**Supplementary materials:**

Table S1: Baseline Characteristics

| Variable | Mean (SD) | Unit | Reference |
| --- | --- | --- | --- |
| **PATIENT DEMOGRAPHICS** |  |   |   |
| Start age  | 58 (10) | Years | [[1](#_ENREF_1)] |
| Duration of Diabetes  | 7 (6) | Years | [[1](#_ENREF_1)] |
| Prop. Male  | 0.506 | [0-1] | [[1](#_ENREF_1)] |
|   |  |   |   |
| **BASELINE RISK FACTORS** |  |   |   |
| HbA1c  | 8.14 (0.94) | %-points | [[2](#_ENREF_2)] |
| SBP  | 132.15 (14.69) | mmHg | [[2](#_ENREF_2)] |
| DBP | 80.36 (9.01) | mmHg | [[2](#_ENREF_2)] |
| T Chol  | 181.51 (41.70) | mg/dl | [[2](#_ENREF_2)] |
| HDL  | 45.47 (10.58) | mg/dl | [[2](#_ENREF_2)] |
| LDL  | 115.00 | mg/dl | Recalculated using [[3](#_ENREF_3)]  |
| TRIG  | 103.19 | mg/dl | [[4](#_ENREF_4)] |
| BMI  | 32.82 (6.11) | kg/m2 | [[2](#_ENREF_2)] |
| eGFR | 95.00 (15.00) | ml/min/1.73m2 | [[1](#_ENREF_1)] |
| Haemoglobin | 13.85 | gr/dl | [[4](#_ENREF_4)] |
| WBC | 6.90 | 106/ml | [[4](#_ENREF_4)] |
| Heart rate | 72.00 | Bpm | [[5](#_ENREF_5)] |
| WHR | 0.93 |   | [[6](#_ENREF_6)] |
| uAER | 4.50 | mg/mmol | [[4](#_ENREF_4)] |
| Serum Creatinine | 0.88 | mg/dl | [[4](#_ENREF_4)] |
| Serum albumin | 4.75 | g/dl | [[4](#_ENREF_4)] |
| Prop. smoker  | 0.15 | [0-1] | [[4](#_ENREF_4)] |
| Cigarettes/day  | 3.00 |   | [[7](#_ENREF_7)] |
| Alcohol consumption oz/week  | 3.00 | Oz/week | [[8](#_ENREF_8)] |
|  |  |  |  |
| **RACIAL CHARACTERISTICS** |  |   |   |
| Prop. White  | 0.6200 | [0-1] | [[1](#_ENREF_1)] |
| Prop. Black  | 0.0720 | [0-1] | [[1](#_ENREF_1)] |
| Prop. Hispanic  | 0.2420 | [0-1] | [[1](#_ENREF_1)] |
| Prop. Native American  | 0.0060 | [0-1] | [[1](#_ENREF_1)] |
| Prop. Asian/Pacific Islander  | 0.0600 | [0-1] | [[1](#_ENREF_1)] |
|   |  |   |   |
| **BASELINE CVD COMPLICATIONS** |  |   |   |
| Prop. MI  | 0.013 | [0-1] | [[4](#_ENREF_4)] |
| Prop. Angina  | 0.005 | [0-1] | [[4](#_ENREF_4)] |
| Prop. PVD  | 0.001 | [0-1] | [[4](#_ENREF_4)] |
| Prop. stroke  | 0.060 | [0-1] | [[9](#_ENREF_9)] |
| Prop. HF  | 0.002 | [0-1] | [[4](#_ENREF_4)] |
| Prop. Atrial fibrillation  | 0.013 | [0-1] | [[4](#_ENREF_4)] |
| Prop. LVH  | 0.006 | [0-1] | [[4](#_ENREF_4)] |
|   |  |   |   |
| **BASELINE RENAL COMPLICATIONS** |  |   |   |
| Prop. Microalbuminuria | 0.027 | [0-1] | [[4](#_ENREF_4)] |
| Prop. macroalbuminuria | 0.006 | [0-1] | [[4](#_ENREF_4)] |
| Prop. ESRD  | 0.00118 | [0-1] | [[4](#_ENREF_4)] |
|   |  |   |   |
| **BASELINE RETINOPATHY COMPLICATIONS** |  |   |   |
| Prop. BDR  | 0.047 | [0-1] | [[4](#_ENREF_4)] |
| Prop. PDR  | 0.071 | [0-1] | [[10](#_ENREF_10)] |
| Prop. SVL  | 0.030 | [0-1] | [[11](#_ENREF_11)] |
|   |  |   |   |
| **BASELINE MACULAR EDEMA** |  |   |   |
| Prop. ME  | 0.001 | [0-1] | [[4](#_ENREF_4)] |
|   |  |   |   |
| **BASELINE CATARACT** |  |   |   |
| Prop. cataract  | 0.047 | [0-1] | [[4](#_ENREF_4)] |
|   |  |   |   |
| **BASELINE FOOT ULCER COMPLICATIONS** |  |   |   |
| Prop. uninfected ulcer  | 0.009 | [0-1] | [[4](#_ENREF_4)] |
| Prop. infected ulcer  | 0.000 | [0-1] |   |
| Prop. healed ulcer  | 0.000 | [0-1] |   |
| Prop. history of amputation  | 0.000 | [0-1] |   |
|   |  |   |   |
| **BASELINE NEUROPATHY** |  |   |   |
| Prop. neuropathy  | 0.082 | [0-1] | [[4](#_ENREF_4)] |

SD: Standard deviation; HbA1c: glycated haemoglobin A1c; SBP: systolic blood pressure; DBP: diastolic blood pressure; T Chol: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; TRIG: triglycerides; BMI: body mass index; eGFR: estimated glomerular filtration rate; WBC: white blood cells; WHR: waist-to-hip ratio; uAER: urinary albumin/creatinine ratio; MI: myocardial infarction; PVD: peripheral vascular disease; HF: heart failure; LVH: left ventricular hypertrophy; ESRD: end-stage renal disease; BDR: background diabetic retinopathy; PDR: proliferative diabetic retinopathy; SVL: severe vision loss; ME: macular edema

Table S2: Treatment Effects – First Line

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Empagliflozin | SE | Oral semaglutide | SE | Unit | Source |
| **Treatment Policy estimand** |  |  |  |  |  |  |
| Change in baseline HbA1c | -0.90 | 0.026 | -1.30 | 0.03 | %-points | [[1](#_ENREF_1)] |
| SBP change from baseline  | -4.34 | 0.63 | -4.85 | 0.65 | mmHg | [[2](#_ENREF_2)] |
| DBP change from baseline  | -2.67 | 0.44 | -2.27 | 0.45 | mmHg | [[2](#_ENREF_2)] |
| T Chol change from baseline | 4.74 | 1.57 | -5.08 | 1.62 | mg/dl | [[2](#_ENREF_2)] |
| HDL Chol change from baseline | 3.11 | 0.34 | 0.73 | 0.35 | mg/dl | [[2](#_ENREF_2)] |
| BMI Change from baseline | -1.29 | 0.03 | -1.36 | 0.03 | kg/m2 | Recalculated\* [[1](#_ENREF_1)] |
|  |  |  |  |  |  |  |
| **Trial Product estimand** |  |  |  |  |  |  |
| Change in baseline HbA1c | -0.79 | 0.05 | -1.30 | 0.05 | %-points | [[2](#_ENREF_2)] |
| SBP change from baseline  | -4.34 | 0.63 | -4.85 | 0.65 | mmHg | [[2](#_ENREF_2)] |
| DBP change from baseline  | -2.67 | 0.44 | -2.27 | 0.45 | mmHg | [[2](#_ENREF_2)] |
| T Chol change from baseline | 4.74 | 1.57 | -5.08 | 1.62 | mg/dl | [[2](#_ENREF_2)] |
| HDL Chol change from baseline | 3.11 | 0.34 | 0.73 | 0.35 | mg/dl | [[2](#_ENREF_2)] |
| BMI Change from baseline | -1.37 | 0.09 | -1.73 | 0.10 | kg/m2 | [[2](#_ENREF_2)] |
|  |  |  |  |  |  |  |

SE: Standard error; HbA1c: glycated haemoglobin A1c; SBP: systolic blood pressure; DBP: diastolic blood pressure; T Chol: Total Cholesterol; HDL Chol: High Density Lipoprotein Cholesterol; BMI: Body Mass index

In Rodbard et al [[1](#_ENREF_1)] starting body weight, BMI and absolute decrease in body weight is reported. Based on this the decrease in BMI per arm was calculated.

Table S3: Adverse Events

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Empagliflozin | Oral semaglutide | Unit | Source |
| **Treatment Policy estimand** |  |  |  |  |
| NSHE rate | 9.535 | 10.976 | /100 pt. yrs | Recalculated [[1](#_ENREF_1)] |
| SHE1 rate | 0.244 | 0.244 | /100 pt. yrs | Recalculated [[1](#_ENREF_1)] |
| SHE2 rate | 0 | 0 | /100 pt. yrs | Recalculated [[1](#_ENREF_1)] |
| **Trial product estimand** |  |  |  |  |
| NSHE rate | 1.90 | 2.25 | /100 pt. yrs | [[2](#_ENREF_2)] |
| SHE1 rate | 0.24 | 0.25 | /100 pt. yrs | [[2](#_ENREF_2)] |

NSHE: Non-severe hypoglycaemia rate; SHE1: Severe hypoglycaemia rate (not requiring medical assistance); SHE2: Severe hypoglycaemia rate (requiring medical assistance).

Rodbard et al [[1](#_ENREF_1)] report incidence and we recalculated them to rates per 100 patient years assuming that study duration was 1 year for all patients.

Table S4: Treatment effects for second/third line treatments (treatment policy estimand)

|  |  |  |  |
| --- | --- | --- | --- |
|   | 2nd line Insulin | 3rd line Insulin | Source |
| HbA1c (change from baseline) | -0.5682 | -0.7109 | [[12](#_ENREF_12)] |
| BMI (change versus previous line | 0 | +1.294/1.357\* | Assumption |
| NSHE event rate | 486 | 486 | [[13](#_ENREF_13)]  |
| SHE1 event rate (req. non. med. assist.) | 1.76 | 1.76 | [[13](#_ENREF_13)] |
| SHE2 event rate (req. med. assist.)  | 0.24 | 0.24 | [[13](#_ENREF_13)] |

HbA1c: glycated haemoglobin A1c; BMI: body mass index; NSHE: non-severe hypoglycaemia event; SHE: severe hypoglycaemia event

\* for empagliflozin and oral semaglutide

Table S5: Proportion of patients on preventive medication

|  |  |  |
| --- | --- | --- |
| Item | Value | Source |
| Prop 1° prevention aspirin | 0.551 | [[14](#_ENREF_14)] |
| Prop 2° prevention aspirin | 0.912 | [[15](#_ENREF_15)] |
| Prop 1° prevention Statins | 0.378 | [[14](#_ENREF_14)] |
| Prop 2° prevention Statins | 0.898 | [[15](#_ENREF_15)]  |
| Prop 1° prevention ACEI/ARB | 0.310 | [[14](#_ENREF_14)] |
| Prop 2° prevention ACEI/ARB | 0.840 | [[15](#_ENREF_15)] |

ACEI/ARB: angiotensin-converting enzyme inhibitor/angiotensin-receptor blocker

Table S6: Screening and patient management proportions

|  |  |  |
| --- | --- | --- |
| Item | Value | Source |
| Prop screened eye disease | 0.870 | [[16](#_ENREF_16)],[[17](#_ENREF_17)]  |
| Prop screened for renal disease | 0.910 |
| Prop receiving intensive insulin after MI | 1.000 | Assumption |

MI - Myocardial infarction

Table S7: Sensitivity and specificity of tests.

|  |  |  |
| --- | --- | --- |
| Item | Value | Source |
| Sensitivity eye screening | 0.920 | [[18](#_ENREF_18)] |
| Specificity eye screening | 0.960 |
| Sensitivity microalbuminuria screening | 0.830 | [[19](#_ENREF_19)] |
| Sensitivity macroalbuminuria screening | 0.830 |
| Specificity renal screening | 0.960 |

Table S8 Annual treatment costs applied (DKK, AIP 2020, [[20](#_ENREF_20)])

|  |  |
| --- | --- |
| INTERVENTION | Annual Cost (DKK) |
| Empagliflozin  | 4,164.70 |
| Oral semaglutide | 9,326.05 |
| Metformin | 84.25 |
| Long-acting insulin 2L 0.7 IU/kg (including administration costs) | 10,036.52  |
| Long-acting insulin 3L 0.9 IU/kg (including administration costs) | 11,447.76  |
| *Administration costs* |  |
| Disposable needles (BD Thin Wall Penkanyle 31G 5mm) | 1,203.33 |
| SMBG testing (FreeStyle Precision) | 3,479.05 |
| SMBG testing (BD Microfine) | 414.81 |

DKK: Danish Krone; AIP: Apotekets Indkøbspris (Pharmacy Purchase Price); SMBG: Self-monitoring of blood Glucose

Table S9 Cost Inputs for the CDM (Costs inflated to 2020 values, DKK)

| Variable | Value | Reference |
| --- | --- | --- |
| **Discounting** |
| Clinical discount rate | 4.0% | [[20](#_ENREF_20)] |
| Costs discount rate | 4.0% | [[20](#_ENREF_20)] |
|  |  |  |
| **Management Costs** |  |  |
| Annual statins treatment | 61.08 | [[21](#_ENREF_21)], AIP  |
| Annual Aspirin | 32.14 | [[21](#_ENREF_21)], AIP  |
| Annual ACE inhibitor/ARB | 58.01 | [[21](#_ENREF_21)], AIP  |
| Annual screening microalbuminuria | 191.95 | [[20](#_ENREF_20)] |
| Annual screening GRP | 191.95 | [[22](#_ENREF_22)] |
| Stopping ACE inhibitor due to side effects | 143.44 | [[22](#_ENREF_22)] |
| Annual eye screening | 757.42 | [[22](#_ENREF_22)] |
|  |  |  |
| **Direct Costs CVD Complications** |  |  |
| Myocardial infarction 1st year | 146,950 | [[23](#_ENREF_23)] |
| Myocardial infarction 2nd+ years | 3,585 | [[23](#_ENREF_23)] |
| Angina 1st year | 146,950 | [[23](#_ENREF_23)] |
| Angina 2nd+ years | 3,585 | [[23](#_ENREF_23)] |
| Congestive heart failure 1st year | 127,449 | [[23](#_ENREF_23)] |
| Congestive heart failure 2nd plus years | 3,346 | [[23](#_ENREF_23)] |
| Stroke 1st year | 121,729 | [[24](#_ENREF_24)] |
| Stroke 2nd+ years | 21,628 | [[24](#_ENREF_24)] |
| Stroke death within 30 days | 59,731 | [[25](#_ENREF_25)] |
| Peripheral vascular disease 1st year | 23,103 | [[25](#_ENREF_25)] |
| Peripheral vascular disease 2nd+ years | 4,188 | [[26](#_ENREF_26)] |
|  |  |  |
| **Direct Costs Renal Complications** |  |  |
| Haemodialysis 1st year | 514,588 | [[27](#_ENREF_27)] |
| Haemodialysis 2+ years | 514,588 | [[27](#_ENREF_27)] |
| Peritoneal dialysis 1st year | 149,230 | [[27](#_ENREF_27)] |
| Peritoneal dialysis 2+ years | 149,230 | [[27](#_ENREF_27)] |
| Renal transplant costs 1st year | 307,901 | [[28](#_ENREF_28)] |
| Renal transplant 2+ years | 25,379 | [[28](#_ENREF_28)] |
|  |  |  |
| **Direct Costs Acute Events** |  |  |
| Non-severe hypoglycemic event | 25.50 | [[29](#_ENREF_29)] |
| Severe hypoglycemic event 1 (requiring non-medical assistance) | 25.50 | [[29](#_ENREF_29)] |
| Severe hypoglycemic event 2 (requiring medical assistance) | 12,160 | [[29](#_ENREF_29)] |
|  |  |  |
| **Direct Costs Eye Disease** |  |  |
| Laser treatment | 2,061 | [[25](#_ENREF_25)] |
| Cataract operation | 8,970 | [[25](#_ENREF_25)] |
| Following cataract operation | 244,66 | [[22](#_ENREF_22)] |
| Blindness - year of onset | 87,280 | [[30](#_ENREF_30)] |
| Blindness - following years | 87,280 | [[30](#_ENREF_30)] |
|  |  |  |
| **Direct Costs Neuropathy/Foot Ulcer/Amputation** |  |  |
| Neuropathy, 1st year | 28,256 | [[24](#_ENREF_24)] |
| Neuropathy, 2nd+ years | 143.44 | [[20](#_ENREF_20)] |
| Cost of active ulcer | 13,794 | [[29](#_ENREF_29)] |
| Cost of Amputation (lower extremity) | 89,715 | [[24](#_ENREF_24)] |
| Cost of Amputation follow up | 15,989 | [[31](#_ENREF_31)] |

CDM: Core diabetes model; DKK: Danish Krone; AIP: Apotekets Indkøbspris (Pharmacy Purchase Price); ACE: angiotensin-converting enzyme; ARB: angiotensin-receptor blockers; GRP: Gross renal proteinuria; CVD: cardiovascular disease

Table S10: Utilities used in CDM

|  Variable | Input values | Reference |
| --- | --- | --- |
| U T2D no complications  | 0.785 | [[32](#_ENREF_32)]  |
| DisU MI event | -0.055 | [[32](#_ENREF_32)] |
| U post MI  | 0.73 | Calculated |
| DisU angina event  | -0.09 | [[32](#_ENREF_32)] |
| U angina  | 0.695 | Calculated |
| DisU heart failure event  | -0.108 | [[32](#_ENREF_32)] |
| U heart failure  | 0.677 | Calculated |
| DisU stroke event | -0.164 | [[32](#_ENREF_32)] |
| U post Stroke  | 0.621 | Calculated |
| DisU PVD | -0.061 | [[32](#_ENREF_32)] |
| U PVD  | 0.724 | Calculated |
| QoL microalbuminuria | 0 | Assumed null |
| U microalbuminuria | 0.785 | Calculated |
| DisU macroalbuminuria | -0.048 | [[32](#_ENREF_32)] |
| U macroalbuminuria | 0.737 | Calculated |
| DisU HD | -0.164 | [[32](#_ENREF_32)] |
| U HD  | 0.621 | Calculated |
| DisU PD | -0.204 | [[32](#_ENREF_32)] |
| U PD  | 0.581 | Calculated |
| U RT  | 0.762 | [[32](#_ENREF_32)] |
| DisU BDR  | -0.04 | [[32](#_ENREF_32)] |
| U BDR  | 0.745 |  Calculated |
| U BDR wrongly treated  | 0.745 |  Calculated |
| DisU PDR | -0.07 | [[32](#_ENREF_32)] |
| U PDR laser treated  | 0.715 | Calculated |
| U PDR no Laser  | 0.715 | Calculated |
| DisU ME | -0.04 | [[32](#_ENREF_32)] |
| U ME  | 0.745 | Calculated |
| DisU SVL | -0.074 | [[32](#_ENREF_32)] |
| U SVL  | 0.711 | Calculated |
| DisU cataract | -0.016 | [[32](#_ENREF_32)] |
| U cataract  | 0.769 | Calculated |
| DisU neuropathy | -0.084 | [[32](#_ENREF_32)] |
| U neuropathy  | 0.701 | Calculated |
| QoL healed ulcer  | 0 | Assumed null |
| U healed ulcer  | 0.785 | Calculated  |
| QoL active ulcer | -0.17 | [[32](#_ENREF_32)] |
| U active ulcer  | 0.615 | Calculated |
| DisU amputation event  | -0.28 | [[32](#_ENREF_32)] |
| U post amputation  | 0.505 | Calculated |
| Diminishing NSHE disutility  | Yes | [[33](#_ENREF_33)] |
| DisU for SHE1 (during daytime)  | -0.0137 | [[34](#_ENREF_34)] |
| DisU for SHE1 (nocturnal)  | -0.0137 | [[34](#_ENREF_34)] |
| DisU for SHE2 (during daytime)  | -0.0578 | [[34](#_ENREF_34)] |
| DisU for SHE2 (nocturnal)  | -0.0578 | [[34](#_ENREF_34)] |
| DisU for UTI/GI | -0.00476 | Calculated based on [[35](#_ENREF_35)] and [[36](#_ENREF_36)] |

CDM: Core diabetes model; U: health state utility; T2: Type 2 diabetes; DisU: disutility of an event; MI: Myocardial infarction; PVD: Peripheral vascular disease; QoL: Quality of life; HD: Haemodialysis; PD: Peritoneal dialysis; RT: Renal transplant; BDR: Background Retinopathy; PDR: Proliferative diabetic retinopathy; ME: Macular edema; SVL: Severe vision loss; NSHE: Non-Severe Hypoglycaemia; SHE1: Severe hypoglycaemia rate (not requiring medical assistance); SHE2: Severe hypoglycaemia rate (requiring medical assistance); UTI/GI: urinary tract infection/gastrointestinal infection

Table S11: Scenario analysis results

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   | LY | QALY | Cost (DKK) | ICER |
| **Oral sema + met** | **Empa****+ met** | **Oral sema + met** | **Empa****+ met** | **Oral sema + met** | **Empa****+ met** | **Oral sema + met vs empa + met** |
| Base case (time horizon 50 years) | 13.21 | 13.21 | 8.78 | 8.75 | 447,633 | 387,786 | 1,930,548 |
| Time horizon 5 years | 4.31 | 4.31 | 3.00 | 2.98 | 99,767 | 86,282 | 612,931 |
| HbA1c threshold of 8%  | 13.21 | 13.21 | 8.82 | 8.79 | 432,106 | 371,308 | 1,961,225 |
| 3 lines of therapy (discontinuation of oral sema and empa and switch to higher dose long-acting insulin alone in 3rd line) | 13.24 | 13.21 | 8.74 | 8.69 | 373,513 | 355,797 | 328,076 |
| Trial product estimand - 50 years | 13.20 | 13.22 | 8.81 | 8.76 | 446,914 | 388,438 | 1,124,537 |
| Trial product estimand - 3 lines of therapy (discontinuation of oral sema and empa and switch to higher dose long-acting insulin alone in 3rd line) | 13.24 | 13.22 | 8.76 | 8.70 | 373,869 | 356,279 | 293,175 |

LY: life years; QALY: quality-adjusted life years; DKK: Danish Krone; ICER: incremental cost-effectiveness ratio; sema: semaglutide; met: metformin; empa: empagliflozin; HbA1c: glycated haemoglobin A1c

Table S12: Breakdown of costs (DKK, per average patient)

| Breakdown of costs | Accumulated over 50 years | Accumulated over 5 years |
| --- | --- | --- |
|  | Oral semaglutide + met | Empagliflozin + met | Oral semaglutide + met | Empagliflozin + met |
| Total | 447,633 | 387,786 | 99,767 | 86,282 |
| Treatment | 238,073 | 176,301 | 57,204 | 43,442 |
| Management | 10,631 | 10,615 | 3,630 | 3,627 |
| Cardiovascular disease | 80,247 | 79,622 | 18,416 | 18,215 |
| Renal disease | 8,388 | 8,323 | 1,981 | 1,820 |
| Ulcer/amputation/neuropathy | 16,412 | 16,670 | 4,455 | 4,692 |
| Eye disease | 92,044 | 94,287 | 13,681 | 13,954 |
| NSHE | 1,476 | 1,582 | 322 | 428 |
| SHE (req. nonmed. assistance) | 7 | 7 | 2 | 2 |
| SHE (req. med. assistance) | 355 | 380 | 75 | 102 |

DKK: Danish Krone; met: metformin; NSHE: No severe hypoglycemic events, SHE: Severe hypoglycemic events

**References**

1. Rodbard HW, Rosenstock J, Canani LH *et al*. Oral Semaglutide Versus Empagliflozin in Patients With Type 2 Diabetes Uncontrolled on Metformin: The PIONEER 2 Trial*.* *Diabetes Care* 42(12), 2272-2281 (2019).

2. Bain SC, Hansen BB, Malkin SJP *et al*. Oral Semaglutide Versus Empagliflozin, Sitagliptin and Liraglutide in the UK: Long-Term Cost-Effectiveness Analyses Based on the PIONEER Clinical Trial Programme*.* *Diabetes Ther* 11(1), 259-277 (2020).

3. Friedawald William (Creator). LDL Calculated <https://www.mdcalc.com/ldl-calculated> (JUN 2019).

4. Ridderstråle M, Rosenstock J, Andersen KR, Woerle HJ, Salsali A. Empagliflozin compared with glimepiride in metformin-treated patients with type 2 diabetes: 208-week data from a masked randomized controlled trial*.* *Diabetes Obes Metab* 20(12), 2768-2777 (2018).

5. Hayes AJ, Leal J, Gray AM, Holman RR, Clarke PM. UKPDS outcomes model 2: a new version of a model to simulate lifetime health outcomes of patients with type 2 diabetes mellitus using data from the 30 year United Kingdom Prospective Diabetes Study: UKPDS 82*.* *Diabetologia* 56(9), 1925-1933 (2013).

6. Folsom AR, Chambless LE, Duncan BB, Gilbert AC, Pankow JS. Prediction of coronary heart disease in middle-aged adults with diabetes*.* *Diabetes Care* 26(10), 2777-2784 (2003).

7. World Health Organization. The tobacco atlas: 2002 <https://www.who.int/tobacco/resources/publications/tobacco_atlas/en/>.

8. World Health Organization. Global Status Report on Alcohol; 2004 <https://www.who.int/substance_abuse/publications/global_status_report_2004_overview.pdf>.

9. Kingry C, Bastien A, Booth G *et al*. Recruitment strategies in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial*.* *Am J Cardiol* 99(12a), 68i-79i (2007).

10. Patel A, Macmahon S, Chalmers J *et al*. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes*.* *N Engl J Med* 358(24), 2560-2572 (2008).

11. Ismail-Beigi F, Craven T, Banerji MA *et al*. Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial*.* *Lancet* 376(9739), 419-430 (2010).

12. Willis M, Asseburg C, Nilsson A, Johnsson K, Kartman B. Multivariate Prediction Equations for HbA(1c) Lowering, Weight Change, and Hypoglycemic Events Associated with Insulin Rescue Medication in Type 2 Diabetes Mellitus: Informing Economic Modeling*.* *Value Health* 20(3), 357-371 (2017).

13. Fonseca V, Gill J, Zhou R, Leahy J. An analysis of early insulin glargine added to metformin with or without sulfonylurea: impact on glycaemic control and hypoglycaemia*.* *Diabetes Obes Metab* 13(9), 814-822 (2011).

14. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyörälä K, Keil U. EUROASPIRE III: a survey on the lifestyle, risk factors and use of cardioprotective drug therapies in coronary patients from 22 European countries*.* *Eur J Cardiovasc Prev Rehabil* 16(2), 121-137 (2009).

15. Kotseva K, Wood D, De Backer G, De Bacquer D, Pyörälä K, Keil U. Cardiovascular prevention guidelines in daily practice: a comparison of EUROASPIRE I, II, and III surveys in eight European countries*.* *Lancet* 373(9667), 929-940 (2009).

16. Rkkp. Dansk Diabetes Database. National årsrapport 2016/2017 (1. marts 2016 - 28. februar 2017) (in Danish). Danish Diabetes Database. Annual national report 2016/2017*.* (2017).

17. Rkkp. Dansk Diabetes Database. National årsrapport 2017/2018 (1. marts 2017 - 28. februar 2018) (in Danish). Danish Diabetes Database. Annual national report 2017/2018*.* (2018).

18. Lopez-Bastida J, Cabrera-Lopez F, Serrano-Aguilar P. Sensitivity and specificity of digital retinal imaging for screening diabetic retinopathy*.* *Diabet Med* 24(4), 403-407 (2007).

19. Cortés-Sanabria, L. M-R, R. H, L.,, Rojas-Campos E, Canales-Muñoz L, Cueto-Manzano M. Utility of the Dipstick Micraltest II™ in the screening of microalbuminuria of diabetes mellitus type 2 and essential hypertension*.* *Revista de Investigación Clínica* 58 190-197 (2006).

20. The Finance Ministry. Nøgletalskatalog 19 Dec 2019, <https://www.fm.dk/oekonomi-og-tal/finansministeriets-regnemetoder>

21. Lægemiddelstyrelsen, medicinpriser.dk (Danish Medicines Agency, official price list). <https://medicinpriser.dk/default.aspx>]

22. Danish Regions. Overenskomster og aftaler mv. gældende i regioner på løn-. personale-. og praksisområdet (Collective agreement and rates - Danish regions - including general practice and specialists): Danish Regions okportal.dk

23. Vive Rapport. En helhjertet indsat - En artikelbaseret klinisk, patientnær og sundhedsøkonomisk kortlægning af hjerte-kar-området, 2018 (VIVE report: A Whole-hearted Effort – a publication based clinical, patient centric and health economic mapping of the cardiovascular area, 2018) <https://hjerteforeningen.dk/wp-content/uploads/sites/17/2018/02/11162-en-helhjertet-indsats-web.pdf>

24. Jennum P, Iversen HK, Ibsen R, Kjellberg J. Cost of stroke: a controlled national study evaluating societal effects on patients and their partners*.* *BMC Health Serv Res* 15 466 (2015).

25. Sundhedsdatastyrelsen (Danish Health Data Authority). DRG

26. Gerdtham UG, Clarke P, Hayes A, Gudbjornsdottir S. Estimating the cost of diabetes mellitus-related events from inpatient admissions in Sweden using administrative hospitalization data*.* *Pharmacoeconomics* 27(1), 81-90 (2009).

27. Region Hovedstaden, Center for Økonomi, svar på spørgsmål nr 141 af 30.8.2016 til forslag til budget 2017-20: Hvad koster en dialysepatient regionen pr. år? (Capital Region, Centre for Financial Affairs, response to question no 141 of 30.8.2016 to the proposal for the budget 2017-20: What is the cost for the region of a dialysis patient per year?) <https://www.regionh.dk/om-region-hovedstaden/oekonomi/Budget/Documents/Sp>ørgsmål%20og%20svar%202017/Svar%20141.pdf

28. Jensen CE, Sørensen P, Petersen KD. In Denmark kidney transplantation is more cost-effective than dialysis*.* *Dan Med J* 61(3), A4796 (2014).

29. Hoskins N, Tikkanen CK, Pedersen-Bjergaard U. The economic impact of insulin-related hypoglycemia in Denmark: an analysis using the Local Impact of Hypoglycemia Tool*.* *J Med Econ* 20(4), 363-370 (2017).

30. Sundhedsstyrelsen (Danish Health Authorities]. Type 2-diabetes – Medicinsk teknologivurdering af screening, diagnostik og behandling. Medicinsk Teknologivurdering. *5* 1 (2003).

31. Ghatnekar O, Persson U, Willis M, Odegaard K. Cost effectiveness of Becaplermin in the treatment of diabetic foot ulcers in four European countries*.* *Pharmacoeconomics* 19(7), 767-778 (2001).

32. Beaudet A, Clegg J, Thuresson PO, Lloyd A, Mcewan P. Review of utility values for economic modeling in type 2 diabetes*.* *Value Health* 17(4), 462-470 (2014).

33. Lauridsen JT, Lønborg J, Gundgaard J, Jensen HH. Diminishing marginal disutility of hypoglycaemic events: results from a time trade-off survey in five countries*.* *Qual Life Res* 23(9), 2645-2650 (2014).

34. Foos V, Mcewan P. Conversion of Hypoglycaemia Utility Decrements from Categorical Units Reflecting Event History into Event Specific Disutility Scores Applicable to Diabetes Decision Models Value in Health, S223. *.* 21 (2018).

35. Turner KM, Round J, Horner P *et al*. An early evaluation of clinical and economic costs and benefits of implementing point of care NAAT tests for Chlamydia trachomatis and Neisseria gonorrhoea in genitourinary medicine clinics in England*.* *Sex Transm Infect* 90(2), 104-111 (2014).

36. National Institute for Health and Care Excellence. Healthcare-associated infections: prevention and control in primary and community care: Clinical guideline [CG139] <https://www.nice.org.uk/guidance/cg139>