Institution: The University of Oxford

Unit of Assessment: 1

Title of case study:

PLANNING FOR A FUTURE WITH DIABETES: TOOLS TO ASSESS DIABETES RISK AND OUTCOMES

Summary of the impact:

We are facing a diabetes epidemic: the number of people affected worldwide is estimated to rise from 366 million in 2011 to 552 million by 2030, representing a huge financial burden on society. Using data from the United Kingdom Prospective Diabetes Study (UKPDS), the University of Oxford's Diabetes Trials Unit developed two assessment tools - the UKPDS Risk Engine (a diabetes-specific heart attack and stroke risk calculator) and the UKPDS Outcomes Model (a lifetime simulator for people with diabetes) to better understand and plan for diabetes risk and its outcomes on both individuals and society as a whole. Patients, clinicians and policymakers globally are now using these tools to assist in planning for future health economic needs, and for predicting health risks for people with diabetes.

Underpinning research:

Predictive models are useful tools to help healthcare systems plan for the future. Using data from the United Kingdom Prospective Diabetes Study (UKPDS), the University of Oxford's Diabetes Trials Unit (DTU) developed two key risk assessment models to evaluate the medical and economic impacts of diabetes, in individual patients and on patient populations globally.

UKPDS Risk Engine: helping doctors and patients assess heart and stroke risk

Ensuring a patient's risk is estimated correctly is essential to inform both patient and healthcare professionals with respect to treatment decisions. It is also important to know that high-risk patients, who might otherwise receive suboptimal care, are not overlooked. Prior to the UKPDS, heart disease and stroke risks were calculated using Boston University's Framingham Heart Study, but this underestimates heart disease and stroke risks in patients with diabetes[1]. To estimate accurate risks specifically for people with type 2 diabetes, the DTU used UKPDS data from over 5,100 diabetic patients to develop the UKPDS Risk Engine. This provides robust risk estimates and 95% confidence intervals for coronary heart disease (nonfatal and fatal)[2] and stroke (nonfatal and fatal)[3]. It is available as a free, easy-to-use software package fully compatible with computing platforms used in primary care, and can be used to:

- Help determine likely event rates in clinical trials and calculate more accurate outcome trial sample sizes;
- Calculate single risk estimates for multiple risk factors;
- Illustrate likely effects of therapeutic interventions;
- Support the need for more intensive therapy; or Empower patients and motivate therapy adherence.

A new enhanced version of the UKPDS Risk Engine, to be released shortly, incorporates the 10-year post-trial UKPDS follow-up data, and provides risk estimates for individuals with established, as well as newly-diagnosed type 2 diabetes. It will also provide risk estimates for individuals with, as well as without, a prior history of cardiovascular disease.

The UKPDS Outcomes Model: simulating the impact of health interventions

The UKPDS Outcomes Model is a computer simulation model developed specifically for people with type 2 diabetes[4] by the DTU in collaboration with Oxford University's Health Economics Research Centre, using UKPDS data supplemented by cross-sectional surveys of non-inpatient

healthcare use and quality of life statistics[4]. As described by Adler[5], the model simulates the burden of complications for a hypothetical population with diabetes by predicting the series of events that unfold over time. The UKPDS Outcomes Model can determine life expectancy, quality-adjusted life expectancy and cost-effectiveness, and can also calculate event rates. It models four functions:

- Incidence and interdependence of complications;
- Changes in risk factors over time;
- Quality of life associated with each complication; and
- Costs associated with complications and therapies.

Because of this, the Model is particularly valuable to health economists in facilitating evaluations of both individual patient and entire populations.

References to the research:

1. Guzder, R. N., Gatling, W., Mullee, M. A., Mehta, R. L. & Byrne, C. D. Prognostic value of the Framingham cardiovascular risk equation and the UKPDS risk engine for coronary heart disease in newly diagnosed Type 2 diabetes: results from a United Kingdom study. *Diabet. Med.* **22**, 554–562 (2005). doi: 10.1111/j.1464-5491.2005.01494.x ***Paper stating the Framingham risk equation underestimates risk for coronary heart disease in people with newly-diagnosed diabetes.***

2. Stevens, R. J., Kothari, V., Adler, A. I., Stratton, I. M. United Kingdom Prospective Diabetes Study (UKPDS) Group The UKPDS risk engine: a model for the risk of coronary heart disease in Type II diabetes (UKPDS 56). *Clin. Sci.* **101**, 671–679 (2001). ***Paper describing the coronary heart disease risk calculation capability of the UKPDS Risk Engine.***

3. Kothari, V. *et al.* UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine. *Stroke* **33**, 1776–1781 (2002). doi: 10.1161/01.STR.0000020091.07144.C7 ***Paper describing the stroke risk calculation capability of the UKPDS Risk Engine.***

4. Clarke, P. M. *et al.* A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia* **47**, 1747–1759 (2004). doi 10.1007/s00125-004-1527-z
Paper describing the UKPDS Outcomes Model.

5. Adler A.I. Chapter 13, "UKPDS – modelling of cardiovascular risk assessment and lifetime simulation of outcomes". From *UKPDS: The First 30 Years, First Edition*. Edited by Rury R Holman and Peter J Watkins. Published 2008 by Blackwell Publishing Ltd (John Wiley & Sons). ***Commentary describing the impact and use of the UKPDS Outcomes Model.***

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Details of the impact:

The UKPDS Risk Engine and UKPDS Outcomes Model are currently being used in a range of clinical, commercial and administrative settings – evaluating long-term medical risks in patients, as well as economic and clinical outcomes for patient populations worldwide.

The UKPDS Risk Engine

The UKPDS Risk Engine has become a significant tool in managing the risk of cardiac complications in patients with diabetes, both in the UK and internationally, and is recommended by the NHS[6]. The UKPDS Risk Engine calculates the real risk of diabetes rather than the assessed risk. Influencing national healthcare procedure, the UK National Institute for Clinical Excellence (NICE) guidelines recommend the UKPDS Risk Engine for[7]: annually estimating cardiovascular risk in patients not considered to be at high cardiovascular risk; educational purposes, when discussing cardiovascular complications and risk estimates with individual patients; patients 40 years old and above with low cardiovascular risk from non-hyperglycaemia-related factors[7].

As described and referenced by Adler[5], the Risk Engine has also been used to: assess the cost-effectiveness of screening for diabetes; evaluate the cost-effectiveness of treatments; assist health planners to direct scarce resources to high-risk patients; help clinical trialists to determine likely event rates and calculate more accurate outcome trial sample sizes; and enable actuaries and epidemiologists to forecast disease distribution.

The Risk Engine was the most successful model of its type at the worldwide Mount Hood Challenge Meeting in 2004. Its equations have been incorporated in many other leading models[8]. The UKPDS Risk Engine was licenced by ISIS Innovation – the technology transfer arm of The University of Oxford – in 2002. It is provided free of charge to academic and clinical groups, but there is a charge for commercial companies to use the model. Over 180,000 free copies have been downloaded to date. In addition, approximately 14 commercial licences have been sold by ISIS (10 to pharmaceutical companies, two to medical publishers, and two to IT companies)[9].

The UKPDS Outcomes Model

Intended to facilitate health economic evaluations of both individual patient and entire populations, the UKPDS Outcomes Model can be used to:

- Evaluate likely rates and sequences of complications (*e.g.* myocardial infarction, stroke, heart failure, renal failure, amputation) over a patient's simulated lifetime;
- Assist health service planning for populations with diabetes[4]. For example, it can help healthcare systems decide how many future coronary care or renal units they need to build, or estimate the overall difference a new diabetes treatment might make in terms of quality of life and costs;
- Help ensure more accurate calculations for life insurance premiums by specifically estimating the life expectancy of people with type 2 diabetes[4];
- Assist academic or clinical groups, or pharmaceutical companies, to model or design clinical trials[4]; or
- Assist healthcare providers to evaluate applications for new diabetes drugs.

The UKPDS Outcomes Model is now the preferred healthcare analysis tool used by NICE[10] to benchmark and evaluate applications for new licensed diabetes drugs. The UKPDS Outcomes Model is capable of facilitating large scale economic evaluations by estimating changes in life expectancy and quality of life, when risk factors are altered[3]. The Model has been used to assess economic impact of diabetic populations in the United Kingdom, Australia and Canada. The UKPDS Outcomes Model was touted the "best diabetes economic model in existence," for the purposes of the Ontario Diabetes Economic Model[11]. The Ontario Model was created to provide policymakers with a tool for assessing the long-term economic benefits of diabetes management, how to best allocate healthcare resources, and to estimate the cost of treating diabetes in Ontario[11]. The UKPDS Outcomes Model was also used in a cost-effectiveness study of diabetes health services in Australia, improving health outcomes for patients with type 2 diabetes[12]. The UKPDS Outcomes Model was the subject of an invited Keynote speech at the 2012 Second Annual PharmaCoEconomics Middle East Forum in Abu Dhabi, attended by international and regional experts, regulators, and other key stakeholders. It is now being used by the Health Authority of Abu Dhabi to assess future diabetes health care requirements.

The UKPDS Outcomes Model was licenced by ISIS Innovation – the technology transfer arm of

The University of Oxford – in 2005. It is provided free of charge to academic and clinical groups, but there is a charge for commercial companies to use the model. Since 2005, ISIS Innovation has provided over 170 licences worldwide in total for the UKPDS Outcomes Model. Of these, around 140 are non-commercial and 28 are commercial licences. The commercial licences sold by ISIS (three to healthcare providers, three to insurance companies, 17 to pharmaceutical and biotech companies, one to a university doing paid consultancy and four to individuals undertaking paid consultancy) have generated contracts worth over £450,000 in revenue for The University of Oxford[9].

Sources to corroborate the impact:

6. National Institute for Health and Care Excellence NHS Clinical Knowledge Summaries - Clinical topic - CVD risk assessment and management. CVD risk calculators. Available at: http://cks.nice.org.uk/cvd-risk-assessment-and-management#!scenarioclarification (accessed 2013) . ***Cardiovascular risk assessment and management advice from the NHS, recommending the use of the UKPDS Risk Engine for people with type 2 diabetes.***

7. National Institute for Health and Clinical Excellence (NICE) Type 2 diabetes:The management of type 2 diabetes, NICE Clinical Guideline 87 March 2009. Available at: http://www.nice.org.uk/nicemedia/live/12165/44320/44320.pdf. ***Clinical guidelines outlining recommendations for management of type 2 diabetes in the NHS in England and Wales.***

8. Mount Hood 4 Modeling Group. Computer modeling of diabetes and its complications: a report on the Fourth Mount Hood Challenge Meeting. *Diabetes Care* 30 (6): 1638–1646 (2007). doi:10.2337/dc07-9919. ***Paper reporting outcomes of the Mount Hood Challenge Meeting where the UKPDS Risk Engine was shown to be the most successful model of its type.***

9. Sales statistics have come from Brendan Spillane, Senior Technology Transfer Manager, ISIS Innovation Ltd. Oxford. Email from Brendan Spillane confirming statistics kept on file. ***Statistics and licence information from ISIS innovation.***

10. National Institute for Health and Clinical Excellence (NICE) Type 2 diabetes: newer agents, NICE Short clinical guideline 87, May 2009. Available at http://www.nice.org.uk/nicemedia/pdf/CG87ShortGuideline.pdf ***Clinical guidelines outlining recommendations for use of newer agents in the management of type 2 diabetes in the NHS in England and Wales.***

11. O'Reilly, D et al. on behalf of Ontario Ministry of Health and Long-term Care Development of an Ontario Diabetes Economic Model (ODEM) and Application to a Multidisciplinary Primary Care Diabetes Management Program. November 2006 Available at http://www.path-hta.ca/Libraries/Reports/Development_of_an_Ontario_Diabetes_Economic_Model_ODEM_and_Application_to_a_Multidisciplinary_Primary_Care_Diabetes_Management_Program.sflb.ashx (accessed 2013) ***Report recommending the use of the UKPDS Outcomes model in Ontario.***

12. McRae, I. S. *et al.* A cost effectiveness study of integrated care in health services delivery: a diabetes program in Australia. *BMC Health Serv Res* **8**, 205 (2008). doi: 10.1186/1472-6963-8-205 ***Paper describing how the UKPDS Outcomes model was used in an Australian cost effectiveness study.***