health professionals | Influence of health professionals to promote adherence | (Whetten, Leserman et al. 2006) – Mean level of trust in care providers (on scale from 3 to 15) was 13.5 (standard deviation of 2.4). Trust in care providers leads to patients being 1.15 times more likely to use their medication. | Level of trust in health professionals selected randomly on normal distribution with mean of 13.5 and standard deviation of 2.4. If this trust level >= 7.5, then the person is influenced by their physician. |
| 95 | Relationship with / trust in health professionals | Frequency of research of information on the internet | (Murray, Lo et al. 2003) – 71% of patients reported an excellent / very good level of care from their physician, compared to 21% good and 8% fair / poor. Of those who rated their level of care as excellent / very good or good, 32% searched for health information on the internet. Of those who rated their level of care as fair / poor, 40% searched for health information on the internet. | If trust in health professionals (calculated in relationship #94) >= 7.5, then there is a 32% probability of being influenced by information found on the internet, otherwise there is a 40% probability of being influenced by information found on the internet. |
| 98 | Frequency of research of information on the internet | Influence of information found on the internet | (Incorporated in relationships #10, #88, #95) | (Incorporated in relationships #10, #88, #95) |
| 105 | Frequency of interaction with health professionals | Influence of health professionals to promote adherence | (Bezie, Molina et al. 2006) – 16.03% of Type 2 Diabetes have regular appointments | There is a 16.03% probability of frequent contact with health professionals (if primary |

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| | | | with a medical practitioner (Hospital doctor, GP or nurse).<br><br>(Corsico, Cazzoletti et al. 2007) – If patient has regular appointments and current adherence is low/medium then increased adherence is 3.32 times more likely<br>If patient has regular appointments and current adherence is high adherence at the continued level is 1.23 times more likely. | language is English). If there is frequent contact, then person is influenced by their physician (overriding relationship #75). |
| 106 | Reluctance to consult with professionals for fear of "wasting their time" | Frequency of interaction with health professionals | (Nichols 1983) – 90/1140 (7.89%) of women reluctant to visit the doctor due to believing they are a nuisance. | 7.89% probability that the person will be reluctant to consult with doctor. If this is the case, then patient does not have frequent contact with health professionals (overriding calculations in relationship #8 and #105) |
| 119 | Perceived adverse effects | Concerns about potential long term effects | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 120 | Perceived adverse effects | Expectations of drug adverse effects | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 121 | Perceived adverse effects | Perceived "wellness" | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 122 | Sensitivity to drug adverse effects | Perceived adverse effects | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 123 | True adverse effects | Perceived adverse effects | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 125 | True adverse effects | True "wellness" | Captured by Reinforcement | Captured by Reinforcement |

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| | | | Learning algorithm | Learning algorithm |
| 133 | True clinical benefits | True “wellness” | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 134 | True clinical benefits | Perceived benefits | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 136 | Sensitivity to drug benefits | Perceived benefits | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 138 | Perceived benefits | Expectations of drug benefits | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 139 | Perceived benefits | Perceived “wellness” | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 140 | True “wellness” | Perceived “wellness” | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 143 | Experience of taking similar / equivalent medication | Expectations of drug adverse effects | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 144 | Experience of taking similar / equivalent medication | Expectations of drug benefits | Captured by Reinforcement Learning algorithm | Captured by Reinforcement Learning algorithm |
| 155 | Level of forgetfulness | Adherence | (Blaiss, Kaliner et al. 2009) – 7.3% of reported asthma patients fail to take medication because they forget (5.2% of asthma patients reported the same).<br><br>(Gaude 2011) – 10% of asthma patients said they fail to take medication because they forget. | Level of forgetfulness for the person is randomly selected from uniform distribution with lower bound 0.052 and upper bound 0.1. The proposed action from this influence is to not adhere for the percentage of time represented by the level of forgetfulness (so if level of forgetfulness is 0.1, the proposed action will be to not adhere 10% of the time). |
| 157 | Pattern of condition progression | Adherence | User specified in prototype | User specified in prototype |
| 158 | Time since onset | Pattern of condition progression | User specified in prototype | User specified in prototype |
| 161 | Caring responsibilities | Adherence | (Pourghaznein, Ghaffari et al. 2013) – there is a negative | User specifies level of caring responsibility. If level = “none”, |

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| | | | correlation between medication adherence and the number of children a person has.<br><br>(Barr, Somers et al. 2002) – 7% of older women with asthma care for an ill spouse. Of those that care for ill spouse 1-8 hours per week, 60% are adherent. Of those that care for ill spouse 9-20 hours per week, 42% are adherent. Of those that care for ill spouse >= 21 hours per week, 37% are adherent. | then proposed action from this influence is to adhere. If level = "low", then proposed action from this influence is to not adhere 40% of the time. If level = "medium", then proposed action from this influence is to not adhere 58% of the time. If level = "high", then proposed action from this influence is to not adhere 63% of the time. |

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