“Turning mirrors into windows”: A study of participatory dynamic simulation modelling to inform health policy decisions

Louise Freebairn

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Chapter 7: Results Part 4: ‘Turning the tide’ on diabetes in pregnancy: Insights from advanced dynamic simulation modelling

This chapter presents the model developed for the primary case study focusing on diabetes in pregnancy (DIP) and reports on the model findings. These results are presented using three methods of communication: an academic manuscript for publication as a journal article, communication products that I developed and used to disseminate insights arising from the model to decision makers within the ACT Health service, and some technical supplementary information about the model itself.

Section 7.1 includes the journal manuscript describing the model development, structure and logic, and reporting on the insights from scenario testing (model findings) to inform decision making. The manuscript included in this chapter is currently undergoing external clinical review prior to journal submission. The communication products aimed at disseminating knowledge about both the project and the policy insights to a non-technical, policy audience are included in Section 7.2 and Appendix 9. These communication products included a plain language fact sheet about the project, an interactive dashboard and a podcast interview. The detailed documentation of the model structure and associated parameters, functions and data sources are included in Appendix 10. Some of this material was included in a technical paper on which I am a contributing co-author (as listed in the front of this thesis) that was led by the computer science members of the modelling team. The model documentation will also be published as supplementary material to the manuscript included in Section 7.1.
7.1. ‘Turning the tide’ on diabetes in pregnancy: Insights from advanced dynamic simulation modelling

Authors (order to be confirmed)

Louise Freebairn\textsuperscript{a,c}, Jo-An Atkinson\textsuperscript{b,d}, Yang Qin\textsuperscript{e}, Paul M Kelly\textsuperscript{a,h,f}, Luke Penza\textsuperscript{g}, Ante Prodan\textsuperscript{g}, Anahita Safarishahrbijari\textsuperscript{e}, Weicheng Qian\textsuperscript{e}, Christopher Nolan\textsuperscript{a,f}, Alison L Kent\textsuperscript{e,h}, Louise Maple-Brown\textsuperscript{b}, Roland Dyck\textsuperscript{k}, Allen McLean\textsuperscript{e}, Geoff McDonnell\textsuperscript{b} and Nathaniel D Osgood\textsuperscript{a},

\textsuperscript{a}ACT Health, GPO Box 825, Canberra ACT 2601, Australia
\textsuperscript{b}Australian Prevention Partnership Centre, the Sax Institute, PO Box K617, Haymarket NSW 1240, Sydney Australia
\textsuperscript{c}University of Notre Dame, PO Box 944, Broadway NSW 2007, Sydney Australia
\textsuperscript{d}Sydney Medical School, University of Sydney, Sydney NSW 2006
\textsuperscript{e}CEPHIL Lab, Department of Computer Science, University of Saskatchewan
\textsuperscript{f}The Australian National University, Canberra ACT 2601
\textsuperscript{g}Western Sydney University, Sydney NSW 2052, Australia
\textsuperscript{h}University of Rochester, Golisano Children’s Hospital at URMC, Rochester, 14642, NY, USA
\textsuperscript{i}Menzies School of Health Research, Darwin
\textsuperscript{j}Division of Medicine, Royal Darwin Hospital
\textsuperscript{k}Department of Medicine, University of Saskatchewan

Email: louise.freebairn@act.gov.au

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Abstract

Introduction: Diabetes in pregnancy is rapidly increasing, with both short- and long-term risks to the health of women and their babies. Strategies to manage and prevent this condition are contested. Dynamic simulation models (DSM), developed using participatory methods, can be used to explore and test policy and program scenarios before they are implemented in the real world. This paper reports on the development and use of an advanced DSM to explore the impact of interventions on maternal weight status and incidence of diabetes in pregnancy (DIP, including gestational diabetes and pre-existing type 1 and type 2 diabetes).

Method: A consortium of experts worked collaboratively to develop a hybrid dynamic simulation model of diabetes in pregnancy comprising of integrated system dynamics, agent-based and discrete event model components. The structure and parameterisation of the model drew on a range of data sources. A series of scenarios comparing the impact of population-level and individually targeted prevention interventions were investigated to identify the combination of interventions that would deliver the greatest impacts.

Results: Population interventions promoting weight loss in early adulthood were found to be more effective (17.6% reduction in incidence by 2030) than targeted pre-pregnancy (5.2% reduction) and post-pregnancy (4.2% reduction) interventions in reducing the population incidence of DIP. Combining targeted interventions for high risk groups with population interventions promoting healthy weight in early adulthood was most effective for reducing DIP incidence (28.8% reduction by 2030). Scenarios exploring the impact of scaling up or scaling back interventions promoting healthy weight in childhood demonstrated significant changes in the selected outcome measure for glycemic regulation, insulin sensitivity, in the short term and diabetes in pregnancy in the long term.

Discussion: Population-level weight reduction interventions will be necessary to “turn the tide” on DIP. Weight reduction interventions targeting individuals identified as high risk, while beneficial for those individuals, did not significantly impact forecasted diabetes in pregnancy incidence rates. The importance of maintaining interventions promoting healthy weight in childhood was also demonstrated.
Keywords

Dynamic simulation modelling, evidence synthesis, public health policy, prevention policy, diabetes in pregnancy, gestational diabetes, multimethod modelling, hybrid modelling

Research in context

Evidence before this study: The rising prevalence of diabetes in pregnancy (DIP) is having a significant impact on health service demand and resources, yet the strategies for screening, diagnosing, preventing and managing DIP remain contested. Exploration of effective decision support tools is needed to guide evidence-informed policy and programs for this complex problem. We searched PubMed and Medline (OVID) databases from inception up to August 24, 2018 using the search terms: “dynamic simulation” “agent-based model” “system dynamics” with a combination of “diabetes” and “pregnancy” and “gestational diabetes”, without language restrictions. We identified only one Canadian study, by members of this modelling consortium, reporting on a dynamic simulation model exploring the intergenerational effects of DIP on the development of type 2 diabetes in an Indigenous population.

Added value of this study: This study brought together local, national and international researchers, clinicians and policy makers to collaboratively develop a multi-scale DSM for DIP capable of exploring the likely impact of policy and health service scenarios to prevent and manage DIP before they are implemented in the real world. The DSM incorporated the complex and interrelated causal factors that contribute to the development of DIP and explored intervention options and combinations, spanning the spectrum from clinical to population health interventions. For the first time, this study brings together the best available evidence and data with integrated DSM approaches to deliver insights for the challenging problem of DIP. Additionally, the unique tripartite structure of the model incorporates multiple integrated dynamic modelling methods. This represents unparalleled sophistication and allows representation of the problem of DIP at multiple integrated levels of abstraction (biological dynamics, individual-level behavioural dynamics and service dynamics) which accommodates a complex systems perspective, while also optimising model performance.
Implications of all the available evidence: The scenario testing capacity enabled by this multi-scale DSM advanced the findings from previous studies and provided guidance for decision making for the prevention of DIP. The scenarios reported in this paper confirmed the importance of public health interventions to maintain healthy weight status in childhood and support women to achieve healthy weight prior to pregnancy. These interventions were shown to improve insulin sensitivity and reduce the incidence of DIP in the modelled population.
Introduction

Diabetes in pregnancy (DIP), including gestational and pre-existing type 1 and 2 diabetes, is increasing both in Australia and internationally [1-3], challenging the capacity of health care services. The increase in DIP is directly associated with the increasing prevalence of risk factors including overweight, obesity, older maternal age and shifts in population demographics and ethnicities [2-4]. With increasing prevalence of risk factors, service providers report that women are more frequently presenting with more complex diabetes and obstetric care needs [5]. Additionally, diabetes during pregnancy increases risk for later chronic disease for the woman [3] and early onset of type 2 diabetes for her children [2, 6].

The available evidence for DIP policy and treatment planning is not definitive [1] and current challenges include: determining the timing and methods of screening, criteria for diagnosis, targets for treatment, resource allocation, identification and management of pre-existing diabetes during pregnancy, risk stratification, timing and type of prevention activities and individual differential effects of treatment [1, 7-9]. To address the increasing incidence of DIP, there have been increasing calls for upstream prevention activities to focus on lifestyle risk factors pre-conception rather than during or post-pregnancy [10-12]. These contested intervention options cross the spectrum from primary prevention approaches to highly specialised clinical management, which can be implemented independently or in combination and may be phased or implemented simultaneously. Sophisticated analytical tools are required to synthesise diverse evidence types across disciplines and support decision making.

Systems science methods provide decision makers with insights into how multiple causal pathways interact to generate the patterns of disease we see in the real world and how interventions modify those pathways [13, 14]. Dynamic simulation modelling (DSM) is a method that recreates complex systems and human behaviours as a computer, or mathematical, model. The models can answer ‘what if’ questions, via computer simulation, about the likely impacts over time of different policy and intervention options and their combinations [15, 16]. This is important for prevention policy and practice, where decision support tools must steer a course through the complexity of interactions that give rise to real-world public health problems, such as the rapid increase in DIP [15-17]. They are also useful for conditions with slow and variable development, like diabetes mellitus, that
involves underlying dynamics between physiological factors, such as the non-linear interrelationships between weight status, pregnancy, insulin sensitivity, insulin production and glycemic regulation [18-20]. These physiological variables interact and some are difficult to measure empirically, meaning that conditions like diabetes present significant challenges for traditional experimental methods [18, 21]. Analytic methods like dynamic modelling and simulation play an important role in improving understanding of the dynamics of disease progression [18, 22, 23]. The multi-scale, hybrid model reported in this paper builds on current understanding of glycemic regulation dynamics related to weight status and pregnancy [19, 20], leveraging existing peer-reviewed mathematical models of diabetes [18, 22, 23] and explores the dynamics of glycemic regulation, weight status and pregnancy on the development of DIP [24].

Recent advances in modelling software have increased model transparency, making them more accessible to non-modellers. This has facilitated expert stakeholder participation in the model development process, increasing the opportunities for interdisciplinary learning about complex health problems and building trust in the model outputs [25-29]. The aim of this study was to develop a DIP decision support tool for policy and program decision makers, using participatory DSM [30]. The model development process, and discussions of the model outputs enable key stakeholders to explore the likely impacts of both clinical and population level intervention options for DIP, via simulation, before they are implemented in the real world. The process has been reported elsewhere [25, 29-31]. The aim of this paper is to explore the impact of prevention interventions targeting weight status on DIP incidence and insulin sensitivity. Insulin sensitivity, while not being a commonly utilised clinical measure, was selected as an outcome measure of glycemic regulation for these scenarios as it reflects metabolic dynamics both during pregnancy and with changing weight status and is potentially responsive to lifestyle interventions [19, 20]. Intervention scenarios were tested to explore the impact of timing, subgroup targeting, and adherence to lifestyle changes on the incidence of DIP and insulin sensitivity.
Methods

Box 1: Study context

The model explored DIP in Australian Capital Territory (ACT) and was built in partnership with the ACT Government Health Directorate (ACT Health). Approximately 16% of ACT resident women who gave birth in the ACT in 2016 were diagnosed with DIP (increasing from 6% in 2008) [32]. ACT Health services provide government funded health services for the population of the ACT (approximately 410,000) and are the major health referral centre for the Greater Southern Region of New South Wales. The total catchment area population is over 600,000 people. The number of women giving birth in the ACT is over 6,000 per year. Approximately 15% of these women are non-ACT residents who access services in the ACT for high risk pregnancy complications (i.e. those requiring tertiary level care). Models of antenatal maternity care provided in the ACT include hospital based out-patient care, tertiary level care, private midwifery care, and shared care (that is, integrated with primary health care providers). A specialist gestational diabetes service operating from one public hospital with satellite clinics in community health centres works with generalist maternity services to provide education and health services for women with DIP.

Model development

The model development process drew on best practice guidelines for computational modelling and included the grounding of assumptions in theory and evidence, sensitivity testing and calibration [33, 34]. The model was built using a participatory approach that engaged a consortium of academics, clinicians, public health policy makers, program planners, modellers and health economists in the process. This approach has been described in detail elsewhere [25, 30, 31]; and a diagrammatical overview of the process is depicted in Figure 1.
The hybrid model was constructed using AnyLogic simulation software (http://www.anylogic.com/). Detailed information is available in the supplementary resources, including the model documentation and technical paper.

Model inputs and data sources

The structure and parameterisation of the model drew on a range of data sources, including census and population data, systematic reviews, meta-analyses, accepted formulas and conceptual models, survey data, policy/programme effectiveness data, economic data and the expert knowledge of the multidisciplinary stakeholders who participated in model development. Local data was prioritised where this was available. Expert opinion was utilised when other evidence options were exhausted or for...
triangulation of multiple data sources when parameters were uncertain. The data included statistics relating to demographic characteristics and trends, the incidence of DIP and associated risk factors, and the underlying physiology determining individual glycemic control including beta cell mass and function based on previous mathematical models of diabetes progression [18, 22, 23]. Census, population and health system data were sourced from the Australian Bureau of Statistics and ACT Health administrative data collections. Model input parameter values, their sources and the data used for model calibration are provided in the supplementary resource. The model was calibrated to the incidence of DIP in ACT Health maternal and perinatal statistics from 2008 to 2016.

Model structure

The tripartite model incorporates system dynamics (SD), agent based modelling (ABM) and discrete event simulation (DES) components with construction and analysis implemented in AnyLogic® version 7.3.6 Professional (http://www.anylogic.com/). The model structure has been described elsewhere [24] and is described in detail in the supplementary resource. A summary is provided here of the following representations:

A. Pregnancy
B. Dysglycemia classification
C. Glycemic regulation including beta cell mass and function
D. Population structure
E. Weight status
F. Clinical service

The overall model structure is depicted in Figure 2 which is intended to depict a high level overview of model components rather than full details. The model population is initialised using demographic characteristics e.g., age and country of birth, of the female population of the Australian Capital Territory (ACT) from the 2011 Australian Census [35]. The model is initialised in 1948 with time units in years. The model then undergoes a burn-in period of 60 years to 2008. Model outputs from 2008 to 2016 have been calibrated against retrospective data [24].
Figure 2: Overview of model components and structure
The model incorporates a dynamic representation of the underlying physiological regulation associated with an individual’s glycemic status that is based on previous mathematical models of diabetes progression [18, 22, 23]. The mechanism for glycemic regulation included in the model is referred to as an endogenous dynamic mechanism. This means that the model represents, over time, the evolution of specific, latent factors related to the level of dysglycemia and metabolic load that a woman experiences. Glycemic regulatory capacity is represented as a stock (an accumulation), allowing the level of an individual’s regulatory capacity to increase and decrease over time. Therefore, the factors that influence glycemic regulatory capacity such as increased metabolic load due to pregnancy, changes to diet and physical activity and pharmacological interventions can be modified within the model and the impact measured over time and between generations.

Glycemic regulatory capacity is a function of two factors in the model. Firstly, it is a function of biologic regulatory capacity; that is, the changes in insulin sensitivity and insulin production associated with underlying physiology [18, 20, 22, 23]. Secondly, there is a component of external regulation by the individual, that is, their conscious regulation through adherence to blood testing, medication regimens and lifestyle interventions including diet and physical activity. The model mechanism allows for changes in an individual’s adherence to medical and lifestyle interventions over time. The model also incorporates the impact of beta cell decline associated with exposure to dysglycemia based on modelling carried out by De Gaetano et al. [18, 22, 23]. Exposure to dysglycemia results in a decline of beta cell function over time and this eventually limits the individual’s regulatory capacity. Reduced beta cell function decreases the effectiveness of lifestyle interventions on glucose regulation, meaning that, even if an individual with reduced beta cell function makes significant changes to their diet and activity levels, the impact on the blood glucose regulation will be minimal.

Pregnancy occurs according to the ACT age and ethnicity specific fertility rate. The model tracks relevant risk factor information for the occurrence of dysglycemia in the current pregnancy, for example, Body Mass Index (BMI), age, history of diabetes, and family history of diabetes. Insulin sensitivity decreases significantly during pregnancy for both normoglycemic and dysglycemic women, based on findings of studies by Catalano [19, 20]. When a woman gives birth, there is a birth event in which a baby is introduced into the model. The baby inherits characteristics, including the mother’s DIP status and history of diabetes, maternal weight status and ethnicity. Outcomes, including birthweight, type of
birth e.g., caesarean section, neonatal intensive care admission and Apgar scores, are recorded at birth. The model incorporates the glycemic changes occurring during pregnancy [36]; it is notable that such changes can impart physiological impact for mother and child (e.g., on beta cell mass and function) that persists beyond that pregnancy. Responsive to the focus on DIP, the model includes only female agents. Births for male babies occur in the model, however these agents are deleted from the population. Model outputs reflect the impact of interventions on females in the population.

High weight status is an important risk factor for declining insulin sensitivity and the development of diabetes. Weight is represented in the model as a continuous variable that changes dynamically with age [37] and pregnancy [38]. An individual's weight status (BMI) impacts on their insulin sensitivity [18-20], with increasing weight leading to decreasing insulin sensitivity. This paper reports on weight reduction intervention scenarios tested in the model as described below.

Simplifying assumptions about individual behaviour were made to ensure the model is parsimonious, while allowing it to approximate real-world behaviour over time. A summary of the key assumptions is presented below:

1. Age specific fertility rates were calculated using birth rates from 2013. The model assumes that age specific fertility rates will remain stable over the period of the simulation.
2. The model assumes that 60% of pregnancies were intended, providing opportunities for intervention during pregnancy planning [10]. The assumption was applied uniformly across age groups.
3. Adherence to healthy lifestyle behaviours was assumed to increase after exposure to intervention and then decline over the subsequent two years.
4. Individuals, who were eligible, had an equal chance of receiving interventions.

Underlying the model structure and assumptions described above are simple mathematical relationships designed to capture the concept they represent. For instance, the decline in intervention adherence was assumed to follow a curve whose coefficients cause adherence to the weight management intervention to increase immediately following an intervention and decline over the subsequent two-year period.

Health services are captured in the model, with the current service model being represented as a DES component. Future planned work for the model will explore the impact of alternative service models on resources and outcomes.
Scenarios tested in this analysis

The scenarios tested in this analysis focused on the impact of targeted and population-level weight reduction strategies. Many of the risk factors for DIP are not modifiable, however weight status is an important modifiable risk factor for both DIP and type 2 diabetes mellitus. The scenarios prioritised for this analysis are described below.

1. **Impact of population vs targeted weight management interventions**

These scenarios compared the impact of weight management interventions delivered across the population of females aged 20 to 35 years with targeted interventions delivered to females who were at high risk according to the Australian Diabetes in Pregnancy criteria [1] either before or after their pregnancies. The interventions are described below.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Population intervention</td>
<td>This intervention targets all women aged 20 to 35 years through a public health intervention. The goal of the intervention is to support women to maintain or achieve a healthier weight status.</td>
</tr>
<tr>
<td>2. Targeted pre-pregnancy intervention</td>
<td>This intervention targets women who have one or more risk factor for DIP. It is available to all women who are considering pregnancy (60% of pregnancies [10]). The intervention aims to achieve a healthy weight via adherence to diet and physical activity recommendations and.</td>
</tr>
<tr>
<td>3. Targeted post-pregnancy</td>
<td>This post pregnancy intervention targets women who have had diabetes in a previous pregnancy. The intervention aims to increase adherence to diet and physical activity recommendations and to achieve a healthy weight before the next pregnancy.</td>
</tr>
<tr>
<td>4. Combined</td>
<td>This scenario combines all the above interventions</td>
</tr>
</tbody>
</table>
The effectiveness of each intervention in reducing weight is a model parameter that can be varied. For simplicity, the interventions in these scenario runs were assumed to result in weight reductions that were normally distributed with a mean weight reduction of 1.3 kg/m² (SD = 1.7 kg/m²). The distribution was based on an Australian study of mobile phone based public health intervention aimed at preventing weight gain in young adults [39] and an Australian study of post pregnancy lifestyle change supported by motivational interviewing [40]. Weight loss results for individuals who received the interventions were drawn from this distribution. It was assumed that all eligible individuals received the intervention and that the intervention effectiveness degraded over time, with adherence diminishing over a two-year period.

2. Impact of childhood weight interventions

These interventions explored the impact of childhood weight interventions. As childhood weight dynamics had not yet been fully articulated in the model, these hypothetical scenarios were simulated by modifying the weight distribution of the population on entry to adulthood. Increasing population-wide interventions to reduce childhood overweight and obesity was simulated by shifting the weight distribution of the population to the “left”, so that more individuals entered adulthood within the healthy weight range (normal distribution with mean BMI = 22). Scaling back population-wide interventions addressing childhood overweight and obesity was also simulated. The scaling back intervention shifted the population weight distribution to the “right” so that more individuals entered adulthood either overweight or obese (normal distribution with mean BMI = 30). The interventions were implemented for individuals born from 2018 and the simulations were run for 42 additional years (2060) to allow individuals to age and enter their reproductive years.

Model outputs and data analysis

For the scenario testing, key outcome indicators against which the impacts of scenarios were compared to the baseline were: (1) incidence of DIP (%) and (2) insulin sensitivity (KxgI). Diabetes in pregnancy incidence was calculated as a percentage based on the proportion of all women giving birth in each year who were diagnosed with DIP. KxgI was
used as a mathematical index of insulin sensitivity representing insulin dependent glucose tissue reuptake [22].

To estimate latent or poorly measured parameters and to support the projection of status quo future incidence of DIP using model outputs, we calibrated a baseline model without interventions against the following historical data: the incidence of DIP for sub-populations in ACT from 2008-2016 according to ADIPS risk profiles[1]; the prevalence of macrosomia by DIP status in the ACT from 2010-2016 [24].

Outputs from the model were summarised using the R statistical package to obtain means, standard errors and 95% confidence intervals; summary data was tabulated and graphed in Microsoft Excel. Given that runs of the model were computationally expensive, 36 runs were deemed sufficient to account for stochasticity and provide stable predictions of scenario performance and of the variance in performance. The comparison of simulation results between baseline and intervention scenarios was expressed as a percent difference in reported outcomes. 95 % confidence intervals about the means were reported as estimates of the variation between simulation runs and to test statistical significance.

Results

Results for scenario testing simulations are presented below.

Scenario testing results

1. Impact of population vs. targeted weight management interventions

Diabetes in pregnancy incidence for the baseline and scenario simulation are presented as a percentage, based on the proportion of all women giving birth in each year who were diagnosed with DIP, in Table 1 and Figure 3. The baseline incidence of DIP was 15.9% (95%CI 15.5 to 16.3) in 2020; 16.1% (95% CI 15.8 to 16.4) in 2030 and 17.3% (95% CI 16.9 to 17.7) in 2040. The population weight loss intervention in early adulthood resulted in a non-significant 3.0% reduction in DIP incidence by 2020 (15.5%; 95% CI 15.1 to 15.9), however by 2030 the 17.6% reduction in DIP incidence (13.3%; 95% CI 13.0 to 13.6) was statistically significant. In comparison, the impact of targeted pre- and post-pregnancy
interventions on population level DIP incidence ranged from a non-significant reduction of just over 2% in 2020, a small but statistically significant reduction of 4-5% in 2030 and 4-6% in 2040, respectively. Incidence rates with confidence intervals for these scenarios are presented in Table 1. Combining targeted interventions for high risk groups with population weight loss interventions was the most effective scenario for reducing DIP incidence, with a reduction of 14.4% by 2020 to 13.6% (95% CI 13.2 to 14.0), two years after the simulated interventions were implemented, 28.8% by 2030 (11.5%; 95% CI 11.2 to 11.8) and 32.1% by 2040 (11.8%; 95% CI 11.5 to 12.1).

*Figure 3: Comparative impact of scenarios on DIP incidence simulated from 2018 to 2040*
Table 1: Summary DIP incidence statistics for baseline and scenarios simulated from 2018 to 2040

<table>
<thead>
<tr>
<th></th>
<th>2020</th>
<th></th>
<th></th>
<th>2030</th>
<th></th>
<th></th>
<th>2040</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>95% CI (±)</td>
<td>% reduction</td>
<td>%</td>
<td>95% CI (±)</td>
<td>% reduction</td>
<td>%</td>
<td>95% CI (±)</td>
</tr>
<tr>
<td>Baseline</td>
<td>15.9</td>
<td>0.4</td>
<td>-</td>
<td>16.1</td>
<td>0.3</td>
<td>-</td>
<td>17.3</td>
<td>0.4</td>
</tr>
<tr>
<td>1. Population intervention</td>
<td>15.5</td>
<td>0.4</td>
<td>-3.0</td>
<td>13.3</td>
<td>0.3</td>
<td>-17.6</td>
<td>13.8</td>
<td>0.3</td>
</tr>
<tr>
<td>2. Targeted pre-pregnancy</td>
<td>15.5</td>
<td>0.3</td>
<td>-2.8</td>
<td>15.3</td>
<td>0.3</td>
<td>-5.2</td>
<td>16.2</td>
<td>0.4</td>
</tr>
<tr>
<td>3. Targeted post-pregnancy reduction</td>
<td>15.6</td>
<td>0.3</td>
<td>-2.1</td>
<td>15.5</td>
<td>0.3</td>
<td>-4.2</td>
<td>16.7</td>
<td>0.4</td>
</tr>
<tr>
<td>4. Combined - population and targeted pre and post pregnancy</td>
<td>13.6</td>
<td>0.4</td>
<td>-14.4</td>
<td>11.5</td>
<td>0.3</td>
<td>-28.8</td>
<td>11.8</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table 2: Summary insulin sensitivity (KxgI) statistics for baseline and scenario simulations simulated from 2018 to 2040

<table>
<thead>
<tr>
<th></th>
<th>2020</th>
<th></th>
<th></th>
<th>2030</th>
<th></th>
<th></th>
<th>2040</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KxgI</td>
<td>95% CI (±)</td>
<td>% increase</td>
<td>KxgI</td>
<td>95% CI (±)</td>
<td>% increase</td>
<td>KxgI</td>
<td>95% CI (±)</td>
</tr>
<tr>
<td>Baseline</td>
<td>50.3</td>
<td>0.02</td>
<td>48.4</td>
<td>46.4</td>
<td>0.03</td>
<td>25.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Population intervention</td>
<td>52.2</td>
<td>0.03</td>
<td>3.8</td>
<td>56.5</td>
<td>0.03</td>
<td>16.7</td>
<td>58.0</td>
<td>0.03</td>
</tr>
<tr>
<td>2. Targeted pre-pregnancy</td>
<td>50.5</td>
<td>0.02</td>
<td>0.3</td>
<td>49.3</td>
<td>0.03</td>
<td>1.8</td>
<td>47.7</td>
<td>0.03</td>
</tr>
<tr>
<td>3. Targeted post-pregnancy reduction</td>
<td>50.5</td>
<td>0.02</td>
<td>0.4</td>
<td>51.5</td>
<td>0.06</td>
<td>6.3</td>
<td>50.1</td>
<td>0.07</td>
</tr>
<tr>
<td>4. Combined - population and targeted pre and post pregnancy</td>
<td>55.7</td>
<td>0.02</td>
<td>10.6</td>
<td>67.9</td>
<td>0.11</td>
<td>40.3</td>
<td>70.7</td>
<td>0.13</td>
</tr>
</tbody>
</table>

KxgI - an index of insulin sensitivity representing insulin dependent glucose tissue reuptake
Insulin sensitivity results for the baseline and intervention simulations are presented in Table 2. Baseline projections of insulin sensitivity (KxgI) were 50.3 (95% CI 50.1 to 50.5) in 2020; 48.4 (95% CI 48.2 to 48.6) in 2030 and 46.4 (95% CI 46.1 to 46.7) in 2040. The population intervention targeting weight loss in early adulthood resulted in a non-significant 3.8% increase in insulin sensitivity by 2020 and a significant 25.2% increase by 2040 (KxgI = 58.0; 95% CI 57.7 to 58.3). Smaller increases in population level insulin sensitivity were found for the targeted pre- and post-pregnancy interventions, with targeted pre-pregnancy weight loss interventions resulting in an increase in insulin sensitivity of 2.3% in 2040 (KxgI = 47.7; 95% CI 47.4 to 50.0). The targeted post-pregnancy interventions had a significantly higher impact by 2040 with an increase in insulin sensitivity of 8.1% (KxgI = 50.1; 95% CI 49.4 to 50.8). Combining targeted weight loss interventions for high risk groups with population-level weight loss interventions was the most effective scenario for increasing insulin sensitivity across the population, with an increase of 10.6% two years after the simulated interventions were implemented (2020) (KxgI = 55.7; 95% CI 55.5 to 55.9) increasing to 52.4% in 2040 (KxgI = 70.7; 95% CI 57.7 to 58.3).

2. Impact of childhood weight status on entry to adulthood

The interventions were implemented for female agents born from 2018 and were simulated to 2060 to allow time for individuals to age into adulthood and their reproductive years. Minimal impact of the interventions was observed on DIP incidence until 2060 (Figure 5), when the scenario with all females entering adulthood at a healthy weight resulted in a 21.2% decrease in the percentage of women diagnosed with DIP from baseline (Table 4) (2060 Baseline 17.0%, 95% CI 16.7 to 17.3; Scenario 13.4%, 95% CI 13.1 to 13.7).
Changes in insulin sensitivity (KxgI) were observed earlier in the simulation, from 2030, for the childhood weight interventions (Figure 5). The scaling up simulation -- with all individuals entering adulthood at a healthy weight -- increased insulin sensitivity, as measured by KxgI, for the population by 8.5% from the baseline simulation by 2030, increasing to 47.3% by 2060 (Table 4). The scaling back simulation shifted the weight distribution for the population further toward overweight and obesity as they entered adulthood. This resulted in a decrease in insulin sensitivity for the population of 31% from baseline by 2060 (Table 4).
Figure 5: Impact of scaling up and scaling back childhood weight interventions on population insulin sensitivity (KxgI)

KxgI - an index of insulin sensitivity representing insulin dependent glucose tissue reuptake
Table 3: Summary DIP (percentage) incidence statistics for baseline and child weight status interventions scenarios simulated from 2018 to 2060

<table>
<thead>
<tr>
<th></th>
<th>2020</th>
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<td>16.9</td>
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<td>0.4</td>
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Table 4: Summary population insulin sensitivity (KxgI) statistics for baseline and scaling up and scaling back scenarios simulated from 2018 to 2060

<table>
<thead>
<tr>
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<td>1.2</td>
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<td>54.2</td>
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KxgI - an index of insulin sensitivity representing insulin dependent glucose tissue reuptake
The simulations reported here prioritised scenario testing of several lifestyle prevention interventions promoting healthy weight status. Population-level interventions promoting weight loss in early adulthood were found to be more effective than targeted pre- and post-pregnancy interventions in reducing the population incidence of DIP. Combining targeted interventions for high risk groups with population health promotion supports was shown to be the most effective scenario for reducing DIP incidence, especially in the longer term. Scaling up childhood health weight interventions, resulting in all female children entering adulthood at a healthy weight, achieved a significant improvement in insulin sensitivity in the short term and decreased DIP in the long term. Scenarios testing the impact of scaling back childhood healthy weight interventions, i.e., having more children entering adulthood overweight or obese, resulted in declines in insulin sensitivity across the population and, therefore increasing risk of early development of diabetes mellitus.

The study presented in this paper is unique in that dynamic simulation modelling was used to explore the metabolic dynamics underlying the development of DIP and compare the likely impact of population level interventions with interventions targeting high risk individuals. This simulation study builds on other research assessing the effectiveness of targeted lifestyle prevention programs to prevent DIP incidence [10, 12, 41]. Given the substantial time needed to achieve weight reduction, it has been argued that early intervention at a population level will be necessary to reduce obesity-related outcomes in pregnancy [10], and this was confirmed by the modelling. The scenarios presented in this paper demonstrated that population level interventions will be needed to make an impact on DIP incidence across the population. Targeted interventions, both pre- and post-pregnancy, did not substantially impact on population DIP incidence.

Over half of pregnancies are planned [10], and this was reflected in the model, with only individuals who were planning to become pregnant being eligible to receive the targeted pre-conception intervention. Therefore, the small proportion of the total population receiving the intervention and individual variations in adherence, included in the model to reflect reality, impacted on intervention effectiveness. The targeted interventions resulted in only a modest impact on population incidence rates for DIP. This result should not devalue the role of targeted interventions, as these are important and beneficial for
individuals and their offspring [11]. However, the results emphasise the need for population interventions to support healthy lifestyle behaviours for all individuals, whether they actively plan their pregnancy or not [10].

A recent review of research into antenatal lifestyle programs for high risk women found that they did not successfully prevent DIP [12]. Further examination of the individual and intervention characteristics that facilitated adoption and adherence to interventions has been identified as a priority [12]. The DIP model presented here incorporated representations of the non-linear dynamics and feedback loops that impact intervention effectiveness e.g., the impact of age and pregnancy related weight changes across the life course and the impact of individual adherence to diet and physical activity recommendations on both DIP incidence and insulin sensitivity. The reduction in DIP incidence was only achieved when individuals remained adherent to the lifestyle changes associated with the intervention.

Scenario testing provides an important tool for exploring hypothetical policy options, including “do nothing” alternatives that forecast the impact of ceasing current interventions [14, 33, 42]. In these scenarios, the DIP model hypothetically tested the impact of scaling back interventions promoting healthy weight for children in school settings. This scenario forecasted the impact of more children entering adulthood at a higher weight status on insulin sensitivity, placing them at risk of early development of diabetes mellitus. These results signify the potential importance of the current global focus and efforts to reduce childhood overweight and obesity.

Diverse local perspectives and interests can provide decision makers with conflicting advice regarding the best course of action [16]. Data limitations, insufficient local analytic capacity and inadequate tools to support longer term planning in a context of changing local needs, contribute to the persistence of a trial and error approach to program planning that may delay or prevent the realisation of significant impacts on important public health issues like DIP [15, 42]. The DSM approach described in the present study is one way to address these challenges and can also contribute to prioritising data gaps for future research and data collection, and infrastructure to better support interventions to prevent and manage DIP. The participatory approach facilitated opportunities for interdisciplinary dialogue and combining diverse perspectives in the consideration of policy options. The developed
partnerships and relationships were critical to the model development and to its likely subsequent use to inform health service and policy decisions.

Future applications of the model include further exploration of the: intergenerational impacts resulting from exposure to DIP; factors that influence childhood weight gain e.g. breastfeeding and other aspects of diet, school-based health promotion interventions, and physical activity etc.; impact of model of care alternatives; and impact of prevention interventions on health service utilisation. Health economic considerations will also be added to future iterations of the model.

Limitations

There are limitations to consider when interpreting the findings of this paper. There is potential measurement bias in the range of secondary data used to parameterise the model. Where possible, routinely collected local health service information was obtained to estimate population-based estimates of DIP, birth outcomes, weight status, and fertility rates. There were also some parameters relating to the heterogeneity of aetiology of DIP and the dynamics of glycemic regulation where data were not available, and these are identified as priorities for future research. The model acknowledges these potential sources of measurement bias, and commonly used strategies were employed to address them, including the triangulation of multiple data sources, calibration to refine parameter estimates and the engagement of stakeholders with detailed knowledge of the limitations and likely direction and size of potential measurement biases in key data sources. In addition, sensitivity analysis was undertaken to estimate the impact of uncertainty on primary outcome indicators and guide priorities for new data collection and quality improvement of existing data collection.

Conclusion

Population health interventions will be necessary to “turn the tide” on DIP. Interventions targeting high risk individuals, while beneficial for those individuals, delivered small reductions in DIP incidence rates. The importance of maintaining interventions promoting healthy weight in childhood was demonstrated. Scenarios simulating the impact of scaling back these interventions showed that insulin sensitivity decreased significantly, increasing...
the risk for early development of diabetes mellitus. DSMs are learning support tools that can mature over time as new evidence becomes available and methods are advanced to facilitate further development. This decision support tool for DIP was developed as a working model and is being published for transparency and to invite input. A key priority for future research is improved knowledge about the dynamics and heterogeneity in the aetiology of glycemic dysregulation and diabetes mellitus development, and the impact of glycemic control during pregnancy on perinatal outcomes.

Authors’ contributions

LF, JA, GM, NO, CN, AK and PK were involved in the planning for this study. Model and scenario programming were done by NO, WQ, YQ, AS and AM. Model outputs were produced by YQ. Data processing was conducted by LP and AP. LF conceptualised the manuscript and wrote the first and subsequent drafts. All authors have made important intellectual contributions to multiple draft revisions.

Acknowledgements

The authors acknowledge the valuable contributions of Professor Lucie Rychetnik to the study design and her comments on this manuscript. The authors also acknowledge the Diabetes in Pregnancy Modelling Consortium (members listed below) for generously contributing their expertise and time to participate in this study.

Members of the Diabetes in Pregnancy Modelling Consortium

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<tr>
<th>Name</th>
<th>Position</th>
<th>Organisation</th>
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<tbody>
<tr>
<td>Jo-An Atkinson</td>
<td>Director, Decision Analytics</td>
<td>Sax Institute</td>
</tr>
<tr>
<td>Tracey Baker</td>
<td>General Practitioner</td>
<td>Chapman Medical Practice</td>
</tr>
<tr>
<td>Lynelle Boisseau</td>
<td>Diabetes Educator</td>
<td>ACT Health Diabetes Service</td>
</tr>
<tr>
<td>Jacqui Davison</td>
<td>Project Officer</td>
<td>The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Roland Dyck</td>
<td>Professor Emeritus</td>
<td>University of Saskatchewan, Canada</td>
</tr>
<tr>
<td>Jeff Flack</td>
<td>Associate Professor, Endocrinology and Medical Informatics</td>
<td>Liverpool Hospital, University of New South Wales</td>
</tr>
<tr>
<td>Name</td>
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</tr>
<tr>
<td>Louise Freebairn</td>
<td>Research lead and Manager, Epidemiology Section and PhD Candidate</td>
<td>ACT Health, The Australian Prevention Partnership Centre and University of Notre Dame Australia</td>
</tr>
<tr>
<td>Alison Hayes</td>
<td>Associate Professor, Health Economics</td>
<td>School of Public Health, University of Sydney, and CRE</td>
</tr>
<tr>
<td>Paul Kelly</td>
<td>Chief Health Officer and Deputy Director, General, Population Health Prevention and Protection</td>
<td>ACT Health</td>
</tr>
<tr>
<td>Alison Kent</td>
<td>Professor and Senior Staff Specialist, Neonatology</td>
<td>Australian National University and ACT Health</td>
</tr>
<tr>
<td>Louise Maple-Brown</td>
<td>Professor, Endocrinologist</td>
<td>Menzies School of Health Research, Royal Darwin Hospital.</td>
</tr>
<tr>
<td>Geoff McDonnell</td>
<td>Adviser, Simulation Modelling</td>
<td>The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Allen McLean</td>
<td>PhD Candidate, Simulation Modelling</td>
<td>University of Saskatchewan, Canada, The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Chris Nolan</td>
<td>Professor of Endocrinology, Director of Diabetes Services ACT</td>
<td>Australian National University, ACT Health</td>
</tr>
<tr>
<td>Eloise O’Donnell</td>
<td>Project Officer</td>
<td>The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Nathaniel Osgood</td>
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<td>University of Saskatchewan, Canada, The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Michael Peek</td>
<td>Professor of Obstetrics and Gynaecology, Maternal Fetal Medicine Specialist,</td>
<td>Australian National University, ACT Health</td>
</tr>
<tr>
<td>Luke Penza</td>
<td>Computer scientist</td>
<td>University of Western Sydney and The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Ante Prodan</td>
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<td>University of Western Sydney and The Australian Prevention Partnership Centre</td>
</tr>
<tr>
<td>Winchell Qian</td>
<td>Computational Science, Simulation Modeller,</td>
<td>Department of Computer Science, University of Saskatchewan, Canada</td>
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<tr>
<td>Lucie Rychetnik</td>
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<tr>
<td>Anahita Safarishahrbijari</td>
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<td>Department of Computer Science, University of Saskatchewan, Canada</td>
</tr>
<tr>
<td>David Simmons</td>
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<td>Western Sydney University, Western Sydney Area Health Service</td>
</tr>
<tr>
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<td>University of Adelaide, Country SA Primary Health Network</td>
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**Role of the funding source**

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- Australian Postgraduate Award scholarship
- CRN top-up scholarship for supervision travel expenses
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7.2 Communication products developed to facilitate model use and knowledge dissemination

Three key products were developed to support communication about this technical modelling project to a non-technical policy audience. The products were a plain language fact sheet, an interactive dashboard and a podcast. The fact sheet and interactive dashboard communication products are described in this section and the podcast transcript is included in Appendix 9.

Project fact sheet

I led the development of plain language fact sheet (below) to facilitate communication about the modelling project. The factsheet was developed with Ms Helen Signy and Ms Ainsley Burgess, communication officers with The Australian Prevention Partnership Centre, and was aimed at Ministerial advisors and a wider health policy audience.

The fact sheet provided background information about diabetes in pregnancy as a priority issue impacting on health services in the ACT, information about the model development process and preliminary results from the model. A local Canberra woman with diabetes in pregnancy was interviewed by Ms Signy and her story was included to illustrate the local impact of diabetes in pregnancy and the importance of prevention interventions.
Preventing diabetes in pregnancy

Diabetes in pregnancy is putting more and more strain on the ACT’s health system. We need to do things differently

Diabetes in pregnancy, including gestational diabetes, is increasing both in the ACT and Australia. This is due to the rise in risk factors such as overweight and obesity, older mothers and more women from high-risk ethnic groups.

Gestational diabetes occurs when high levels of blood glucose are detected during pregnancy that, if untreated, increase the risk of poor pregnancy outcomes. It also predicts a future higher risk of permanent diabetes in mothers and obesity and diabetes in children.

Pregnancy is a time when public health interventions can have a big impact. Women are more motivated to make changes, and these can also positively affect the health of future generations.

Achieving even small delays in the development of diabetes will have significant implications for the longer-term burden of disease and costs to the health system.

CASE STUDY

Pip is 37, she is about to have her first baby – and has gestational diabetes

Both Pip and her new daughter will be at increased risk of type 2 diabetes in future. Pip is one of about 800 women diagnosed every year in the ACT with gestational diabetes. She joins an ever increasing number of women whose future health and that of her children is at risk.

"Before I conceived, no-one ever suggested to me my history of polycystic ovary syndrome, diet, weight or age put me at risk of gestational diabetes. If I had known, I could have made changes before I became pregnant to try and reduce my risk.

Sometimes I feel like I’m doing this alone. Better support before and during my pregnancy would make a big difference, and would mean a better outlook for both me and the baby."
What did we do?

We brought together diabetes in pregnancy experts including leading academics, policy makers and clinicians from across Australia. Their insights were combined with research and data to develop a dynamic simulation model of diabetes in pregnancy in the ACT.

“With the collaborative modelling approach, the people in the room have accumulated knowledge and expertise in the area over many years. To have that wealth and depth of knowledge involved is incredibly valuable.”

Professor Christopher Nolan, Director of Endocrinology and Diabetes, ACT Health

A dynamic simulation model is a sophisticated computer ‘what if’ tool that can test the likely impact of a range of possible solutions over time. It considers the short, intermediate, and long-term implications of the increasing prevalence of risk factors for diabetes in pregnancy and looks at alternative models of care.

Based on real data, the model can be used to test out different solutions to see which will be most effective and cost effective. The expert group identified, clarified and prioritised gaps in current knowledge and evidence which can be used to guide future research and, in turn, further improve the model.

BUILDING AND USING A DYNAMIC SIMULATION MODEL WITH STAKEHOLDERS

**1. EVIDENCE SOURCE**
- Research evidence
- Health service and survey data
- Expert knowledge
- Local practice experience

**2. BUILD**
- Build a conceptual map of the problem collaboratively
- Convert to a computer model

**3. VALIDATE**
- Does the model reproduce historic data trends?
- Refine the model
- Compare model output to real data

**4. APPLY**
- Switch on different intervention combinations. For example:
  - A. Pre-pregnancy intervention to lose weight
  - B. Family–centred programs to reduce weight
- Run ‘what if’ scenarios through the model
- Compare predicted impact over time
- Facilitate discussion to help drive policy action

---

Gestational diabetes, increases the subsequent risk of type 2 diabetes in mothers almost ten fold.

Babies of mothers who have gestational diabetes are at short-term risk of high birthweight, birth complications and hypoglycaemia.

Children of mothers who had gestational diabetes have a 2–4 fold increased risk of being overweight/obese and having long-term impaired glucose tolerance.

Both gestational diabetes and type 2 diabetes are associated with modifiable lifestyle risk factors such as diet and physical activity.

There are also strong genetic and family related risk factors which are not modifiable.
What did we find?

Early findings from the model reinforce the long-term benefits for women and their children of preventing diabetes in pregnancy:

- Women with obesity experience a sharper decline in insulin sensitivity compared with normal weight women (see image below)
- Interventions delivered between pregnancies or after pregnancy for women who have experienced diabetes in pregnancy could reduce their risk of progressing to Type 2 diabetes
- Pregnancy and pre-conception is a time when interventions can improve health outcomes for whole families
- It is possible to significantly reduce the number of women with diabetes in pregnancy by focusing on risk factors like diet, physical activity and weight
- These lifestyle interventions should target women in early adulthood, before pregnancy, to reduce the incidence of diabetes in pregnancy.

What happens to insulin sensitivity during pregnancy?

- High insulin-sensitivity helps keep blood glucose levels in the normal range
- Low insulin-sensitivity, or insulin resistance, is associated with type 2 diabetes.

Source: Early results from the diabetes in pregnancy dynamic simulation model.
Next steps

This project has demonstrated that participatory dynamic simulation modelling is an effective way of informing program and policy decision-making for diabetes in pregnancy in the ACT. Dynamic simulation models mature over time and can be continuously refined as new knowledge and evidence becomes available.

One of the main benefits of the modelling process was that it brought together a large group of stakeholders, including key decision makers, to discuss the causes of diabetes in pregnancy and impacts of interventions. Building these networks is a crucial step in driving a multi-sector approach that can lead to practical changes on the ground.

What interventions could be modelled in the future?

- Pre-pregnancy population level interventions, for example app-based support for women and couples to make lifestyle changes
- Targeted pre-pregnancy interventions for women with multiple risk factors
- Post-pregnancy interventions to support families to maintain a healthy lifestyle
- Different models of care for women with diabetes in pregnancy.

About this project

This project was implemented as a collaboration between the Prevention Centre and Australian Capital Territory Government Health Directorate (ACT Health).

The model harnesses advances in technology incorporating multiple methods including agent-based modelling, system dynamics and discrete event simulation into a logically consistent decision support tool for health policy and program decision making.

The model incorporates best available evidence, data and expert opinion. We collaboratively developed the model structure with recognised experts in providing care, planning services, undertaking research and developing policy for the diagnosis and management of diabetes. We used an iterative process of model development where we presented the model back to participants at meetings and workshops to continually incorporate their feedback and refine the structure. The model was built by systems modelling experts based in Canada.

Papers published


This factsheet was prepared by The Australian Prevention Partnership Centre

For questions about this topic please contact Louise Freebairn
Tel: (02) 6205 2608  Email: louise.freebairn@act.gov.au
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Interactive dashboard

I led the development of an interactive dashboard designed for use by a policy audience. The dashboard was programmed by Mr Luke Penza and Dr Ante Prodan, computer scientists employed by The Australian Prevention Partnership Centre, in Tableau© using model output data.

The dashboard was designed to be presented to the ACT Minister for Health and Wellbeing; therefore, priority was given to displaying the results in a simplified and clear format. This was intended to facilitate the communication of key messages about the insights derived from the simulated scenarios. To achieve this purpose, it was decided to remove measures of model output variation and uncertainty, such as 95% confidence intervals from the dashboard. These measures of uncertainty were included in papers prepared for publication.

The dashboard allowed policy makers to engage with model outputs dynamically to test “What if” scenarios relating to the impact of population health and targeted interventions. Contextual information about the model and its development were provided on the first tabs viewed by the user. The scenario testing tabs allowed users to select interventions and compare their effect on outcome measures, including insulin sensitivity and diabetes in pregnancy incidence, against the baseline. Being able to forecast the number of women receiving services is important for resource allocation and service planning decisions. Therefore, the dashboard included forecasted estimates of the number of women receiving the selected interventions and the number diagnosed with diabetes in pregnancy for each year. Screen shots from the dashboard are displayed and explained below.
1. **Home tab.** This screen provided an overview of the model development process. It displayed photographs depicting modelling participants engaging in activities to map the causal factors contributing to the development of diabetes in pregnancy. The conceptual maps developed in the activities shown in the photographs were used to inform the model structure and logic.
2. **Model structure tab.** This screen provided a strategic overview of the model structure and showed the relationships between model components. The model structure presented on this tab shows that individual characteristics, weight status and pregnancy status all contribute to an individual’s internal dynamics of glucose regulation e.g. their blood glucose levels and insulin sensitivity. Glucose regulation in turn effects an individual agent’s risk of developing and being diagnosed with diabetes in pregnancy and impacts on their use of health services. The background photograph shows a Canberra woman who was receiving diabetes in pregnancy care. She is depicted in a distinctive local setting to illustrate the local focus for the model.
1. **Scenario testing screen 1.** On this screen, users could choose up to five interventions to compare against the baseline scenario over time. A description of each scenario was displayed when users hovered their cursor over the drop-down arrow. Users selected to display either insulin sensitivity (shown) or diabetes in pregnancy incidence as the outcome presented in the graph at the top left. The percentage difference from baseline for each scenario was displayed in the graphs in the bottom right of the screen. Impact on BMI categories for the agent population for each scenario are displayed in the graphs in the bottom left of the screen.
2. **Scenario testing screen 2.** On this screen users could choose up to four interventions to compare against the baseline scenario in the graph at top left. Users selected to display either insulin sensitivity (shown) or diabetes in pregnancy incidence as the outcome. The percentage difference from baseline for each scenario is displayed in the graphs in the bottom right of the screen. Impact on BMI categories for the agent population for each scenario are displayed in the graphs in the bottom left of the screen.
3. **Model outputs compared with retrospective data.** The ability to replicate historical trends is commonly used to assess model performance. The validation of this model was demonstrated by its ability to closely replicate the percentage of women diagnosed with diabetes in pregnancy from the ACT maternal and perinatal data collection. The retrospective data is shown in black below and the model results are shown in orange.
4. **Forecasted number of women diagnosed with diabetes in pregnancy.** This tab presented the forecasted number of women diagnosed with diabetes in pregnancy for each scenario. The graphs displayed on this tab updated dynamically with the intervention selected on previous tabs or could be manipulated manually by the user on this tab.
5. **Forecasted number of women receiving interventions.** The forecasted number of women receiving interventions was displayed along with more detailed descriptions for each intervention. A grid of graphs was utilised for this presentation to accommodate the significant difference in numbers receiving interventions. For example, the forecasted number of women receiving the population intervention each year settled at around 15,000 after the initial implementation period, whereas the targeted interventions were delivered to significantly smaller numbers of women.