

Causal Dynamic Bayesian Networks for the Management of Glucose Control in Gestational Diabetes

Mariana Neves, Bridget Daley, Graham Hitman, Mohammed Huda, Scott McLachlan, Sarah Finer and William Marsh

EasyChair preprints are intended for rapid dissemination of research results and are integrated with the rest of EasyChair.

April 29, 2021

Causal Dynamic Bayesian Networks for the Management of Glucose Control in Gestational Diabetes

Mariana R. Neves^{*}, Bridget J. Daley[†], Graham A. Hitman[†], Mohammed S. B. Huda[§], Scott McLachlan^{*}, Sarah Finer[‡], and William Marsh^{*}

*School of Electronic Engineering and Computer Science, Queen Mary University of London, London, UK [†]Centre for Genomics and Child Health, Blizard Institute, Queen Mary University of London, London, UK [‡]Primary Care and Public Health, Blizard Institute, Queen Mary University of London, London, UK [§]Department of Diabetes & Metabolism, Barts Health NHS Trust, Royal London Hospital, London, UK Email: m.r.neves@qmul.ac.uk, b.j.daley@qmul.ac.uk, g.a.hitman@qmul.ac.uk, bobby.huda1@nhs.net, scott.mclachlan@qmul.ac.uk, s.finer@qmul.ac.uk, d.w.r.marsh@qmul.ac.uk

Abstract-Patients suffering from chronic conditions may need to make frequent decisions about the management of their condition in partnership with their health professionals. However, this may not be possible as appointments are not always scheduled according to necessity but instead at a fixed frequency. Remote monitoring technology has the potential to generate patient data but without intelligent systems capable of analysing the data and offering advice, more data just increase the person's dependency on clinical staff for its interpretation. Decision-support systems that can give people more autonomy in the management of their condition can therefore benefit both the affected person and clinicians. We propose the use of Dynamic Bayesian Networks built from expert knowledge to interpret data and support decision-making, offering advice to patients suffering from a chronic condition. We argue that expert knowledge is needed as well as data to build such a decision-support system as the data that would be required to use machine learning will never be available in the current clinical system with all treatment decisions made at appointments scheduled at fixed intervals. We illustrate the methodology using a case study in Gestational Diabetes.

Index Terms—Dynamic Bayesian Networks, Chronic diseases, Patient monitoring, Gestational Diabetes Mellitus

I. INTRODUCTION

People suffering from chronic conditions whose treatment needs to be adjusted must wait for their next appointment with a clinician. From the point of view of a clinician, the frequent appointments needed to manage the condition effectively may be a burden, especially when some patients require no modification to their treatment. The development of sensor and communication technologies has made it possible to keep track of vital signs and monitor health using simple devices and tools such as smartwatches, smart bands and phone apps. However, the advance in technology able to collect data has not been accompanied by progress in the interpretation of the data generated. Without tools that can process and analyse data in real time, the use of these new technologies to manage chronic health conditions will be limited as clinicians will not have the resources to analyse the quantity of data generated. Gestational Diabetes Mellitus (GDM) is a condition that develops during pregnancy and require close clinical supervision because of its consequences for both the mother and infant. The blood glucose levels (BGL) of the pregnant women are recorded daily as well as dietary and lifestyle factors. Women with GDM may be seen at hospitals and clinics, for example in fortnightly appointments, when the treatment can be adjusted depending on how well the person's BGL is controlled and on their treatment adherence. Some women are able to control their BGL by following a diet and exercise routine whilst others need medication and frequent adjustments to the dose taken.

Both patients and clinicians could benefit from a decision support tool to monitor patients' BGL to optimize the frequency of clinic appointments and to further encourage the person to take more autonomy in the management of their condition. In Section II we show that BGL control is complicated by the person's adherence to the recommended diet and lifestyle regimes, suggesting that simple deterministic rules will not be adequate.

We therefore propose a methodology to develop a probabilistic model that takes into account the uncertainty and dynamics of a disease progression. This model would be embedded in a decision support system that could be used to allow increase in patient independence and reduce the frequency of appointments for patient monitoring when no adjustment to treatment is necessary. We demonstrate the methodology using a case study of GDM.

A. Dynamic Bayesian Networks

Bayesian Networks (BNs) are probabilistic graphical models consisting of a set of nodes and arcs. The nodes represent random variables and the arcs their direct probabilistic interactions. BNs are widely used in medicine and they offer a natural way of modelling uncertainties involved in diagnosis, treatment selection and prognosis of a disease ([1], [2] and [3]). Dynamic Bayesian networks (DBNs) can incorporate the causal and temporal nature of medical domain knowledge elicited from domain experts and offer detailed prognostic predictions [4]. They were first proposed by [5] and can be seen as an extension to BNs that enables modelling of changes over time (e.g., [5], [6], [7], [8]). A DBN is composed by a set of static and dynamic variables (or nodes), organised in 'time slices'. An intra-time-slice arc connects variables in the same time slice, while the inter-time-slice arcs represents the relationship between variables in different time slices.

It is assumed that the time is discretized into a set of fixed time slices. Conditional probability distributions (CPDs), also called conditional probability tables (CPTs) in the discrete case, model the relationships between variables. Both the structure and the CPDs do not change over time [8]. Extensions of DBNs were proposed by relaxing some of the assumptions described previously (for example, [9], [7], [10], [11] and [12]).

II. GESTATIONAL DIABETES MELLITUS

During pregnancy, the body produces hormones that can have a blocking effect on insulin. Gestational diabetes [13] is a condition in which a hormone produced by the placenta prevents the body from using insulin effectively, therefore the level of glucose in the blood remains high. To compensate the increased amount of glucose in the blood, the body should produce more insulin. Occasionally, the amount of insulin produced is not enough to transport glucose into the cells, or the body cells become more resistant to insulin. Gestational Diabetes Mellitus can therefore be defined as carbohydrate intolerance ([14], [15]). Complications related to GDM include fetal macrossomia, preterm delivery, clinical neonatal hypoglycemia and cesarean delivery ([16], [17], [18]). Evidence suggests that early treatment in order to maintain normal glucose levels can reduce future complications ([19]).

A. GDM management practice

Women with GDM need to control their blood glucose levels at fasting time (before breakfast) and after each meal. Lifestyle advice is provided as soon as a diagnosis is given, including the amount of carbohydrate ingested and appropriate exercise. Women are asked to record their blood glucose levels in a logbook (see Figure 1) 4 times a day: when they wake up, after breakfast, after lunch, and after dinner.

They are also requested to use the same logbook for comments on their lifestyle choices. As these choices have an impact on the person's blood glucose levels (BGL), they are necessary information for the clinician when selecting the best treatment for a specific person at a specific time of the day. The times of the day are often treated separately and the best treatment is selected based on the blood glucose control at that specific time of the day. Some people can manage their blood glucose levels just by following the diet and exercise recommendations throughout the pregnancy, while others need medication such as metformin and or insulin either because

You may find the following pages useful to record your blood glucose test results on, alternatively you can continue to use your home monitoring diary. Use one line per day and enter the result in the box beside the correct date and time. Your specialist team will set agreed blood glucose targets which you may wish to record in the boxes below. My blood before meals $4-55$ In here $4-7.8$												
Day Blood Glucose Level Insulin dose in units												
of Month	Before BF	After BF	Before	After L	Bafore EM	After EM	Bètere BT	BF	L	EM	вт	Comments **
							-					
01-21	5	6.7	-	75	~	7.0	-					
01-21	4.8	7.2	~	6.1	-	6.6	~					
01.21	4.6	6.9	_	6./	-	Q.4)	_					
01-21	4.2	6.0	-	2.8	-	6.0	-					
01-21	4.7	1.8		1.2	-	75	-					
01.21	J-1 U.U	54		69	-	(m)	-					Cometer.
01.21	4.1	5.7	É	7.5	\leq	7.3	-					
01.21	4.7	6.4	~	7.0	-	6.9	~					
01-21	4.6	23	-	7.6	-	75	-					
01-21	52	I)	-		-	7.1	-					
01-21	4.6	7.7	\sim	7.3	~	Q	1					Opizza
01.21	(5.8)	7.1	-	6.9		6.3	-					100

Fig. 1. Simulated logbook page showing how BGL and occasionally medication, diet and exercise information are recorded.

they are unable to comply with the recommendations or because diet and exercise alone are not enough to maintain their blood glucose at a normal level. Some people diagnosed with as GDM can control their BGL without needing medication at any time of the day, some need medication at specific times and others at all times.

People with GDM are managed in community settings led by a midwife when medication is not required, BGL levels are maintained in the ideal range and there is no risk due to comorbidities. Decisions regarding the treatment are made based on how well the BGL is controlled and adherence to treatment. People have appointments that in general occur fortnightly until the delivery decision is made by the clinicians. The clinicians decide which is the best delivery age depending on the blood glucose control, if the person is taking any medication and considering other obstetric risks.

B. GDM management data

A dataset containing 127 people diagnosed with GDM in the Newham University Hospital, part of the Barts Health NHS Trust in London was collected as part of an audit of GDM management and made available for this work¹. The variables include age, ethnicity, BMI and other demographic information, information about blood tests (RPG, OGTT, HbA1c), scan results, delivery and neonatal outcomes, and data such as blood glucose monitoring and lifestyle choices (Figure 1).

The dataset contains information about treatment or adjustment of the treatment prescribed during hospital visits. In the dataset, only appointments in which the treatment was modified were recorded so that it is not possible to know how many appointments each woman had. The distribution of treatment by patient can be seen in Table I. The diet only category represents women that did not take medication at any time of the day at any point during the pregnancy.

¹Clinical Audit of the Diabetes in Pregnancy (Gestational Diabetes) Pathway ID number 9861, approved and registered with Barts Health NHS Trust.



Fig. 2. Distribution of number of days of CBG recorded.

TABLE II DISTRIBUTION OF COMMENTS ON CARBOHYDRATE (CHO) INTAKE AND EXERCISE BY TYPE.

	CHO intake	Exercise
Less than usual	0.88%	89.66%
Usual	4.85%	3.45%
More than usual	94.27%	6.90%

117 / 127 people recorded their capillary blood glucose (CBG) measurements 4 times a day, occasionally adding comments about diet, exercise, medication taken and reasons for not recording CBG measurements. These comments were entered as free text (see Figure 1) and were sometimes difficult to relate to a specific CBG measurement. The distribution of the number of days of CBG measurements recorded (Figure 2) reflects the testing regimen (pregnant women are in general tested at 16 and 24 weeks of pregnancy).

For the 117 people with recorded CBG measurements, 84 had one or more comments on the diet (generally regarding carbohydrate intake), exercise, medication taken, other health issues or missed CBG recordings. Comments specifically about the diet and exercise were recorded by 48 people. The maximum number of comments recorded per person was 30. Also, 50% of the people that recorded comments regarding diet and exercise recorded less than 3 comments. Table II shows the distribution of the comments on diet and exercise by type.

C. Existing Systems for GDM Management

Some studies suggest that GDM treatment is not costeffective ([20], [21]) and it is likely that the cost of a clinic appointment every 14 days contributes to this. We briefly survey existing work that has attempted to improve this. Telemedicine can reduce the need for clinic visits and can improve the management of GDM ([22], [23]). Tools have been developed for GDM management, mainly focusing on blood glucose control but there is less emphasis on increasing the affected person's autonomy.

Some tools (for example, [24] and [25], [26] and [27]) allow the BGL to be monitored remotely. Other tools focus on the diet recommendations since reducing dietary carbohydrate helps control BGL. In [28], the authors propose the use of neural networks to estimate the energy expenditure and determine a meal plan for people with GDM. Tools and models have been also used to predict the person's BGL. In [29], gradient boosting models are used to predict postprandial blood glucose based on the meal glycemic load, amount of carbohydrates and starch in the meal, type of meal, amount of food consumed 6 hours before the current meal and other factors. [30] developed an app that collects information about meals, exercises and sleep and using this information predicts the BGL of people suffering from GDM. The app depends on the person being able to enter the exact amount of food ingested, does not consider medication and is supposed to be used only by women in the third trimester of pregnancy.

DIABNET ([31], [32]) is a tool that offers therapy planning for GDM. The model's main parameters are insulin effectiveness, carbohydrate availability and insulin adequacy. The model uses information about BGL, meals and ketonuria to suggest therapy adjustments. A rule is used to propose quantitative insulin dose modifications and dietary advises are also supposed to be offered. The tool was developed to assist clinicians with dietary and insulin therapy adjustments and it is not directed for patient use. Sinedie ([33], [34]) is a web-based platform designed to monitor pregnant women suffering from GDM remotely using BGL data, information about diet and ketonuria. The person's metabolic condition is analysed by a rule-based knowledge base that generates therapy adjustment recommendations. The system offers dietary advice to patients whilst proposed adjustments in insulin dose are sent to clinicians. The use of the tool was compared to the standard care and the number of face-to-face hospital visits was reduced, but clinicians contacted patients by phone, which does not happened in standard care.

Although tools were developed to support GDM management, they do not seem to target patient independence regarding the management of their condition. We propose a probabilistic model to be embedded in a tool to be used by people with GDM, using only the data that is already recorded.

III. METHODOLOGY FOR MODEL BUILDING

When working with BNs and DBNs it is possible to build the structure of the model and define the CPDs using expert knowledge, data or hybrid approaches. This section explains the approach used to define the structure and CPDs of the model.

A. Defining the structure

The structure of the model, including the choice of variables, was elicited from experts. A team of 3 clinicians and a midwife composed the panel of experts. Regular meetings were conducted to build and validate the structure of the model. The structure uses idioms ([35], [36], [37]) and medical idioms [38]. All variables in the model are discrete, i.e. they have a finite number of states. The software AgenaRisk [39] was used to build the models.

B. Options for Defining the CPTs

The data needed to learn the BN's CPTs are not available within the current health system since the treatment decisions are made at appointments scheduled at fixed intervals. Additionally, the BN model contains latent variables, so called because they correspond to underlying states rather than directlyobserved quantities. Our approach is therefore to define all CPTs using expert knowledge .

However, eliciting CPTs directly from experts can be cumbersome task, rarely cost-effective, and can result in incoherent distributions ([40], [41]). When the variables in the BN are discrete and their states are expressed on an ordinal scale, the use of ranked nodes [40] can simplify the process of eliciting CPTs. In our model, the CPTs of the variables were defined using three techniques: rules, ranked nodes as presented in [40] and an elaboration of this, explained in the next section.

C. Use of Ranked Nodes for Defining the CPTs

The method of using ranked nodes allows the variable defined as ranked to be a weighted average of its parents. It is assumed that each state of the variable corresponds to one subinterval of [0,1]. A doubly truncated Normal distribution with mean μ defined as the weighted average of the parent's variable and variance σ^2 is used to calculate the probability of each state of the variable as the probability of a random variable $X \sim TN(\mu, \sigma^2)$ belonging to each of the sub-intervals.

Even when it is illogical to define the variable as a weighted average of its parents, the use of probability distributions with parameters depending on the parent variables can facilitate the construction of the CPTs. We use a doubly truncated Normal distribution on the interval [0,1], with both the mean μ and the variance σ^2 defined depending on assumptions made about the combination of the parents' states and their relationships. We chose to use a Truncated Normal distributions as used as in [40] because we found that it is easy to define the mean and variance using logic extracted from expert knowledge, but other probability distributions could be used.

IV. DBN FOR GLUCOSE CONTROL SUPPORT

In this section, we explain the model's variables, CPTs and structure. In Section IV-A we describe the variables that represent the model's input. In Sections IV-B, IV-C, IV-D and IV-E we describe fragments of the model. In Section IV-F we suggest how the model should be used. The complete BN model is shown in Figure 3.

A. Evidence variables

The variables representing the model's input are called evidence variables and use the daily records kept by women with GDM. In our model the evidence variables (shaded grey in Figure 3) are:

- CBG measurement: the BGL measured using the capillary blood glucose test,
- *Carbohydrate intake*: the amount of carbohydrate in the meal compared with the usual amount and
- *Exercise after meal*: the amount of exercise after the meal, also compared to usual routine.

The meaning of these variables varies depending on the time of the day the tool is used: when using the tool at fasting time (just after waking up) the *CBG measurement* is set from a measurement at that time, but *Carbohydrate intake* and *Exercise after meal* are given by what happened at the end of the previous day.

The additional variable *Data input* is not directly entered but inferred from the other inputs. It is used to handle the case that the woman with GDM does not enter any information for the other inputs for the specific time on a given day. Rather than using a prior distribution for the variables *CBG measurement*, *Carbohydrate intake* and *Exercise after meal*, the distributions used when evidence is not entered depend on *Data input*. If *Data input* is No, past information about the person is used instead of a prior since data was not entered. If the *Data input* is yes, these variables have a uniform distribution. This technique prevents the information entered from flowing backwards to the previous day's variables.

B. Alternative explanation for hyperglycemia episodes

The variable *Glycemia explanation* represents whether there is an alternative explanation for hyperglycemia that is not directly a symptom of GDM, either because the person had a meal with high amount of carbohydrates or because the person did not exercise after the meal (see Figure 4). Since the explanation for a hyperglycemia episode is a balance between the carbohydrate intake and exercise, an increase in carbohydrate intake could, for example, be compensated by more intense exercising. We considered that the weight of carbohydrate intake variable to be twice as the weight of the exercise variable, meaning that even a small increase in carbohydrate ingested would require a lot more exercise to compensate for the effect on the BGL and avoid hyperglycemia.

We use the methodology in section III-C to define the CPT of the variable *Glycemia explanation*. The mean of the distribution for each combination of the states of *Carbohydrate intake* and *Exercise after meal* is defined by the weighted average of the combination, with weight 2 for Carbohydrate intake and 1 for exercise. The variance is defined following the logic: when the states of *Carbohydrate intake* and *Exercise after meal* have the same effect on the BGL (such as eating less carbohydrate and exercising more) the variance is small. When the states of *Carbohydrate intake* and *Exercise after meal* have an opposing effect on the BGL the variance is larger. If only one of the diet or exercise differs from usual, the variance lies in between the previous cases.

For tracking if the person has not been following the recommendations for diet and exercise, the variables *Diet adherence* and *Exercise adherence* are used. They represent the consistency of the behaviour of the person related to the



Fig. 3. Two Time-Slices of the DBN for Managing Glucose Control (Using AgenaRisk [39]).

lifestyle choices. We also used the methodology in section III-C to define the CPT tables of *Diet adherence* and *Exercise adherence* variables. Both variables are defined as a weighted average between adherence in the past and the adherence in the current day.

We assigned values for each state of the parent variables as the center of the interval depending on whether they represent adherence or not. The mean is then calculated as a weighted average with weight 4 for the past adherence and 1 for the current day. We use variance $\sigma^2 = 0.02$. The weights represent how quickly we want the adherence to adapt to the most recent information about diet and exercise.

C. Blood glucose control

The variables (see Figure 4) that model the increased BGL caused by insulin resistance in a woman with GDM are:

- *CBG measurement*: the evidence variable described above,
- *Glycemia explanation*: the alternative explanation for any abnormal BGL (also described above) and
- *Underlying BGL*: representing the blood glucose levels adjusted for the effect of any alternative explanations.

Each *CBG measurement* state corresponds to one of the states of the *Underlying BGL*. Using the methodology in section III-C, when there is no alternative source of disturbance in the BGL (as an increased carbohydrate intake), the mean μ of the distribution will be defined as the center of the interval corresponding to the state of the CBG measurement.

In case the increase in the BGL is caused by one of the alternative explanations for a hyperglycemia episode, the effect is possibly reversible without an increase in the dose of the medication. If there is no alternative explanation for a rise in the BGL, it is often assumed that the rise was caused by a worsening of the condition and an increase in the dose is prescribed. A hyperglycemia episode motivated by non-concordance to the diet and exercise recommendations



Fig. 4. Blood glucose control (Using AgenaRisk [39]).

dislocates the true state of *Underlying BGL* to a higher level. For this reason, when there is a hyperglycemia explanation, we define the mean of the distribution no longer as the center of the interval correspondent to the state of the *CBG measurement* but as the center subtracted by a fraction of the interval size. The variance used in all cases was $\sigma^2 = 0.002$.

D. Overall blood glucose dynamics

Figure 5 shows the variable in this fragment of the BN. The variable *BG average level* represents the weighted average of the previous and current *Underlying BGL* and is used to evaluate if the person is having problems controlling their BGL; if the average is high it could indicate that the person needs medication. We used a ranked node with a weighted mean with weight 5 for *BG average level* in the previous day and 1 for *Underlying BGL* in the current day and variance 0.0003.

It is also important to keep track of the progression of the BGL; if the blood glucose level is increasing, the person could soon need medication, while if the BGL is decreasing after an

intervention, it could indicate that the intervention succeeded. The *Change* variable represents the change in the *Underlying BGL* from the previous to the current day. The CPT table contains 147 entries and was defined by a simple rule: when the *Underlying BGL* for the current day is higher than the previous day the *Change* state is 'Increase', when it is lower 'Decrease' and when it is the same 'No change'.

The variable *Trend* is used to keep track of the BGL dynamics and it depends on the variables *Change* and *Trend* in the previous day. We defined this variable as Ranked with a weighted mean with weight 5 for *Trend* in the previous day and 1 for *Change* and variance 0.0003.

The combined information about the *BG average level* and *Trend* is necessary for defining which people need support. If the average of the blood glucose levels of two people are high but for one the trend is increasing and for the second the trend is decreasing, the first person is more likely to need medication. The variable *Glycemic state* is therefore a combination of *BG average level* and *Trend* and represents the person's overall state (figure 5).

The CPT of the variable Glycemic state was defined using the method explained in section III-C. The mean of the distribution was defined depending on the states of the BG average level variable. For example, if the BG average level of the person is High, she is more likely to be in the state Alarm, so the mean of the distribution over the states of the Glycemic state variable when the BG average level is High should belong to the interval corresponding to Alarm state. We propose to define the variance of the distribution depending on the combination of the states *BG* average level and *Trend*. For example, for the combination of states High and Trend Increasing, Stable and Decreasing we follow the logic: the mean of the distribution is located in the state Alarm so the distribution for the combination High and Increasing should have a small variance since the combination represents high risk for the pregnant woman. The variance for the distribution of High and Decreasing, on the other hand, should be larger than the previous one since there is indication that the person's state is improving and then we should be more uncertain about the person's Glycemic state being Alarm. The same logic is applied for the remaining combinations except the ones including the states High and Low of the variable BG average level, for which the mean was also modified for each combination.

E. Recommendation

People not achieving BGL targets on diet control may require further lifestyle advice or medication to improve glycemic control. If the woman is following the recommendations but still has a high and increasing average BGL she is likely to need an appointment to determine whether she needs medication. If the person's BGL is 'controlled' on diet and lifestyle and there are no other pregnancy complications or the person is not considered at high obstetric or fetal risk, then that person could be safely managed with fewer appointments in the clinic.



Fig. 5. Overall blood glucose dynamics (Using AgenaRisk [39]).

 TABLE III

 CPT FOR THE VARIABLE Treatment adherence.

Diet adherence	N	lo	Yes	
Exercise adherence	No	Yes	No	Yes
Improve Diet	0.0	1.0	0.0	0.0
Improve Exercise	0.0	0.0	1.0	0.0
Improve Diet + Exercise	1.0	0.0	0.0	0.0
Well done	0.0	0.0	0.0	1.0

The variables expressing this reasoning (see Figure 3) are:

- The variable *Treatment adherence* represents the overall adherence to the treatment. The CPT for this variable is defined in table III.
- The variable *Advice* is defined by the *Glycemic state* and *Treatment adherence* variables and represents the advice that should be given. The states of the variable are: Schedule an appointment, Treatment adherence and Monitor.

The CPT table for the *Advice* variable is given by the following rules:

- 1) If the *Glycemic state* is 'Alarm' the *Advice* should be 'Schedule an appointment' for any possible state of *Treatment adherence*.
- 2) If the *Glycemic state* is 'Attention' and *Treatment adherence* is 'Well done' the *Advice* should be 'Schedule an appointment' and for any other state of *Treatment adherence* the *Advice* should be 'Treatment adherence'.
- If the *Glycemic state* is 'Control' and *Treatment adherence* is 'Well done' the *Advice* should be 'Monitor' otherwise the *Advice* should be 'Treatment adherence'.

F. Proposed Use for Decision-Support

The probabilistic model should be part of a tool to be used by pregnant women 4 times a day, entering information for the evidence variables (explained in the section IV-A and represented in grey in Figure 3). The output would be the advice: scheduling the frequency of health-professional appointments when the BGL are uncontrolled and the person has been complying with the treatment, treatment adherence when the person is not following the treatment recommendations and

TABLE IV Description of the Invented Scenarios.

Person	BGL	Trend	CHO intake and Exercise		
1	Normal	Stable	Usual		
2	Normal	Increasing	Usual		
3	Very high	Decreasing	Usual		
4	High	Stable	Usual		
5	Very high	Stable	Usual		
5'	Very high	Stable	Unusual		

self-monitoring when the BGL is controlled and the person is following the treatment recommended.

We propose using four different models for tracking a person's overall glycemic control: one for each time of the day. For example, when tracking BGL control at lunch, the evidence entered for the variable CBG measurement would represent the CBG measured at the current day at lunch time. It means that the evidence entered in the previous day's CBG measurement would correspond to the CBG measured in the previous day at the same time. The same is true for all the evidence variables. This model would only make predictions for lunch time. The final advice would be schedule an appointment, improve treatment adherence, or to continue to monitor (when the BGL is controlled). The complete structure of the model can be seen in Figure 3. A model with the same structure would be used for each of the other times of the day and if the advice from any of the models is to schedule an appointment, that would be the final advice given.

V. EVALUATION

In this section we present the results of two tests of the BN model. It was first tested using invented scenarios and then separately with two real cases from the data set. The AgenaRisk API was used to perform inference in the model. The problem of testing the model using real data is that the model's main recommendation is to seek an appointment, whereas in the data the appointments are at fixed intervals. Therefore a precise correspondence is not possible; instead we look for an appointment where a change was made close to the time this is recommended by the model.

A. Testing with scenarios

To test the model's reasoning, we have invented 6 scenarios covering different simple cases. Each scenario defines the evidence entered over 14 days. The invented scenarios are not necessarily a faithful representation of real people, but they can be used as a first step in the validation of the model. The characteristics of each scenario are described in Table IV.

We used 14 days of fictitious data to test the models reasoning. We do not show the predictions for the first 4 days (since with no past data these are not specific), so the first day in Figure 6 represents the fifth day of the monitoring.

1) Advice in the Invented Scenarios: Figure 6 shows the probabilities for each state of the variable Advice for people 1 to 5 in Table IV (all with usual diet and exercise). The advice



Fig. 6. Probability of Each State of Variable Advice, Invented Scenarios.

given in each scenario to the imaginary person seems to be consistent with the simulated health state.

- For person 1 who has a controlled BGL within the normal limits, the state of largest probability is the state Monitor. We also observe that there is still a reasonably high probability for the state *Treatment adherence*. This is due to the approach used to define the mean and variance of the distribution for the states of the *Treatment adherence* variable and this can be easily adjusted.
- For the people 2 and 3 that simulate scenarios in which a person's health is improving or deteriorating, the probability of the states of the *Advice* variable are coherent with the BGL trajectory.
- People 4 and 5 simulate the difference between a person whose BGL is clearly outside the normal ranges and a person that can be considered borderline. The probability for the states of the *Advice* variable shows that the person whose BGL is Very high would be given the advice to schedule an appointment after fewer days.

2) Hyperglycemia explanation versus no hyperglycemia explanation: For people whose BGL are outside the normal range, possible explanations for hyperglycemia should be considered. In cases where the person has not followed the diet and exercise recommendations, the clinician might emphasise their importance and reevaluate the person's state in the next appointment. In cases where the person's BGL is uncontrolled and there are no possible explanations related to diet and exercise, the clinician might prescribe metformin, insulin, or both.

Figure 6 shows the probabilities of each state of the monitoring and advice variables for people 5 and 5'. A comparison between these 2 people with the same BGL but different input in the explanations show that for person 5 the model's advice is to schedule an appointment whilst for the person 5' the model suggests the person adheres to the treatment at first, but after a longer period of uncontrolled BGL and no change in the adherence, the model suggests that an appointment should be scheduled .



Fig. 7. BGL (modified by a random offset) and advice for a person on lunch time medication.

CBG measurement 10.0 7.5 CBG 5.0 2 5 0.0 21 31 41 51 61 1Ó1 Day Advice 1.00 0.75 Probability 0.50 0.25 0.00 61 Day 2' 3 51 81 91 1Ó1 12 ent adherence Schedule

Fig. 8. BGL (modified by a random offset) and advice for a person not taking medication.

B. Results from Audit Data

We tested the model using 129 days of lunch time monitoring data (CBG measurement, diet and exercise) for two people from audit data. Figure 7 shows the CBG measurements for each day starting from the 5^{th} day. To preserve confidentiality, the actual CBG data plotted in the upper part of the two figures have been modified using a small random offset. At first, the person in Figure 7 was not taking medication, but started taking metformin on the day 113 (shown in the figure by a red vertical dotted line). The dotted blue vertical lines represent days for which the person did not follow the diet or exercise recommendations.

We observe that in the first 20 days of monitoring the person seemed not to adhere to diet and exercise recommendations. Figure 7 shows that the most probable state at that period was Treatment adherence. It is not possible to affirm if the person was offered advice regarding diet and exercise frequency and improved her treatment adherence or if the person simply did not record when she did not follow diet and exercise recommendations after that period but no other days of unusual diet choices or exercise pattern were found in the data.

After approximately 3 months of monitoring, the BGL appears to be uncontrolled. At that time, the model indicates (probability of the state 'Schedule an appointment' in Figure 7) that the person should schedule an appointment. If we consider the advice that should be given as the most probable state at each day, the model would advise this person to schedule an appointment on day 95 in Figure 7, 14 days before the person had an appointment in which the medication was changed. We cannot confirm that the person did not have an appointment before the date in which the medication treatment was initiated, but we can say that the model suggested the person should have an appointment 14 days before the first modification of the treatment.

We also tested the model using 127 days of monitoring data for lunch time for a person who did not have medication for controlling after lunch BGL during the entire pregnancy and seemed compliant to the diet recommendations and exercise routine. We observe (Figure 8) that the model seems to capture the periods in which the person's BGL was outside the normal range but the final advice for the person during the entire period was to continue monitoring.

VI. CONCLUSION

In this paper we have described the difficulties of monitoring people suffering from chronic conditions and the need for decision-support models directed to patient use that can interpret frequent monitoring data. Often, the data that might be used to build these models will not be available in full. We have used a case study in GDM management to present these difficulties and propose solutions.

We propose a probabilistic model to be part of a tool to be used by people suffering from GDM when monitoring their condition. The model is a DBN built from expert knowledge. The structure was elicited from a team of clinicians and we used different techniques to define the CPT tables. We tested the model using invented scenarios and audit data from two real people; the results of both tests show that the model behaves as expected.

We plan to conduct a more extensive evaluation of the model by looking at the time between the model advising a person to schedule an appointment and when the person had an appointment in which medication was initiated or adjusted for everyone in the audit data. We will use experts to evaluate the model's incorrect predictions and make modifications to the model if necessary. We are also developing a model to support people on medication.

ACKNOWLEDGMENT

Support is acknowledged from EPSRC project EP/P009964/1 PAMBAYESIAN for MR, WM, BD, GH and MH. We thank Prof. Norman Fenton, Dr. Evangelia Kyrimi and Ali Fahmi for contributions to the DBN model development.

REFERENCES

- [1] P. Lucas, Bayesian networks in medicine: a model-based approach to medical decision making. na, 2001.
- [2] P. J. Lucas, L. C. Van der Gaag, and A. Abu-Hanna, "Bayesian networks in biomedicine and health-care," *Artificial intelligence in medicine*, vol. 30, no. 3, pp. 201–214, 2004.
- [3] E. Kyrimi, S. McLachlan, K. Dube, M. R. Neves, A. Fahmi, and N. Fenton, "A comprehensive scoping review of bayesian networks in healthcare: Past, present and future," *arXiv preprint arXiv:2002.08627*, 2020.
- [4] M. A. Van Gerven, B. G. Taal, and P. J. Lucas, "Dynamic bayesian networks as prognostic models for clinical patient management," *Journal* of biomedical informatics, vol. 41, no. 4, pp. 515–529, 2008.
- [5] T. Dean and K. Kanazawa, "A model for reasoning about real-time processes," *Computational Intelligence*, vol. 5, no. 2, p. 37 p. ;, feb 1989.
- [6] U. Kjaerulff, "A computational scheme for reasoning in dynamic probabilistic networks," in *Uncertainty in Artificial Intelligence*. Elsevier, 1992, pp. 121–129.
- [7] A. E. Nicholson and J. M. Brady, "Dynamic belief networks for discrete monitoring," *IEEE Transactions on Systems, Man, and Cybernetics*, vol. 24, no. 11, pp. 1593–1610, 1994.
- [8] K. P. Murphy and S. Russell, "Dynamic bayesian networks: representation, inference and learning," 2002.
- [9] T. Dean and K. Kanazawa, "A model for reasoning about persistence and causation," *Computational intelligence*, vol. 5, no. 2, pp. 142–150, 1989.
- [10] U. Nodelman, C. R. Shelton, and D. Koller, "Continuous time bayesian networks," arXiv preprint arXiv:1301.0591, 2012.
- [11] J. Robinson and A. Hartemink, "Non-stationary dynamic bayesian networks," Advances in neural information processing systems, vol. 21, pp. 1369–1376, 2008.
- [12] L. Song, M. Kolar, and E. Xing, "Time-varying dynamic bayesian networks," Advances in neural information processing systems, vol. 22, pp. 1732–1740, 2009.
- [13] A. D. Association *et al.*, "Gestational diabetes mellitus," *Diabetes care*, vol. 27, p. S88, 2004.
- [14] S. L. Kjos and T. A. Buchanan, "Gestational diabetes mellitus," New England journal of medicine, vol. 341, no. 23, pp. 1749–1756, 1999.
- [15] T. A. Buchanan, A. H. Xiang et al., "Gestational diabetes mellitus," *The Journal of clinical investigation*, vol. 115, no. 3, pp. 485–491, 2005.
- [16] P. M. Catalano, H. D. McIntyre, J. K. Cruickshank, D. R. McCance, A. R. Dyer, B. E. Metzger, L. P. Lowe, E. R. Trimble, D. R. Coustan, D. R. Hadden *et al.*, "The hyperglycemia and adverse pregnancy outcome study: associations of gdm and obesity with pregnancy outcomes," *Diabetes care*, vol. 35, no. 4, pp. 780–786, 2012.
- [17] K. Kamana, S. Shakya, and H. Zhang, "Gestational diabetes mellitus and macrosomia: a literature review," *Annals of Nutrition and Metabolism*, vol. 66, no. Suppl. 2, pp. 14–20, 2015.
- [18] A. Gilmartin, S. H. Ural, and J. T. Repke, "Gestational diabetes mellitus." *Reviews in obstetrics & gynecology*, vol. 1, no. 3, pp. 129– 134, 2008.
- [19] O. Langer, Y. Yogev, O. Most, and E. M. Xenakis, "Gestational diabetes: the consequences of not treating," *American journal of obstetrics and gynecology*, vol. 192, no. 4, pp. 989–997, 2005.
- [20] D. Farrar, M. Simmonds, S. Griffin, A. Duarte, D. A. Lawlor, M. Sculpher, L. Fairley, S. Golder, D. Tuffnell, M. Bland *et al.*, "The identification and treatment of women with hyperglycaemia in pregnancy: an analysis of individual participant data, systematic reviews, meta-analyses and an economic evaluation," *Health technology assessment*, pp. 1–348, 2016.
- [21] N. Fitria, A. D. van Asselt, and M. J. Postma, "Cost-effectiveness of controlling gestational diabetes mellitus: a systematic review," *The European Journal of Health Economics*, vol. 20, no. 3, pp. 407–417, 2019.
- [22] W. Xie, P. Dai, Y. Qin, M. Wu, B. Yang, and X. Yu, "Effectiveness of telemedicine for pregnant women with gestational diabetes mellitus: an updated meta-analysis of 32 randomized controlled trials with trial sequential analysis," *BMC pregnancy and childbirth*, vol. 20, pp. 1–14, 2020.
- [23] N. Pérez-Ferre, M. Galindo, M. D. Fernández, V. Velasco, I. Runkle, M. J. de la Cruz, P. Martín Rojas-Marcos, L. Del Valle, and A. L. Calle-Pascual, "The outcomes of gestational diabetes mellitus after a

telecare approach are not inferior to traditional outpatient clinic visits," *International journal of endocrinology*, vol. 2010, 2010.

- [24] L. Mackillop, J. E. Hirst, K. J. Bartlett, J. S. Birks, L. Clifton, A. J. Farmer, O. Gibson, Y. Kenworthy, J. C. Levy, L. Loerup *et al.*, "Comparing the efficacy of a mobile phone-based blood glucose management system with standard clinic care in women with gestational diabetes: randomized controlled trial," *JMIR mHealth and uHealth*, vol. 6, no. 3, p. e71, 2018.
- [25] H. Miremberg, T. Ben-Ari, T. Betzer, H. Raphaeli, R. Gasnier, G. Barda, J. Bar, and E. Weiner, "The impact of a daily smartphone-based feedback system among women with gestational diabetes on compliance, glycemic control, satisfaction, and pregnancy outcome: a randomized controlled trial," *American journal of obstetrics and gynecology*, vol. 218, no. 4, pp. 453–e1, 2018.
- [26] M. Rigla, I. Martínez-Sarriegui, G. García-Sáez, B. Pons, and M. E. Hernando, "Gestational diabetes management using smart mobile telemedicine," *Journal of diabetes science and technology*, vol. 12, no. 2, pp. 260–264, 2018.
- [27] M. Peleg, Y. Shahar, S. Quaglini, T. Broens, R. Budasu, N. Fung, A. Fux, G. García-Sáez, A. Goldstein, A. González-Ferrer *et al.*, "Assessment of a personalized and distributed patient guidance system," *International journal of medical informatics*, vol. 101, pp. 108–130, 2017.
- [28] H. T. Huynh and T. M. Hoang, "A novel approach for determining meal plan for gestational diabetes mellitus using artificial intelligence," *The Computer Journal*, 2020.
- [29] E. A. Pustozerov, A. S. Tkachuk, E. A. Vasukova, A. D. Anopova, M. A. Kokina, I. V. Gorelova, T. M. Pervunina, E. N. Grineva, and P. V. Popova, "Machine learning approach for postprandial blood glucose prediction in gestational diabetes mellitus," *IEEE Access*, vol. 8, pp. 219308–219321, 2020.
- [30] E. Pustozerov, P. Popova, A. Tkachuk, Y. Bolotko, Z. Yuldashev, and E. Grineva, "Development and evaluation of a mobile personalized blood glucose prediction system for patients with gestational diabetes mellitus," *JMIR mHealth and uHealth*, vol. 6, no. 1, p. e6, 2018.
- [31] M. Hernando, E. Gómez, F. Del Pozo, and R. Corcoy, "Diabnet: a qualitative model-based advisory system for therapy planning in gestational diabetes," *Medical Informatics*, vol. 21, no. 4, pp. 359–374, 1996.
- [32] M. E. Hernando, E. J. Gómez, R. Corcoy, and F. del Pozo, "Evaluation of diabnet, a decision support system for therapy planning in gestational diabetes," *Computer methods and programs in biomedicine*, vol. 62, no. 3, pp. 235–248, 2000.
- [33] E. Caballero-Ruiz, G. García-Sáez, M. Rigla, M. Villaplana, B. Pons, and M. E. Hernando, "A web-based clinical decision support system for gestational diabetes: automatic diet prescription and detection of insulin needs," *International journal of medical informatics*, vol. 102, pp. 35– 49, 2017.
- [34] L. Albert, I. Capel, G. García-Sáez, P. Martín-Redondo, M. E. Hernando, and M. Rigla, "Managing gestational diabetes mellitus using a smartphone application with artificial intelligence (sinedie) during the covid-19 pandemic: Much more than just telemedicine," *Diabetes research and clinical practice*, vol. 169, p. 108396, 2020.
- [35] M. Neil, N. Fenton, and L. Nielson, "Building large-scale bayesian networks," *The Knowledge Engineering Review*, vol. 15, no. 3, pp. 257– 284, 2000.
- [36] D. A. Lagnado, N. Fenton, and M. Neil, "Legal idioms: a framework for evidential reasoning," *Argument & Computation*, vol. 4, no. 1, pp. 46–63, 2013.
- [37] N. Fenton and M. Neil, *Risk assessment and decision analysis with Bayesian networks*. Crc Press, 2018.
- [38] E. Kyrimi, M. R. Neves, S. McLachlan, M. Neil, W. Marsh, and N. Fenton, "Medical idioms for clinical bayesian network development," *Journal of Biomedical Informatics*, vol. 108, p. 103495, 2020.
- [39] Agena Ltd, "Agenarisk." [Online]. Available: https://www.agenarisk.com/
- [40] N. E. Fenton, M. Neil, and J. G. Caballero, "Using ranked nodes to model qualitative judgments in bayesian networks," *IEEE Transactions* on *Knowledge and Data Engineering*, vol. 19, no. 10, pp. 1420–1432, 2007.
- [41] C. A. Pollino, O. Woodberry, A. Nicholson, K. Korb, and B. T. Hart, "Parameterisation and evaluation of a bayesian network for use in an ecological risk assessment," *Environmental Modelling & Software*, vol. 22, no. 8, pp. 1140–1152, 2007.