# **Research: Health Economics**

# Estimating the impact of better management of glycaemic control in adults with Type 1 and Type 2 diabetes on the number of clinical complications and the associated financial benefit

M. Baxter<sup>1</sup>, R. Hudson<sup>1</sup>, J. Mahon<sup>2</sup>, C. Bartlett<sup>2</sup>, Y. Samyshkin<sup>3</sup>, D. Alexiou<sup>3</sup> and N. Hex<sup>2</sup>

<sup>1</sup>Sanofi, Guildford, <sup>2</sup>York Health Economics Consortium Ltd, University of York, York and <sup>3</sup>IMS Health, London, UK

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# Abstract

**Aim** To estimate potential cost avoidance through modest and achievable improvements in glycaemic control in adults with Type 1 or Type 2 diabetes mellitus in the UK healthcare system.

**Methods** The IMS Core Diabetes Model was used to examine the impact of improved glycaemic control (indicated by reduction in  $HbA_{1c}$  level), in a representative cohort of adults with Type 1 or Type 2 diabetes. The cumulative incidence of microvascular and macrovascular complications was modelled across 5-year periods to a 25-year time horizon. Complication costs were applied to the data to estimate potential accrued cost avoidance.

**Results** Significant cost avoidance of ~£340 m is apparent in the first 5 years, increasing to ~£5.5bn after 25 years of sustained improvement in control. The overwhelming majority of cost avoidance arises from reductions in microvascular complications. In people with Type 1 diabetes the greatest cost avoidance comes from a reduction in renal disease (74% of cost avoidance), while in people with Type 2 diabetes it is generated by a reduction in foot ulcers, amputations and neuropathy: 57% cost avoidance). Greater cost reduction is accrued more rapidly in people with higher starting HbA<sub>1c</sub> levels.

**Conclusion** Modest improvements in glycaemic control generate significant reductions in the incidence and, therefore, cost of microvascular complications in people with Type 1 or Type 2 diabetes. This study provides clear support for the premise that prioritized and sustained investment in early and better intervention can provide concrete financial benefits in both the short and longer term.

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# Introduction

Previous research has estimated that, in 2010/2011, the total annual cost of Type 1 and Type 2 diabetes to the UK National Health Service (NHS) was £9.8 bn. A major component of this cost (80%) arises from dealing with potentially avoidable long-term complications of the disease. Only 8% is spent on direct therapeutic intervention [1].

Many studies have highlighted the heightened risk of complications with increasing HbA<sub>1c</sub> levels [2–4]. Both the UK Prospective Diabetes Study (UKPDS) in Type 2 diabetes [5] and the Diabetes Control and Complications Trial

(DCCT) in Type 1 diabetes [6] recorded a 37% reduction in microvascular complications for an 11 mmol/mol (1%) reduction in HbA<sub>1c</sub> level. A 25% reduction in microvascular endpoints was also reported in people whose HbA<sub>1c</sub> level was 53 mmol/mol (7.0%) rather than 63 mmol/mol (7.9%) over a 10-year period [5,6].

The UK National Institute for Health and Care Excellence (NICE) guideline on Type 2 diabetes has a monitoring and treatment escalation algorithm that aims to maintain HbA<sub>1c</sub> below 59 mmol/mol (7.5%) [7]; however, evidence shows that therapy escalations currently take place at higher HbA<sub>1c</sub> thresholds than detailed in the algorithm, with increasing delays being encountered as treatment complexity increases [8–10]. The UKPDS suggests that 75% of people with Type 2 diabetes will require insulin within 5 years of diagnosis to maintain HbA<sub>1c</sub> targets; however, the average time to initiation of insulin in people with Type 2 diabetes in the

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# What's new?

- This study provides estimates of the potential costs avoided as a consequence of reducing the incidence of complications by improving glycaemic control in the current UK adult population with diabetes.
- By implementing modest and achievable reductions in HbA<sub>1c</sub> levels, a significant cost avoidance of ~£340 m is apparent after 5 years. This increases to ~£5.5bn after 25 years of sustained improvement in glycaemic control.
- These results suggest that action taken now could produce demonstrable clinical and financial benefit within the next 5 years; sustained intervention will ensure this accrues for decades to come.

UK is 9 years. The average  $HbA_{1c}$  on initiation of insulin is 84 mmol/mol (9.8%), which is the highest in Europe [8]. Furthermore, after initiation of insulin, up-titration of doses to achieve optimum control is also poor [11].

For Type 1 diabetes, despite the use of human insulin, insulin analogues, basal-bolus insulin and an increasing use of insulin pumps, < 30% of people with Type 1 diabetes have HbA<sub>1c</sub> levels < 59 mmol/mol (7.5%) and > 30% have HbA<sub>1c</sub> levels > 75 mmol/mol (9%) (Table S1). This failure to achieve recommended targets and the consequent exposure of people to a higher risk of avoidable and costly complications has been described as clinical inertia [8].

The commonly presented argument to explain and justify this situation is that the care of people with diabetes is complex, the achievement of targets too difficult, and the actual benefits, in terms of reduced complications (and potential cost savings), of improved glycaemic control are ill defined.

In the present study we report our estimate of the potential cost avoidance that may be achieved through reducing complication rates by making achievable, incremental improvements in glycaemic control, when compared with the levels currently delivered in clinical practice. It is not predicated on any specific therapy, but simply more timely and appropriate interventions to improve care.

Recognizing that the development of complications is a function of both glycaemic control and time, we estimated the impacts of improved glycaemic control at 5-year intervals up to 25 years. This was carried out for the prevalent cohort of adults with Type 1 and Type 2 diabetes estimated within 1 year. We did not consider incident (or newly diagnosed) cases in subsequent years.

It is important to note that the study did not consider the costs of the interventions associated with changing clinical practice, but simply the avoided costs accrued by a reduction in complication rates. It is for NHS commissioners to determine how best to invest to generate improvements in care for people with diabetes. The results of the present study could be used in financial arguments to encourage investment in early, more aggressive diabetes therapy and/or to inform possible population-based intervention strategies. The study included costs to UK NHS only, and did not consider societal costs.

# Methodology

A four-stage methodology was used to estimate cost reductions.

- 1) Modelled cumulative rates of complications comparing current and better glycaemic management scenarios for adults with Type 1 and Type 2 diabetes using the IMS Core Diabetes Model ('the model') and individual UK patient primary care data from IMS Disease Analyzer.
- 2) Applied complication treatment costs.
- 3) Calculated per-person complication costs by starting HbA<sub>1c</sub> level subgroup.
- 4) Estimated aggregate cost reduction, multiplying perperson cost reductions by national numbers of adults with Type 1 or Type 2 diabetes.

# IMS Core Diabetes Model

The IMS Core Diabetes Model is a widely published and validated [12,13] model for Type 1 and Type 2 diabetes. It is a non-product-specific computer simulation model designed to translate surrogate endpoints into long-term health and economic outcomes [14]. It is the most widely adopted economic model by academia and the pharmaceutical industry, as well as healthcare payers and decision-makers. Results from the model have been widely published.

In the present study we used the model to analyse the impact of a reduction in the level of  $HbA_{1c}$  for representative cohorts of adults with treated Type 1 or Type 2 diabetes drawn from the IMS Disease Analyzer (UK database), a longitudinal database containing more than two million anonymous patient records.

These cohorts were fixed at the beginning of the analysis and modelled for the 25 years. The model structure comprises a number of interdependent submodels that simulate the microvascular and macrovascular complications of diabetes, in addition to non-specific mortality. The study projects outcomes and costs over 25 years at 5-yearly intervals to provide a link with the forecast future cost burden of diabetes from Hex *et al.* [1] The assumption is that complication treatment and costs remain the same over the time horizon.

The Type 1 and Type 2 diabetes cohorts were differentiated into subgroups depending on their range of HbA<sub>1c</sub>, based on the Quality and Outcomes Framework definitions [ $\leq$  59 mmol/mol (7.5%); > 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%); > 64 mmol/mol (8.0%) to 75 mmol/ mol (9.0%); and > 75 mmol/mol (9.0%). The base cases for the study were: 1) Type 1 diabetes: modelling assuming the trajectory of HbA<sub>1c</sub> would follow the natural history of disease for each of the HbA<sub>1c</sub> segments (baseline). For the comparator scenario it was assumed that the HbA<sub>1c</sub> trajectory would be parallel to the baseline but at 4 mmol/mol (0.4%) below and 2) Type 2 diabetes: modelling of modification of treatment at HbA<sub>1c</sub> thresholds indicated by current NICE guidelines [7], as opposed to current UK practice which indicates that therapy modifications currently take place at higher HbA<sub>1c</sub> thresholds (baseline) [8–10].

# Extrapolation to current UK adult population with Type 1 or Type 2 diabetes

The numbers of avoided complications were estimated by applying the incremental changes in the cumulative incidence of complications for each cohort subgroup based on  $HbA_{1c}$  to the estimated UK adult population currently diagnosed with, and being treated for, Type 1 or Type 2 diabetes. The proportions of people with Type 1 and Type 2 diabetes in each subgroup were drawn from Cegedim Strategic Data and applied to total UK adult population estimates for Type 1 and Type 2 diabetes (Table S1).

The study estimated reductions in the rates of complications compared with the base case for both Type 1 and Type 2 diabetes. Around 81 000 microvascular and 7000 macrovascular events could be avoided over 25 years through a 4-mmol/mol (0.4%) reduction in HbA<sub>1c</sub> levels for people with Type 1 diabetes (Table S4) [15]. Scenario analysis for Type 1 diabetes explored the range 2–9 mmol/ mol (0.2–0.8%) for reduction in HbA<sub>1c</sub> levels and also the maintenance of HbA<sub>1c</sub> at 58 mmol/mol (7.5%) over 25 years. For Type 2 diabetes, if HbA<sub>1c</sub> levels were managed at levels specified in NICE guidance then 789 000 microvascular and 81 000 macrovascular events could be avoided (Table S5). Scenario analysis for Type 2 diabetes explored a more modest reduction in  $HbA_{1c}$  thresholds, at 11 mmol/ mol (1%) below the base case.

### **Complication treatment costs**

Costs of diabetes management are not included but treatment costs for complications are derived from peer-reviewed literature where available. All costs are inflated to 2014 [16]. Estimated costs were not discounted as the study was a budget impact analysis. A summary of costs is provided in Table S6.

# Results

Cost results are reported per person, and in aggregate, for each of the four complication areas considered, and for the scenario analyses undertaken. The cost reductions reflect the costs of avoided complications but not the total cost of treatment and management of diabetes.

#### Total costs avoided

Virtually all of the cost reductions related to avoided microvascular complications after 25 years of improved glycaemic control for people with Type 1 or Type 2 diabetes (Tables 1 and 2). The cost reduction estimates do not include any estimates of the costs of interventions to improve glycaemic control.

#### Type 1 diabetes

Assuming that better management could result in a 4-mmol/ mol (0.4%) lower HbA<sub>1c</sub> level in people with Type 1 diabetes, the cost reduction from complications avoided per person after 25 years ranged from £2057 for people with a starting HbA<sub>1c</sub> of < 59 mmol/mol (7.5%), to £4136 for people with HbA<sub>1c</sub> > 75 mmol/mol (9.0%). The total cost reductions in the current UK adult Type 1 diabetes popula-

Table 1 Type 1 diabetes cost reductions per person, and for the total current UK adult population with Type 1 diabetes, from avoided complications for the reduction of HbA<sub>1c</sub> from baseline by 0.4% point

HbA <sub>1c</sub>	5 years	10 years	15 years	20 years	25 years
Adult Type 1 diabetes, per-person cost reductions					
< 59 mmol/mol (7.5%)	£66	£271	£719	£1379	£2057
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£89	£358	£901	£1713	£2621
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£103	£494	£1224	£2138	£2831
> 75 mmol/mol (9.0%)	£184	£808	£1880	£3147	£4136
Adult Type 1 diabetes, total population cost reduction	ons				
< 59 mmol/mol (7.5%)	£6 221 012	£25 543 854	£67 771 332	£129 981 455	£193 888 21
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£3 556 036	£14 304 053	£35 999 865	£68 443 695	£104 723 24
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£9 046 940	£43 390 178	£107 509 267	£187 789 880	£248 659 09
> 75 mmol/mol (9.0%)	£19 906 668	£87 416 238	£203 394 216	£340 468 935	£447 467 27
Total	£38 730 656	£170 654 323	£414 674 680	£726 683 966	£994 737 84

tion could be £39 m over 5 years, rising to £995 m after 25 years of improved control. People with HbA<sub>1c</sub> > 75 mmol/mol (9.0%) account for 45% of the total cost reduction over 25 years of improved control, and renal disease accounts for 74% of the 25-year cost reduction (Tables 3 and S7).

#### Type 2 diabetes

Assuming people with Type 2 diabetes might receive up to five treatment modifications at the levels of  $HbA_{1c}$  recommended in NICE guidance, over 25 years, the cost reduction from avoided complications ranged from £1280 per person for people with starting  $HbA_{1c}$ 

 $\leq$  59 mmol/mol (7.5%), to £2223 for people with HbA<sub>1c</sub> > 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%). Cost reductions in the current UK adult Type 2 diabetes population could be £299 m over 5 years, rising to £4.506 bn over 25 years. People with lower starting HbA<sub>1c</sub> levels generate most of the cost reductions because they are the largest cohort, with people at a starting HbA<sub>1c</sub> level of < 59 mmol/mol (7.5%) accounting for 50% of the cost reductions. Renal complications resulted in substantial cost reductions but the majority of cost reductions (57%) were generated from reduced cumulative incidence of foot ulcer and amputations, and neuropathy (Tables 4 and S8).

Table 2 Type 2 diabetes cost reductions per person, and for the total current UK adult population with Type 2 diabetes, from avoided complications for management of HbA<sub>1c</sub> at treatment levels specified by the National Institute for Health and Care Excellence

HbA <sub>1c</sub>	5 years	10 years	15 years	20 years	25 years
Adult Type 2 diabetes, per-person cost reduc	ctions				
< 59 mmol/mol (7.5%)	£83	£317	£682	£1078	£1280
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£132	£449	£995	£1510	£1678
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£138	£607	£1366	£1999	£2223
> 75 mmol/mol (9.0%)	£105	£622	£1274	£1591	£1559
Adult Type 2 diabetes, total population cost	reductions				
< 59 mmol/mol (7.5%)	£146 891 319	£561 018 652	£1 206 986 500	£1 907 817 371	£2 265 311 900
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£41 540 384	£141 300 247	£313 126 383	£475 196 823	£528 066 403
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£58 477 533	£257 216 394	£578 842 824	£847 076 724	£941 996 777
> 75 mmol/mol (9.0%)	£51 933 835	£307 646 148	£630 130 534	£786 921 255	£771 093 801
TOTAL	£298 843 071	£1 267 181 440	£2 729 086 240	£4 017 012 172	£4 506 468 88

Table 3 Cost reductions of avoided complications for current UK adult Type 1 diabetes population with 4 mmol/mol (0.4%) HbA<sub>1c</sub> reduction

HbA <sub>1c</sub>	5 years	10 years	15 years	20 years	25 years
Eye disease					
< 59 mmol/mol (7.5%)	£188 516	£1 319 609	£4 053 084	£8 106 168	£11 876 478
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£119 866	£559 376	£1 438 396	£2 197 550	£2 077 684
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£87 834	£966 178	£3 074 203	£4 743 056	£4 303 884
> 75 mmol/mol (9.0%)	£432 754	£1 839 203	£3 029 276	£1 406 449	-£5 842 174
Renal disease					
< 59 mmol/mol (7.5%)	£188 516	£3 864 568	£21 396 512	£58 062 782	£105 191 664
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£239 733	£3 196 436	£14 224 142	£37 038 707	£66 206 189
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£1 493 184	£15 546 683	£54 984 315	£117 171 048	£179 709 118
> 75 mmol/mol (9.0%)	£5 733 986	£44 357 249	£133 937 255	£262 465 090	£388 829 156
Foot ulcers and amputations and neuropathy					
< 59 mmol/mol (7.5%)	£4 430 115	£16 023 820	£33 650 021	£51 276 223	£63 906 763
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£2 317 416	£8 110 957	£15 982 182	£23 294 030	£31 564 810
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£6 148 406	£21 782 923	£40 930 816	£56 213 996	£62 625 905
> 75 mmol/mol (9.0%)	£11 792 537	£37 541 379	£63 073 845	£78 544 788	£82 331 382
Cardiovascular disease					
< 59 mmol/mol (7.5%)	£1 413 866	£4 335 857	£8 671 714	£12 536 282	£12 913 314
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	£879 020	£2 437 283	£4 355 145	£5 913 407	£4 874 566
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	£1 317 516	£5 094 393	£8 519 934	£9 661 781	£2 020 190
> 75 mmol/mol (9.0%)	£1 947 391	£3 678 406	£3 353 841	-£1 947 391	-£17 851 08

Table 4 Cost reductions from avoided complications for current UK adult population with Type 2 diabetes for management of HbA<sub>1c</sub> at treatment levels specified by the National Institute for Health and Care Excellence

HbA <sub>1c</sub>	5 years	10 years	15 years	20 years	25 years
Eye disease					
< 59 mmol/mol (7.5%)	12 388 424	42 474 598	95 567 846	159 279 743	214 142 766
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	4 091 098	11 329 196	24 861 291	39 652 185	50 981 381
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	12 712 507	63 138 785	147 041 332	228 401 378	273 318 903
> 75 mmol/mol (9.0%)	5 440 687	26 214 222	56 385 307	81 115 705	98 426 983
Renal disease					
< 59 mmol/mol (7.5%)	5 309 325	37 165 273	143 351 769	353 954 985	585 795 501
> 59 mmol/mol (7.5%) to 64 mmol/mol (8.0%)	-2 202 899	2 202 899	33 672 887	96 612 864	157 035 241
> 64 mmol/mol (8.0%) to 75 mmol/mol (9.0%)	0	12 712 507	67 376 288	161 025 090	241 961 385
> 75 mmol/mol (9.0%)	2 473 040	51 933 835	168 661 312	276 485 846	312 592 227
Foot ulcers and amputations and neuropathy					
Below 59 mmol/mol (7.5%)	54 863 023	307 940 837	690 212 221	1 104 339 554	1 368 036 018
> 59  mmol/mol (7.5%)  to  64  mmol/mol (8.0%)	21 714 292	86 542 468	190 708 129	287 635 693	331 064 276
> 64  mmol/mol (8.0%)  to  75  mmol/mol (9.0%)	24 577 514	123 311 319	276 708 905	400 867 724	450 022 752
> 75 mmol/mol (9.0%)	24 235 790	160 747 585	325 946 642	408 051 562	420 911 369
Cardiovascular disease					
< 59 mmol/mol (7.5%)	74 330 547	173 437 943	277 854 663	290 243 088	97 337 621
> 59  mmol/mol (7.5%)  to  64  mmol/mol (8.0%)	17 937 893	41 225 685£	63 884 076	51 296 081	-11 014 496
> 64  mmol/mol (8.0%)  to  75  mmol/mol (9.0%)	21 187 512	58 053 782	87 716 299	56 782 532	-23 306 263
> 75 mmol/mol (9.0%)	19 784 318	68 750 506	79 137 273	21 268 142	-60 836 778

#### Scenario analysis

# Type 1 diabetes

If HbA<sub>1c</sub> was reduced by just 2 mmol/mol (0.2%), cost reductions from avoided complications could be £515 m after 25 years of improved control. If HbA<sub>1c</sub> was reduced by 9 mmol/mol (0.8%), the cost reduction over 25 years could be £1.865bn. If HbA<sub>1c</sub> was maintained at 58 mmol/ mol (7.5%) over 25 years then the cost reductions from avoided complications could be £3.831bn. The decrement of 4 mmol/mol (0.4%) is modest and achievable compared with the HbA<sub>1c</sub> reductions achieved in the DCCT trial (up to 22 mmol/mol (2%) [6]. If those reductions were realised, cost avoidance would be proportionally higher.

#### Type 2 diabetes

If escalation of therapy was to take place at an  $HbA_{1c}$  level of 11 mmol/mol (1%) lower than the base case then cost reductions from avoided complications over 25 years could be £2.476bn.

#### **Results for individual complications**

Using the base case analysis for the better management scenario for people with Type 1 diabetes [4 mmol/mol (0.4%)], the overall cost reductions after 25 years of improved control were estimated to be £12 m for eye disease; £740 m for renal disease; £240 m for foot ulcer and amputations, and neuropathy; and £2 m for cardiovas-cular disease (Table 3).

For people with Type 2 diabetes, it was estimated that better treatment to the NICE guideline targets, could reduce costs after 25 years by £637 m for eye disease, £1.297bn for renal disease, £2.57bn for foot ulcers and amputations, and neuropathy, and £2 m for cardiovascular disease (Table 4).

#### Discussion

There are several points to note in relation to the present study. First, it does not include the costs associated with implementing strategies to improve glycaemic control. There are a broad range of potential interventions which can positively influence HbA<sub>1c</sub> levels and these will be very dependent on population characteristics, pre-existing infrastructure and even geographical location. Local providers are best placed to determine the optimal use of their own resource.

Second, the study does not take into account the increase in the population of people with diabetes.

Third, only patient records containing the essential information needed for model simulation, such as HbA<sub>1c</sub>, were selected for the study.

Fourth, the model has an ethnicity cohort input. Although ethnicity data are not well recorded in primary care, a data cleaning process was carried out for people with no ethnicity information, based on the UK proportion of different ethnic groups.

Fifth, the perspective is that of the UK NHS, and societal costs are not included. Costs of complication treatment are based on unit costs inflated to 2014 and, as this is a budget impact analysis, quality-adjusted life years are not considered.

Finally, in the better-managed cohort, some people incur higher costs as they have longer exposure to non-fatal events. This group also included a greater number of people alive compared with the poorly managed cohort. The present study clearly shows that in people with Type 1 or Type 2 diabetes, modest, achievable and sustained  $HbA_{1c}$  control improvements can significantly reduce the rates of diabetes-related microvascular complications, and avoid the associated costs of treatment the NHS would otherwise incur. These benefits can been seen in the first 5 years after intervention, and increase over time, with large benefits being accrued up to and including 25 years (Table S7).

The greatest cost reduction from glucose reduction is seen in people with Type 1 or Type 2 diabetes with the highest HbA<sub>1c</sub> levels. In population terms, the majority of people with Type 1 diabetes have high HbA<sub>1c</sub> levels [more than 57% have levels > 64 mmol/mol (8%) and 32% have levels > 75 mmol/mol (9%)] and so the largest NHS cost saving is in this group of people (Table S7).

In Type 2 diabetes the situation is more complex. Although the largest individual benefit still lies with the people with the highest HbA<sub>1c</sub> levels, 59% have HbA<sub>1c</sub> levels < 59 mmol/mol (7.5%) and 70% have HbA<sub>1c</sub> levels < 64 mmol/mol (8%). This means that, although the individual risk of a specific complication is low in this group, at the population level, this is where the greatest cost reduction might be achieved (Table S8).

These estimates may give some strategic insights for the resource-constrained NHS. In the adult population with Type 1 diabetes a strategy might be to target the high-risk population (those with high  $HbA_{1c}$  levels), attempting to improve  $HbA_{1c}$  control as much as possible in order to achieve the largest benefit, both clinically and financially. By contrast, in the Type 2 diabetes population a dual-focus approach might be warranted. Concentrated focus on people with high  $HbA_{1c}$  to achieve the greatest per-person improvement could be combined with less intensive intervention in the wider majority with a comparatively low elevated  $HbA_{1c}$  to optimize the clinical and financial benefits.

The majority of the cost avoidance in adults with Type 1 diabetes arises from a reduction in complications associated with renal disease. This emphasizes the fact that the major, and most costly, complication of Type 1 diabetes is diabetic nephropathy, which occurs as a consequence of microvascular disease. It therefore highlights the importance of good glycaemic control, but also good blood pressure control and regular urinary albumin screening.

By contrast, more than half of the cost avoidance in the Type 2 diabetes population is attributed to microvascular complications related to foot ulcers, amputations, and neuropathy. It is likely that the true cost of foot complications has been underestimated in the present study. Recent data suggest that in hospital admissions, where diabetes-related issues are the main reason for admission (primary diagnosis), 50% of admissions are related to foot complications [17].

Cost reductions for some complications, notably those relating to cardiovascular disease and, to a lesser extent, eye disease, decrease after 15 years and, in some cases, the costs of certain complications increase compared with the base case management scenario. The reasons for the increase are likely to be multifactorial. The low cost reductions from cardiovascular disease complications (macrovascular) at all time points up to, and including, 25 years reinforces evidence that glycaemic control is a weak modifier of cardiovascular risk [18]. This is an important observation, suggesting that attempts to modify cardiovascular disease risk via improvements in glycaemic control alone could be misplaced. The management of cardiovascular disease risk in people with diabetes, which is undoubtedly clinically very important, is most effectively achieved, as in the population without diabetes, by the adequate control of blood pressure and cholesterol levels. For people with diabetes, the avoidance of renal disease will also help to reduce cardiovascular disease risk.

The discussion has been predicated on base-cases for Type 1 and Type 2 diabetes. Further scenario modelling has shown that a modest 2-mmol/mol (0.2%) HbA<sub>1c</sub> reduction in adults with Type 1 diabetes, and treatment modification occurring at HbA<sub>1c</sub> levels only 11 mmol/mol (1%) lower than current clinical norms in adults with Type 2 diabetes would lead to substantial costs avoided. Conversely, if there was a commitment to driving even larger reductions in HbA<sub>1c</sub>, the level of impact would be even more significant.

It is important restress that the present work does not specify which treatment modifications that should be adopted and does not support any particular intervention strategy. It simply shows that improvements in glycaemic control, however it might be achieved, could generate significant clinical and financial benefit, even within 5 years of starting an intervention. Furthermore, the demonstration of cost avoidance should not be interpreted as an argument that this 'saved' money should be spent on a specific intervention. It does, however, indicate for the first time the magnitude of the financial impact on the population that modest improvements in glycaemic control could deliver, as well as the improvement in individual outcomes. As such, it could therefore help to identify the level and urgency of resources that the NHS should dedicate to improved diabetes interventions in an attempt to reduce the rates and costs of diabetes complications in the future. The results also signpost a population-based strategy which recognizes that even modest improvements in HbA1c can result in significant reductions in both the risk of developing, and the costs of managing, complications.

Action now could produce demonstrable financial benefit within the next 5 years and sustained intervention will ensure this accrues for decades to come.

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#### **Competing interests**

C.B. is a member of the JDRF and Diabetes UK. R.H. is an employee of Sanofi and M.B. was at the time of writing a medical advisor contracted by Sanofi but has now become a full time employee of sanofi.

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# **Supporting Information**

Additional Supporting Information may be found in the online version of this article:

 Table S1 Type 1 and Type 2 diabetes current UK adult

 population cohort estimates

Table S2 Incremental changes in cumulative incidence (%) of complications (per person) for Type 1 diabetes, for reduction of HbA<sub>1c</sub> from baseline by 0.4%

Table S3 Incremental changes in cumulative incidence of complications (per person) for Type 2 diabetes for reduction of  $HbA_{1c}$  from baseline to comparator case

Table S4 Extrapolated numbers of avoided complications for people with Type 1 diabetes, for reduction of  $HbA_{1c}$  from baseline by 4 mmol/mol (0.4%) (based on population in Table S1)

Table S5 Extrapolated numbers of avoided complications for people with Type 2 diabetes, for reduction of  $HbA_{1c}$  from baseline to comparator case (based on population in Table S1)

Table S6 Direct costs of complications and management costs

Table S7 Percentage of total cost reductions (at 25 years) from avoided complications for the current UK adult Type 1 diabetes population for reduction of HbA<sub>1c</sub> from baseline by 4 mmol/mol (0.4% point)

Table S8 Percentage of cost reductions from avoided complications (at 25 years) for the current UK adult Type 2 diabetes population for management of HbA<sub>1c</sub> at treatment levels specified by the National Institute for Health and Care Excellence (NICE)