SUPPLEMENTARY MaTERIAL:

EVALUATING THE BURDEN OF POOR GLYCAEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES: A MODELLING ANALYSIS FOR THE UK SETTING

**Table 1 Baseline cohort characteristics**

| Characteristic | Mean (SD) | Reference / Comment |
| --- | --- | --- |
| **Demographic data and baseline risk factors** | | |
| Baseline age (years) | 59.8 (12.6) | NICE THIN Cohort[[1]](#endnote-1) |
| Duration of diabetes (years) | 2.0 | NICE THIN Cohort1 |
| Percentage male (%) | 57.1 | NICE THIN Cohort1 |
| HbA1c (%) | 8.2 (2.0) | NICE THIN Cohort1 |
| Systolic blood pressure (mmHg) | 139.6 (17.1) | NICE THIN Cohort1 |
| Diastolic blood pressure (mmHg) | 80.0 (8.0) | CORE Diabetes Model default |
| Total cholesterol (mg/dL) | 191.8 (44.5) | NICE THIN Cohort1 |
| High density lipoprotein cholesterol (mg/dL) | 45.63 (11.60) | NICE THIN Cohort1 |
| Low density lipoprotein cholesterol (mg/dL) | 102.3 (31.60) | Pratley et al.[[2]](#endnote-2) / data on file\* |
| Triglycerides (mg/dL) | 210.5 (196.3) | Pratley et al.2 / data on file\* |
| Body mass index (kg/m2) | 31.85 (3.19) | NICE THIN Cohort1 |
| Percentage smokers (%) | 19.1 | NICE THIN Cohort1 |
| Mean cigarettes per day (n) | 12 | Office for National Statistics[[3]](#endnote-3) |
| Mean alcohol consumption (oz/week) | 7.52 | World Health Organization[[4]](#endnote-4) |
| **Ethnic group** | | |
| White | 94.6 | NICE THIN Cohort1 |
| Black | 2.7 | NICE THIN Cohort1 |
| Asian/Pacific Islander | 2.7 | NICE THIN Cohort1 |
| **Baseline complications** | | |
| Myocardial infarction (%) | 0.8 | NICE THIN Cohort1 |
| Unstable angina (%) | 2.7 | NICE THIN Cohort1 |
| Peripheral vascular disease (%) | 0.5 | NICE THIN Cohort1 |
| Stroke (%) | 0.5 | NICE THIN Cohort1 |
| Congestive heart failure (%) | 0.5 | NICE THIN Cohort1 |
| Atrial fibrillation (%) | 0.8 | NICE THIN Cohort1 |
| Microalbuminuria (%) | 1.1 | Pratley et al.2 / data on file\* |
| Gross proteinuria (%) | 0.2 | Pratley et al.2 / data on file\* |
| End-stage renal disease (%) | 0.2 | NICE THIN Cohort1 |
| Background diabetic retinopathy (%) | 2.7 | Pratley et al.2 / data on file\* |
| Proliferative diabetic retinopathy (%) | 0 | Pratley et al.2 / data on file\* |
| Macular edema (%) | 1.1 | Pratley et al.2 / data on file\* |
| Cataract (%) | 1.7 | Pratley et al.2 / data on file\* |
| Severe vision loss (%) | 0.4 | NICE THIN Cohort1 |
| Uninfected ulcer (%) | 0.6 | Pratley et al.2 / data on file\* |
| Infected ulcer (%) | 0.3 | Pratley et al.2 / data on file\* |
| Neuropathy (%) | 11.6 | Pratley et al.2 / data on file\* |
| Amputation (%) | 0.1 | NICE THIN Cohort1 |

BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

\* A select set of cohort characteristics was presented in the Prately et al.2 publication due to publication requirements. All cohort characteristics not included in the publication are retained as data on file by Novo Nordisk A/S.

Table 2 Summary of unit costs used in the health economic analysis

| **Cost** | **Value  (2018 GBP)** | **Source** |
| --- | --- | --- |
| **Patient management** |  |  |
| Cost of statins | 9.78 | MIMS 2018 (online version) [Simvastatin 40 mg] |
| Cost of aspirin | 6.78 | MIMS 2018 (online version) [aspirin gastro-resistant 75 mg] |
| Cost of ACE inhibitors | 10.17 | MIMS 2018 (online version) [Ramipril 5 mg capsules] |
| Cost of screening for microalbuminuria | 11.45 | Based on one nurse appointment (PSSRU, band 6, £44/hr with 15.5 minutes consultation) and Albustix (NHS electronic drug tariff, £4.10 per 50 plastic test strips) [(£4.10/50)+(44/(60/15.5))] |
| Cost of screening for gross proteinuria | 11.43 | Based on one nurse appointment (PSSRU, band 6, £44/hr with 15.5 minutes consultation) and Medi-test protein 2 (NHS electronic drug tariff, £3.27 per 50 plastic reagent test strips) [(£3.27/50)+(44/(60/15.5))] |
| Cost of eye screening | 34.24 | NHS reference costs 2016-17, WH15Z unit cost (special screening, examinations or other genetic disorders) |
| **Cardiovascular complications** | | |
| Cost of myocardial infarction (year of event) | 7,857 | Alva et al. 2015. 2012 values for MI event during year: £6,379 (mean inpatient cost) plus £963 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)[[5]](#endnote-5) |
| Cost of myocardial infarction (years 2+) | 1,953 | Alva et al. 2015. 2012 values for history of MI: £1,154 (mean inpatient cost) plus £671 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of angina (year of event) | 2,320 | Danese et al. (2015) mean 2014 incremental acute CV event costs for "unstable angina" across three patient groups (CV low/moderate risk, CV high risk and CV event history)[[6]](#endnote-6) |
| Cost of angina (years 2+) | 388 | Danese et al. (2015) mean 2014 incremental long-term costs for "unstable angina" across three patient groups (CV low/moderate risk, CV high risk and CV event history)6 |
| Cost of heart failure (year of event) | 4,462 | Alva et al. 2015. 2012 values for CHF event during year: £3,191 (mean inpatient cost) plus £979 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of heart failure (years 2+) | 2,617 | Alva et al. 2015. 2012 values for history of CHF: £1,473 (mean inpatient cost) plus £973 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of stroke (year of event) | 8,449 | Alva et al. 2015. 2012 values for non-fatal stroke event during year: £6,805 (mean inpatient cost) plus £1,091 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of stroke (years 2+) | 2,013 | Alva et al. 2015. 2012 values for history of stroke: £1,125 (mean inpatient cost) plus £756 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of stroke death within 30 days | 4,231 | Alva et al. 2015. 2012 value for fatal stroke: £3,954 (mean inpatient cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of peripheral vascular disease (year of event) | 1,661 | NHS reference costs 2016-17, weighted average of HRGs YQ50A/B/C/D/E/F |
| Cost of peripheral vascular disease (years 2+) | 1,661 | NHS reference costs 2016-17, weighted average of HRGs YQ50A/B/C/D/E/F |
| **Renal complications** |  |  |
| Hemodialysis cost (year of event) | 22,632 | NHS reference costs 2016-17, weighted average of HRGs LD01/05/09A and assuming three sessions per week |
| Annual cost of hemodialysis (years 2+) | 22,632 | NHS reference costs 2016-17, weighted average of HRGs LD01/05/09A and assuming three sessions per week |
| Peritoneal dialysis cost (year of event) | 27,690 | NHS reference costs 2016-17, weighted average of HRGs LD11/12/13A and assuming daily use |
| Annual cost of peritoneal dialysis (years 2+) | 27,690 | NHS reference costs 2016-17, weighted average of HRGs LD11/12/13A and assuming daily use |
| Renal transplant cost (year of event) | 26,878 | Kent et al. (2015) 2011 in-hospital care costs in the year of transplantation[[7]](#endnote-7) |
| Annual cost of renal transplant (years 2+) | 1,254 | Kent et al. (2015) 2011 annual cost after transplantation7 |
| **Acute events** |  |  |
| Cost of non-severe hypoglycemic event | 4 | Calculated as a weighted average of daytime and nocturnal events from resource use data summarized in Chubb and Tikkanenen (2015)[[8]](#endnote-8) |
| Cost of severe hypoglycemic event 1 | 427 | Calculated based on direct costs estimates published by Hammer et al (2009) as a weighted average between groups 1-3[[9]](#endnote-9) |
| Cost of severe hypoglycemic event 2 | 427 | Calculated based on direct costs estimates published by Hammer et al (2009) as a weighted average between groups 1-39 |
| **Ocular complications** |  |  |
| Cost of laser treatment | 90 | HS Tariff costs 2017-2019, Annex A, Tab 1a: Admitted Patient Care & Outpatient Procedures, BZ87A Minor Vitreous Retinal Procedures, 19 years and over. Available from: https://improvement.nhs.uk/resources/national-tariff-1719/#h2-tariff-documents |
| Cost of cataract operation | 749 | Alva et al. 2015. 2012 values for cataract operation: £700 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost following cataract operation | 721 | Alva et al. 2015. 2012 values following cataract operation: £674 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of blindness in year of onset | 3,365 | Alva et al. 2015. 2012 values for blindness in one eye: £1,355 (mean inpatient cost) plus £1,790 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of blindness in subsequent years | 1,274 | Alva et al. 2015. 2012 values for history of blindness in one eye: £453 (mean inpatient cost) plus £738 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| **Neuropathy and diabetic foot complications** | | |
| Cost of neuropathy (year of event) | 151 | MIMS UK (June 2018) [generic duloxetine]. The annual cost is based on pack price of £11.57 of 28 units (£0.41 per unit \* 365.25 days per year) |
| Cost of neuropathy (years 2+) | 151 | MIMS UK (June 2018) [generic duloxetine]. The annual cost is based on pack price of £11.57 of 28 units (£0.41 per unit \* 365.25 days per year) |
| Cost of amputation (event based) | 13,103 | Alva et al. 2015. 2012 values for amputation: £9,546 (mean inpatient cost) plus £2,699 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of prosthesis (event based) | 3,642 | Alva et al. 2015. 2012 values for history of amputation: £1,792 (mean inpatient cost) plus £1,611 (mean expected non-inpatient healthcare cost). The costs represent the UKPDS population (a representative individual male, aged 60 years)5 |
| Cost of gangrene treatment | 3,563 | Ghatnekar et al. (2002) cost includes cost of topical treatment, antibacterial, outpatient and inpatient care and orthopaedic appliances among diabetic populations, original 2000 value €3,647 (conversion rate to GBP of 0.60949 [average for year 2000 from oanda.com])[[10]](#endnote-10) |
| Cost after healed ulcer | 270 | Ghatnekar et al. (2002) cost includes orthopaedic appliances only among diabetic populations, original 2000 value €23 (monthly, conversion rate to GBP of 0.60949 [average for year 2000 from oanda.com])10 |
| Cost of infected ulcer | 2,043 | Ghatnekar et al. (2002) cost includes topical treatment, antibacterials, outpatient and inpatient care and orthopaedic appliances among diabetic populations, original 2000 value €2,091 (conversion rate to GBP of 0.60949 [average for year 2000 from oanda.com]) |
| Cost of standard uninfected ulcer | 2,003 | Ghatnekar et al. (2002) cost includes topical treatment, outpatient and inpatient care and orthopaedic appliances among diabetic populations, original 2000 value €2,050 (conversion rate to GBP of 0.60949 [average for year 2000 from oanda.com])10 |
| Cost of healed ulcer (history of amputation) | 270 | Ghatnekar et al. (2002) cost includes orthopaedic appliances only among diabetic populations, original 2000 value €23 (monthly, conversion rate to GBP of 0.60949 [average for year 2000 from oanda.com])10 |

Table 3 Summary of values used in the estimation of indirect costs

|  |  |  |
| --- | --- | --- |
| **Cost** | **Value  (2018 GBP)** | **Source** |
| Retirement age (years) | 65 | <https://www.gov.uk/government/news/proposed-new-timetable-for-state-pension-age-increases> |
| Age at first income (years) | 18 | <https://www.gov.uk/child-employment> |
| Mean salary male\* (GBP) | 28,698 | https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2017provisionaland2016revisedresults |
| Mean salary female\* (GBP) | 28,698 | https://www.ons.gov.uk/employmentandlabourmarket/peopleinwork/earningsandworkinghours/bulletins/annualsurveyofhoursandearnings/2017provisionaland2016revisedresults |
| No. work days/year (days) | 252 | <http://www.work-day.co.uk/workingdays_holidays_2017.htm> |
| Days off work estimates | See publication for details | Ploug and Sørensen (2013)[[11]](#endnote-11) |

\* estimated based on a published median weekly salary in 2017 of GBP 550 (multiplied by (365.25/7)).

Table 4 Cost savings associated with diabetes-related complications avoided for patients reaching glycemic targets (HbA1c 7.0%, 53 mmol/mol) versus having poor glycemic control (HbA1c 8.2%, 66 mmol/mol) (undiscounted results)

|  | **Time horizon** | | | | |
| --- | --- | --- | --- | --- | --- |
|  | **3 years** | **5 years** | **10 years** | **15 years** | **Lifetime** |
| **Intensification delayed by 1 year** | | | | | |
| **Per patient outcomes** |  |  |  |  |  |
| Direct cost savings (GBP) | 77.98 | 117.14 | 206.06 |  | 291.88 |
| Indirect cost savings (GBP) | 456.32 | 795.70 | 720.45 |  | 671.83 |
| Total cost savings (GBP) | 534.30 | 912.83 | 926.52 |  | 963.71 |
| **Population outcomes** |  |  |  |  |  |
| Direct cost savings (GBP millions) | 91 | 136 | 240 |  | 340 |
| Indirect cost savings (GBP millions) | 531 | 926 | 838 |  | 782 |
| Total cost savings (GBP millions) | 622 | 1,062 | 1,078 |  | 1,121 |
| **Intensification delayed by 7 years** | | | | | |
| **Per patient outcomes** |  |  |  |  |  |
| Direct cost savings (GBP) |  |  | 859.06 | 1,372.02 | 1,897.73 |
| Indirect cost savings (GBP) |  |  | 1,704.93 | 1,790.00 | 1,781.13 |
| Total cost savings (GBP) |  |  | 2,563.98 | 3,162.02 | 3,678.86 |
| **Population outcomes** |  |  |  |  |  |
| Direct cost savings (GBP millions) |  |  | 1,000 | 1,596 | 2,208 |
| Indirect cost savings (GBP millions) |  |  | 1,984 | 2,083 | 2,072 |
| Total cost savings (GBP millions) |  |  | 2,983 | 3,679 | 4,281 |

GBP, British Pounds Sterling

Table 5 Cost savings associated with diabetes-related complications avoided for patients reaching glycemic targets (HbA1c 7.0%, 53 mmol/mol) versus having poor glycemic control (HbA1c 9.0%, 75 mmol/mol) (undiscounted results)

|  | **Time horizon** | | | | |
| --- | --- | --- | --- | --- | --- |
|  | **3 years** | **5 years** | **10 years** | **15 years** | **Lifetime** |
| **Intensification delayed by 1 year** | | | | | |
| **Per patient outcomes** |  |  |  |  |  |
| Direct cost savings (GBP) | 136.76 | 211.25 | 353.41 |  | 651.67 |
| Indirect cost savings (GBP) | 854.42 | 1,318.92 | 1,262.10 |  | 1,318.43 |
| Total cost savings (GBP) | 991.19 | 1,530.17 | 1,615.51 |  | 1,970.10 |
| **Population outcomes** |  |  |  |  |  |
| Direct cost savings (GBP millions) | 159 | 246 | 411 |  | 758 |
| Indirect cost savings (GBP millions) | 994 | 1,535 | 1,469 |  | 1,534 |
| Total cost savings (GBP millions) | 1,153 | 1,780 | 1,880 |  | 2,292 |
| **Intensification delayed by 7 years** | | | | | |
| **Per patient outcomes** |  |  |  |  |  |
| Direct cost savings (GBP) |  |  | 1,520.94 | 2,418.83 | 3,424.65 |
| Indirect cost savings (GBP) |  |  | 3,011.92 | 2,987.70 | 3,078.32 |
| Total cost savings (GBP) |  |  | 4,532.86 | 5,406.52 | 6,502.98 |
| **Population outcomes** |  |  |  |  |  |
| Direct cost savings (GBP millions) |  |  | 1,770 | 2,814 | 3,985 |
| Indirect cost savings (GBP millions) |  |  | 3,505 | 3,476 | 3,582 |
| Total cost savings (GBP millions) |  |  | 5,274 | 6,291 | 7,567 |

GBP, British Pounds Sterling

**Table 6 Incidence-estimates of the direct cost burden for immediate intensification versus intensification delayed by 1 year (undiscounted)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Time horizon | | | |
| **3 years** | **5 years** | **10 years** | **50 years** |
| **Intensification from 8.2% to 7.0%** | | | | |
| Direct cost savings (GBP) | 30 million | 72 million | 244 million | 2,320 million |
| **Intensification from 9.0% to 7.0%** | | | | |
| Direct cost savings (GBP) | 53 million | 129 million | 407 million | 5,135 million |

GBP, British Pounds Sterling. Estimates assume 198,000 incident cases of type 2 diabetes each year based on Zghebi et al. (2017).[[12]](#endnote-12) Incidence rate was calculated as 37.21 cases per 10,000 persons per year (weighted average of males and females in 2014) and an adult population (aged 16+ years) at risk of approximately 53.2 million (calculated as 81.1% of the total population).[[13]](#endnote-13)

**Table 7 Incidence-estimates of the direct cost burden for immediate intensification versus intensification delayed by 7 years (undiscounted)**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Time horizon | | |
| **10 years** | **15 years** | **50 years** |
| **Intensification from 8.2% to 7.0%** | | | |
| Direct cost savings (GBP) | 751 million | 1,894 million | 14,282 million |
| **Intensification from 9.0% to 7.0%** | | | |
| Direct cost savings (GBP) | 1,306 million | 3,381 million | 26,043 million |

GBP, British Pounds Sterling. Estimates assume 198,000 incident cases of type 2 diabetes each year based on Zghebi et al. (2017).12 Incidence rate was calculated as 37.21 cases per 10,000 persons per year (weighted average of males and females in 2014) and an adult population (aged 16+ years) at risk of approximately 53.2 million (calculated as 81.1% of the total population).13

References

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