Assessing the economics of a stratified treatment approach for Type 2 Diabetes

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Background

Current guidelines indicate treating type 2 diabetes patients with a standard, stepwise protocol.

However, stratification based on predicted drug response or predicted risk factors has the potential to improve life expectancy and slow progression of diabetes.

Identifying patient subgroups and treating each group of patients in the most appropriate way could reduce risk and prolong patient lifetimes.

Aims

A treatment by subgroup interaction:

Our starting point is the case of two subgroups of patients who respond differently to a pair of treatment options.

	Benefits of Treatment A	Benefits of Treatment B
Group 1	High	Low
Group 2	Low	High

A key goal of the MASTERMIND project is to identify such subgroup and treatment pairs.

The purpose of the work reported here is to assess the benefits that can arise from stratified treatment.

Methods: The UKPDS Model

We used the UKPDS Outcomes Model (version 2.0) to evaluate the benefits of treatment strategies that reduce HbA1c in the patient population.

The model takes as input a patient's pattern of HbA1c and other risk factors over a period of years.

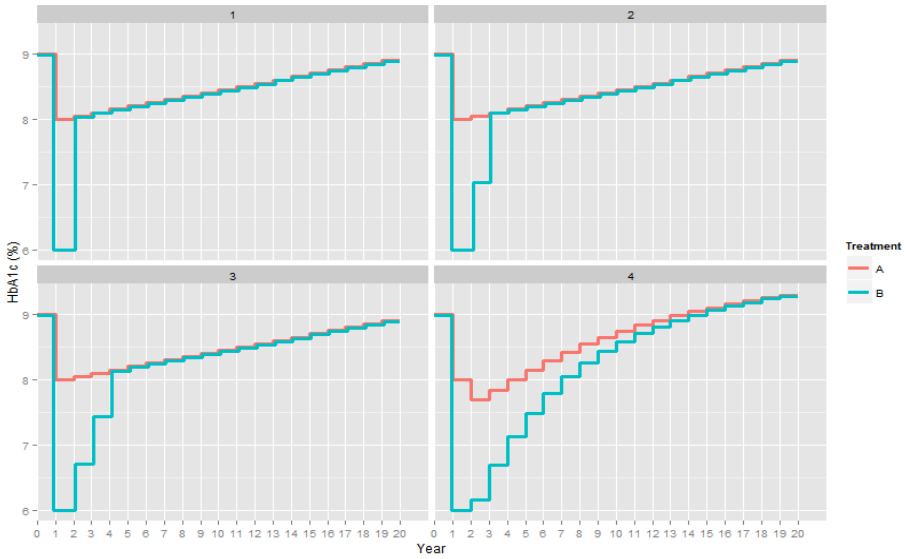
Its output is a prediction of quality adjusted life expectancy and the cost of treating diabetes related complications.

This allows us to asses the effects of reduced HbA1c on patient outcomes.

(1) Subjects + Comparisons of HbA1c sequences

We took four examples of T2D patients whose age, sex, BMI, BP, HKL, smoker, etc., put them at *low / middle / high / very high* risk of complications or death.

We compared their outcomes over 20 years under different patterns of HbA1c: four scenarios A vs B.



Treatment B decreases HbA1c by an additional 2% (22 mmol/mol) in year 1.

(1) Patient characteristics for four patient exemplars

	Patient 1 Very High Risk	Patient 2 High Risk	Patient 3 Medium Risk	Patient 4 Low Risk
Sex	Male	Male	Male	Female
Age at baseline	60	55	50	40
BMI (kg/m^2)	40.1	32.4	27.8	23.7
Current smoker	Yes	Yes	Yes	No
HDL (mmol/l)	0.90	1.05	1.10	1.15
LDL (mmol/l)	5.85	5.65	5.50	4.60
Systolic BP (mmHg)	165	155	140	125
Heart Rate (bpm)	100	85	75	65

(1) Gain in E(QALYs)

The table shows the increase in E(QALYs) over 20 years of follow-up when HbA1c is changed from Pattern A (higher) to Pattern B (lower) in each of the four scenarios.

The areas between the HbA1c curves A and B in the four scenarios are 2, 3, 4 and 8.3 % years

(%)	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Very high risk	0.04	0.05	0.07	0.13
High risk	0.03	0.05	0.07	0.12
Medium risk	0.02	0.03	0.04	0.08
Low risk	0.00	0.00	0.00	0.01

Positive differences indicate higher E(QALYs) on Treatment B

(1) Reduced cost of treating complications

The table shows the decrease in average cost of diabetes related complications over 20 years follow-up when HbA1c is changed from A to B in the 4 scenarios.

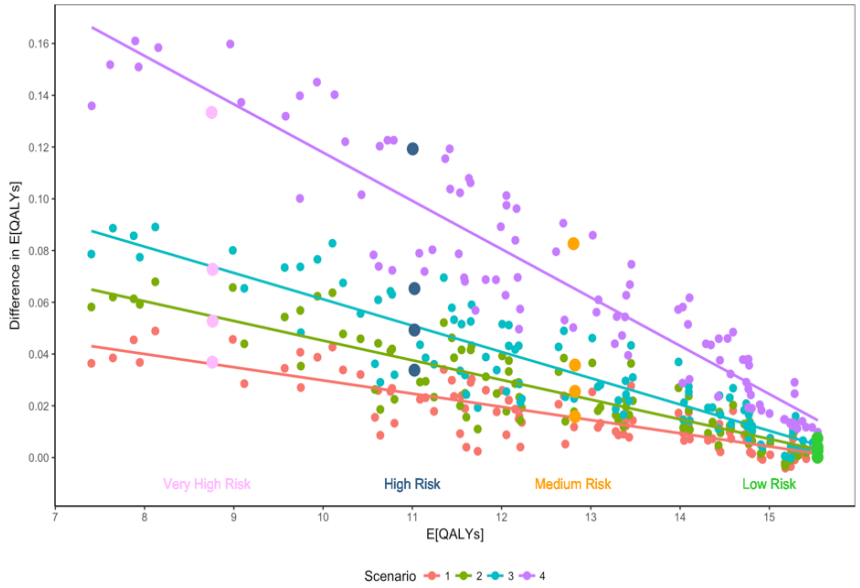
(£)	Scenario 1	Scenario 2	Scenario 3	Scenario 4
Very high risk	70	120	120	150
High risk	30	50	40	120
Medium risk	30	60	90	190
Low risk	20	30	50	80

Positive values indicate lower E(Costs) on Treatment B.

NB: E(Costs) range from £27,000 to £32,500, so these differences represent a small percentage change.

(1) Impact is highest for those at greatest risk

The figure shows the increase in E(QALYs) on moving from Treatment A to B for 100 hypothetical patients, in the 4 scenarios for the effects of Treatments A and B.



Lower average HbA1c gives higher expected quality adjusted life years E(QALYs).

Changes in HbA1c have the greatest impact for patients at the highest risk.

(1) Discussion

1. The benefit of reduced HbA1c (A vs B) depends on patient characteristics.

E(QALYs) under A is a good measure of risk – with high E(QALYs) equating to low risk.

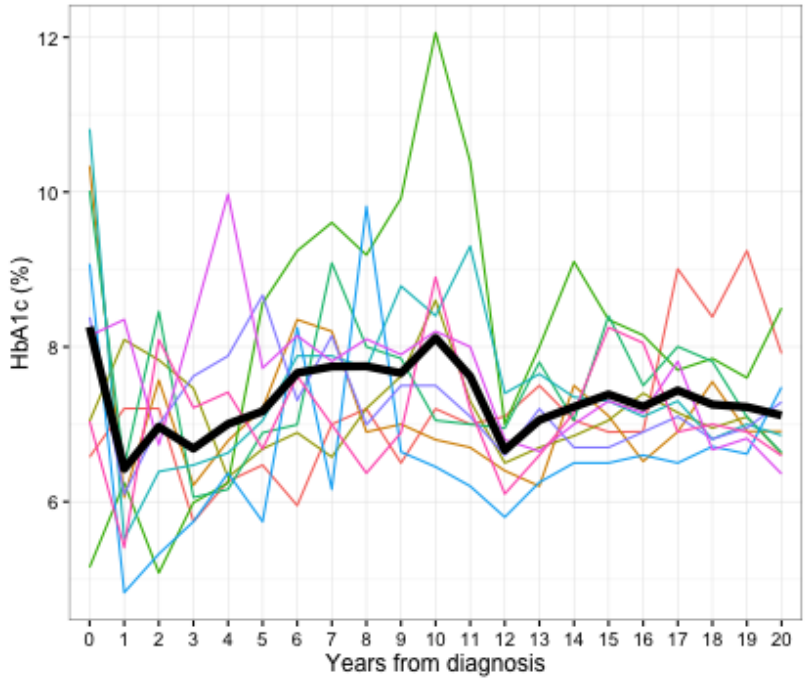
Then, benefits of B vs A increase linearly as E(QALYs) decreases, with slope proportional to the area between A and B curves.

2. We find the benefits for the same % fall in HbA1c to be roughly constant over when this occurs in years 1 to 5.

After that, benefits decrease to about 60% when the fall in HbA1c occurs in year 10, and to about 30% if the fall in HbA1c is in year 15.

(2) Subjects: A sample from the GoDARTS database

To assess the benefits of reducing HbA1c across the patient population, we sampled 100 subjects from the GoDARTS database.



The plot shows HbA1c time-paths for 20 of these patients.

The thick black line shows the mean HbA1c for these 20 cases.

(2) Methods: Assessing outcomes for GoDARTS patients under modified HbA1c sequences

We compared expected quality adjusted life years, E(QALYs), and the cost of treating diabetes-related complications in 3 scenarios:

(A) The original patient data,

(B) With HbA1c reduced for all patients by 2% in Year 1,

(C) With HbA1c reduced for all patients in Year 1 by a random amount, normally distributed with mean = 2% and standard deviation = 0.5%.

(2) Impact of lower HbA1c on E(QALYs)

Reducing HbA1c by an average of 2% (22 mmol/mol) for 1 year in a patient subgroup, in either scenario (B) or (C), gave the following benefits for our sample of 100 GoDARTS subjects:

- Increase in E(QALYS) of 0.0105 (s.e. 0.0004, bootstrap CI 0.0087 – 0.0168)
- A decrease of £25 (s.e. £2) in the costs of treating diabetes-related complications

(3) Impact of lower HbA1c for non-obese males

Reducing HbA1c by an average of 2% (22 mmol/mol) for 1 year, in either scenario (B) or (C), gave the following benefits for a sample of 100 non-obese males from the GoDARTS data set:

- Increase in E(QALYS) of 0.0236 (s.e. 0.0004, bootstrap CI 0.0182 – 0.0317)
- A decrease of £55 (s.e. £2) in the costs of treating diabetes-related complications

(2 & 3) Impact of lower HbA1c on E(QALYs)

Effect on E(QALYs) of reducing HbA1c by 2% for 1 year:

- An increase of 0.0105 in expected QALYs overall,
- An increase of 0.0236 E(QALYs) for non-obese males.

The increase in E(QALYs) can be attributed to a large benefit for a small proportion of patients who avoid a serious event such as MI or stroke.

In general, benefits increase in proportion to average reduction in HbA1c, summed over years.

Average benefits are greater for higher risk patients.

(2) Impact of lower HbA1c on E(QALYs)

The effect on E(QALYs) of reducing HbA1c by 2% for 1 year – or by 1% for 2 years for typical GoDARTS patients:

- An increase of 0.0105 in expected QALYs per patient

Valuing one QALY at £20k, this increase translates to a value of £210 per subgroup patient − to be set against the cost of determining subgroup membership and rise in treatment costs.

Reducing HbA1c by 2% for one year for one tenth of the approx. 3 million UK patients with Type 2 diabetes, would gain

3,150 quality adjusted life years

equivalent to ***£63 million*** at £20,000 per QALY.

Conclusions

- We can quantify the benefits from improvements in HbA1c that follow from a stratified treatment approach.
- Even modest, short-term improvements in HbA1c have quantifiable effects on patient lifetimes and quality of life, and on the costs of treating complications.
- These benefits indicate how much can be spent on stratified treatment, both in identifying a patient subgroup and treating these patients differently, while remaining cost-effective.