**SUPPLEMENTARY MATERIAL**

# Burden of Illness of Type 2 Diabetes Mellitus in the Kingdom of Saudi Arabia: A Five-Year Longitudinal Study

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# Supplementary tables

**Supplementary Table 1: Economic input parameters used in the CDM**

| Variable | Description | Value (SAR) | References/Notes |
|---|---|---|---|
| **Management costs** | | | |
| Annual statins treatment | Annual cost for statin treatment (applied if patient is on 1º or 2º prevention) | 41.23 | Cost from NUPCO.<br>Weighted average cost of different Statins prescribed in Saudi as per published source |
| Annual aspirin treatment | Annual cost for aspirin treatment (applied if patient is on 1º or 2º prevention) | 30.88 | Cost from SFDA.<br>Adult dose of Aspirin 300 mg (SAR3.5, 30 Pack), CIF price calculated by applying pharmacist (20%) and local distributor markups (15%) |
| Annual ACE inhibitor treatment | Annual cost for ACE inhibitor treatment (applied if patient is on 1º or 2º prevention) | 59.76 | Cost from NUPCO.<br>weighted average cost of different ACE-I/ARB prescribed in Saudi |
| Annual screening for MA | Annual cost for MA screening (applied if patient is screened) | 160.00 | MoH service cost list,<br>Cost of "combination of urine albumin and protein ratio (microalbumin)" SAR 160- single test is considered annually |
| Annual screening for GRP | Annual cost for MA (applied if patient is screened) | 40.00 | MoH service cost list,<br>Cost of "urine protein" SAR 40, single test is considered annually |
| ACE inhibitor treatment discontinuation due to AEs | One off-event cost for stopping treatment with ACE inhibitors or ARB due to AEs | 75.00 | MoH service cost list,<br>Assumption of one-time general physician visit cost is considered |
| Screening for retinopathy | Cost for an ophthalmologist visit for eye screening in diabetes-related diseases (assumed annual) | 254.00 | MoH service cost list,<br>Cost of "Examination- eye" (SAR 104) and "ophthalmology cons fee consultation" (SAR 150)- single unit is considered annually |

| | | | |
|---|---|---|---|
| **Direct cost of complications** | | | |
| MI (1st year) | Annual costs applied in the year MI occurs | 65,273.30 | [1] |
| MI (2nd year) | Annual costs applied in the years after MI occurs | 4,603.89 | Assumed same as 1st year |
| Angina (1st year) | Annual costs applied in the year unstable angina occurs | 46,682.45 | [2]<br>Assuming cost of unstable angina for 1st year |
| Angina (2nd + year) | Annual costs applied in the years after angina occurs | 4,603.89 | [3] |
| CHF (1st year) | Annual costs applied in the year CHF occurs | 133,759.51 | [1] |
| CHF (2nd year) | Annual costs applied in the years after CHF occurs | 4,603.89 | Assumed same as 2nd year cost of angina |
| Stroke (1st year) | Annual costs applied in the year stroke occurs | 172,564.33 | [1] |
| Stroke (2nd year) | Annual costs applied in the years after stroke occurs | 57,102.43 | [1]<br>Assumed the annual cost of acute stroke rehabilitation 2nd year onwards |
| Stroke death within 30 days | Annual costs applied in the year stroke occurs and subject dies within 30 days | 21,000.00 | Considered cost of hospitalization for next 30 days as proxy indicator for stroke death within 30 days |
| PVD (1st year) | Annual costs applied in the year PVD occurs | 21,819.38 | [3] |
| PVD (2nd year) | Annual costs applied in the years after PVD occurs | 4,603.89 | Assumed same as 2nd year cost of angina |
| Hemodialysis (1st year) | Annual costs applied in the | 343,892.83 | [4] |

| | | | |
|---|---|---|---|
| | year ESRD occurs and is treated by hemodialysis | | |
| Hemodialysis (2nd year) | Annual costs applied in the year after ESRD occurs and is treated by hemodialysis | 343,896.01 | Calculated by subtracting the 1st year cost from 4 year cost available in the literature and then divided by 3 assuming same cost is incurred in next 3 years |
| Peritoneal Dialysis (1st year) | Annual costs applied in the year ESRD occurs and is treated by peritoneal dialysis | 343,892.83 | Assumed same as annual cost for HD |
| Peritoneal Dialysis (2nd year) | Annual costs applied in the year after ESRD occurs and is treated by peritoneal dialysis | 343,896.01 | Assumed same as annual cost for HD |
| Renal transplant (1st year) | Annual costs applied in the year ESRD occurs and is treated by renal transplant | 414,392.25 | [4] |
| Renal transplant (2nd year) | Annual costs applied in the year after ESRD occurs and is treated by renal transplant | 61,726.02 | [4] |
| Non-severe hypoglycaemia | Cost for a non-severe hypoglycaemic event (not requiring external assistance) | 750.0 | Cost per service captured from MoH service cost list and NUPCO.<br>Cost calculated based on discussion with MoH (including SMBG, test strips and lancets) |
| Severe hypoglycaemia Type 1 | Cost for a type 1 severe hypoglycaemic | 121.68 | Cost per service captured from MoH service cost list and NUPCO. |

| | | | |
|---|---|---|---|
| | event (not requiring medical assistance. e.g. from friends or family members) | | Cost assumed similar to NSHE (plus additional cost for glucagon hydrochloride) |
| Severe hypoglycaemia type 2 | Costs for a type 2 severe hypoglycaemic event (requiring medical assistance e.g. health care practitioners, hospitalization) | 1,711.90 | Cost per service captured from MoH service cost list and drug cost from NUPCO.<br>Based on discussion with MoH |
| Diabetic ketoacidosis | | 3,929.40 | [5]<br>Service costs obtained from MoH service cost list |
| Laser treatment | Cost for laser treatment/retinal photocoagulation | 4,139.93 | [3] |
| Cataract surgical treatment (1st year) | Cost for first or second cataract surgery in the first year | 7,445.63 | [3] |
| Cataract surgical treatment (2nd year) | Cost for subsequent years after cataract surgery | 430.00 | Using proxy services available in MoH price list: Removal post cataract suture/or corneal suture removal" (SAR 280) + "Ophthalmologist consultation" (SAR150) |
| Blindness (1st year) | Annual cost applied in the year blindness occurs | 5,792.78 | Average of laser treatment cost and cost of cataract operation |
| Blindness (2nd year) | Annual cost applied in the year after blindness occurs | 5,792.78 | Considered same as cost of blindness treatment in year of onset |
| Neuropathy (1st year) | Annual cost applied in the year neuropathy occurs | 1,631.05 | Cost per service captured from MoH service cost list and SFDA. |
| Neuropathy (2nd year) | Annual cost applied in the year after neuropathy occurs | 1,631.05 | Assumed same as 1st year |

| | | | |
|---|---|---|---|
| Active ulcer | | 6,684.90 | [6]<br>Per patient cost of diabetic foot ulcer (SAR 6684.9) specific to Saudi |
| Amputation | Cost of amputation event (all medical costs except prosthesis) | 14,690.50 | [3] |
| Post amputation | Annual cost applied in the year after ulcer is healed and treated with amputation | 8,801.81 | [3] |

*ACE-I* angiotensin converting enzyme inhibitor, *AE* adverse events, *ARB* angiotensin receptor blocker, *CDM* Core Diabetes Model, *CIF* cost, insurance, and freight, *CHF* congestive heart failure, *ESRD* end-stage renal disease, *GRP* gross renal proteinuria, *HD* hemodialysis, *MA* microalbuminuria, *MI* myocardial infarction, *MoH* Ministry of Health, *NUPCO* National Unified Procurement Company, *PVD* peripheral vascular disease, *SAR* Saudi Arabian Riyal, *SFDA* Saudi Food and Drug Authority, *SMBG* self-monitoring blood glucose.

**Supplementary Table 2: Sensitivity and specificity of screening tests associated with T2DM-related complications**

| Parameter | Value | Source |
|---|---|---|
| Sensitivity eye screening | 0.987 | [7] |
| Specificity eye screening | 0.800 | [7] |
| Sensitivity GRP screening | 1.000 | [8] |
| Sensitivity MA screening | 1.000 | [8] |
| Specificity MA screening | 0.913 | [8] |

*GRP* gross renal proteinuria, *MA* microalbuminuria.

**Supplementary Table 3: Utility inputs used for the CDM**

| Quality of life utilities | Mean | SE/SD | Sources/Comments |
|---|---|---|---|
| U T2 no complications | 0.7850 | 0.0531 | [9] |
| DisU MI event | -0.05500 | 0.00660 | [9] |
| U post MI | 0.7300 | 0.0066 | [9] |
| U angina | 0.6950 | 0.0184 | [9] |
| U CHF | 0.6770 | 0.0306 | [9] |
| DisU stroke event | -0.16400 | 0.03010 | [9] |
| U post Stroke | 0.6210 | 0.0301 | [9] |
| U PVD | 0.7240 | 0.0286 | [9] |
| U MA | 0.7850 | 0.0531 | [9] |
| U GRP | 0.7370 | 0.0219 | [9] |
| U HD | 0.6210 | 0.0561 | [9] |
| U PD | 0.5810 | 0.1378 | [9] |
| U RT | 0.7620 | 0.0531 | [9] |
| U BDR | 0.7450 | 0.0617 | [9] |
| U BDR wrongly treated | 0.7450 | 0.0617 | [9] |
| U PDR laser treated | 0.7150 | 0.0148 | [9] |
| U PDR no Laser | 0.7150 | 0.0148 | [9] |
| U ME | 0.7450 | 0.0133 | [9] |
| U SVL | 0.7110 | 0.0250 | [9] |
| U cataract | 0.7690 | 0.0077 | [9] |
| U neuropathy | 0.7010 | 0.0138 | [9] |
| DisU active ulcer | -0.17000 | 0.01890 | [9] |
| DisU amputation event | -0.28000 | 0.05610 | [9] |
| U post amputation | 0.5050 | 0.0561 | - |
| Diminishing NSHE disutility | Yes | | [10] |
| DisU NSHE (during daytime) | -0.00335 | 0.00100 | [11] |
| DisU NSHE (nocturnal) | -0.00335 | 0.00100 | [11] |
| Dis U SHE 1 (during daytime) | -0.01370 | 0.00100 | [11] |
| Dis U SHE 1 (nocturnal) | -0.01370 | 0.00100 | [11] |
| Dis U SHE 2 (during daytime) | -0.05780 | 0.00100 | [11] |

| | | | |
|---|---|---|---|
| Dis U SHE 2 (nocturnal) | -0.05780 | 0.00100 | [11] |
| U adverse event 1 | 0.78500 | - | [9] |
| BMI utility approach | Apply static BMI disutility | | - |
| DisU for 1 unit increase in BMI above 25 $Kg/m^2$ | -0.00610 | - | [12] |

*BDR* background retinopathy, *BMI* body mass index, *CHF* congestive heart failure, *DisU* disutility of an event, *GRP* gross renal proteinuria, *HD* haemodialysis, *MA* microalbuminuria, *ME* macular oedema, *MI* myocardial infarction, *NSHE* non-severe hypoglycaemia, Oz ounce, *PD* peritoneal dialysis, *PDR* proliferative diabetic retinopathy, *PVD* peripheral vascular, *RT* renal transplant, *SE* standard error, *SD* standard deviation, *SHE1* severe hypoglycaemia event (requiring non-medical assistance), *SHE2* severe hypoglycaemia event (requiring medical assistance), *SVL* severe vision loss, *T2* Type 2 diabetes mellitus, *U* health state utility

**Supplementary Table 4 Baseline demographics, risk factors and existing complications of the main population**

| Parameters | Description | Overall (N=2226) |
|---|---|---|
| Gender | Male | 1085 (48.8%) |
| | Female | 1139 (51.2%) |
| | Missing (n) | 2 |
| Start age of T2DM | N | 2109 |
| | Mean (SD), (years) | 47.8 (11.1) |
| | Missing (n) | 117 |
| Time of follow-up [a] | N | 2157 |
| | Mean (SD), (years) | 8.3 (1.5) |
| | Missing (n) | 69 |
| Ethnic group | Arab/Saudi | 1347 (71.2%) |
| | White | 272 (14.4%) |
| | Black | 33 (1.7%) |
| | Hispanic | 0 (0.0%) |
| | Native American | 1 (0.1%) |
| | Asian/Pacific Islander | 232 (12.3%) |
| | Other | 7 (0.4%) |
| | Missing (n) | 334 |
| Family history of T2DM | Yes | 651 (73.5%) |
| | No | 235 (26.5%) |
| | Missing (n) | 1340 |
| Alcohol consumption status at initial diagnosis of T2DM | Never | 1372 (100.0%) |
| | Current | 0 (0.0%) |
| | Former | 0 (0.0%) |
| | Missing (n) | 854 |
| Weekly alcohol consumption [b] | N | 0 |
| | Mean (SD), (oz/week) | NA |
| | Missing (n) | 0 |
| Smoking status at initial diagnosis of T2DM | Never | 1085 (90.7%) |
| | Current | 87 (7.3%) |
| | Former | 24 (2.0%) |
| | Missing (n) | 1030 |
| Number of cigarettes smoked per day [b] | N | 43 |
| | Mean (SD) | 13.9 (6.9) |
| | Missing (n) | 68 |
| Pack years [b] | N | 42 |
| | Mean (SD) | 8.6 (5.9) |

| | | |
|---|---|---|
| | Missing (n) | 69 |
| BMI | N | 1244 |
| | Mean (SD), (numerical, $kg/m^2$) | 31.0 (5.8) |
| | Missing (n) | 982 |
| BMI (categorical) | Underweight | 5 (0.4%) |
| | Normal weight | 156 (12.5%) |
| | Overweight | 430 (34.6%) |
| | Obesity | 653 (52.5%) |
| | Missing (n) | 982 |
| Waist-to-hip ratio | N | 112 |
| | Mean (SD) | 0.88 (0.056) |
| | Missing (n) | 2114 |
| Heart rate | N | 886 |
| | Mean (SD), (bpm) | 84.7 (9.7) |
| | Missing (n) | 1340 |
| SBP | N | 1060 |
| | Mean (SD), (mmHg) | 134.8 (16.9) |
| | Missing (n) | 1166 |
| DBP | N | 1060 |
| | Mean (SD), (mmHg) | 79.2 (9.1) |
| | Missing (n) | 1166 |
| **Baseline laboratory data and complications** | | |
| Haemoglobin [c] | N | 390 |
| | Mean (SD), (g/dL) | 13.9 (1.9) |
| | Missing (n) | 1836 |
| WBC [d] | N | 388 |
| | Mean (SD), ($10^6$/mL) | 7.2 (2.3) |
| | Missing (n) | 1838 |
| HbA1c [e] | N | 1055 |
| | Mean (SD), (%) | 9.0 (2.1) |
| | Missing (n) | 1173 |
| Serum creatinine [f] | N | 461 |
| | Mean (SD), (mg/dL) | 0.81 (0.23) |
| | Missing (n) | 1767 |
| Serum albumin [g] | N | 264 |
| | Mean (SD), (g/dL) | 3.8 (0.52) |
| | Missing (n) | 1962 |
| T-Chol [h] | N | 565 |
| | Mean (SD), (mg/dL) | 191.2 (46.7) |
| | Missing (n) | 1663 |
| HDL [h] | N | 400 |
| | Mean (SD), (mg/dL) | 43.9 (16.5) |

| | | |
|---|---|---|
| | Missing (n) | 1828 |
| LDL [h] | N | 461 |
| | Mean (SD), (mg/dL) | 124.4 (40.1) |
| | Missing (n) | 1767 |
| TRIG [i] | N | 737 |
| | Mean (SD), (mg/dL) | 183.6 (171.3) |
| | Missing (n) | 1491 |
| eGFR | N | 10 |
| | Mean (SD), (mL/min/1.73 $m^2$) | 105.3 (35.2) |
| | Missing (n) | 2216 |
| UACR [j] | N | 12 |
| | Mean (SD), (mg/mmol) | 48.6 (60.4) |
| | Missing (n) | 2214 |
| **Baseline existing complications of patients** | | |
| Cardiovascular | Yes | 106 (5.5%) |
| | No | 1828 (94.5%) |
| | Missing (n) | 292 |
| Cardiovascular subcategory [k] | MI | 22 (1.1%) |
| | Angina | 10 (0.5%) |
| | PVD | 2 (0.1%) |
| | Stroke | 4 (0.2%) |
| | CHF | 14 (0.7%) |
| | Atrial fibrillation | 4 (0.2%) |
| | LVH | 1 (0.1%) |
| | Unknown | 49 (2.5%) |
| Renal | Yes | 16 (0.8%) |
| | No | 1912 (99.2%) |
| | Missing (n) | 298 |
| Renal subcategory [k] | MA | 1 (0.1%) |
| | GRP | 0 (0.0%) |
| | ESRD | 1 (0.1%) |
| | Unknown | 14 (0.7%) |
| Ocular | Yes | 80 (4.2%) |
| | No | 1846 (95.8%) |
| | Missing (n) | 300 |
| Ocular subcategory [k] | BDR | 4 (0.2%) |
| | PDR | 11 (0.6%) |
| | SVL | 16 (0.8%) |
| | ME | 0 (0.0%) |
| | Cataract | 35 (1.8%) |
| | Unknown | 15 (0.8%) |
| Foot ulcer | Yes | 14 (0.7%) |
| | No | 1910 (99.3%) |

| | | |
|---|---|---|
| | Missing (n) | 302 |
| Foot ulcer subcategory [k] | Uninfected foot ulcer | 4 (0.2%) |
| | Infected foot ulcer | 1 (0.1%) |
| | Healed foot ulcer | 2 (0.1%) |
| | History of lower limb amputation | 0 (0.0%) |
| | Unknown | 7 (0.4%) |
| Foot ulcer subcategory (aggregated) [k] | Foot ulcer (any type) | 7 (0.4%) |
| Neuropathy | Yes | 29 (1.5%) |
| | No | 1886 (98.5%) |
| | Missing (n) | 311 |

*bpm* beats per minute, *BMI* body mass index, *CHF* congestive heart failure, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *ESRD* end-stage renal disease, GRP gross renal proteinuria, *HbA1c* haemoglobin A1c, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *LVH* left ventricular failure *MA* microalbuminuria, *ME* macular oedema, *MI* myocardial infarction, *N* Total number of patients with available data, *NA* not applicable, *oz* ounce, *PDR* proliferative diabetic retinopathy, *PVD* peripheral vascular disease, *Q* quartile, *SBP* systolic blood pressure, *SD* standard deviation, *SVL* severe visual loss, *T2DM* type 2 diabetes mellitus, *TRIG* triglycerides, *UACR* urinary albumin creatinine ratio, *WBC* white blood cell count.

[a] Time between diagnosis of T2DM and SIV.

[b] For current and former consumers.

[c] Only values in g/dL are used (values in mmol/L inconsistent). Values >100 g/dL are discarded.

[d] Values greater than 30 x $10^6$/mL are discarded.

[e] Values in mmol/L converted as % = (18.015*mmol/L+46.7)/28.7. Two patients with values 60 and 807 mmol/L are discarded.

[f] Only values in mg/dL are used (values in micromole/L inconsistent). Values greater than 3.4 mg/dL are discarded.

[g] Only values in g/dL are used (values in micromole/L and g/L inconsistent). Values greater than 30 g/dL are discarded.

[h] Values in micromole/L converted as 1 micromol/L = 38.67 g/dL. Values lower than 10 or greater than 2000 g/dL are discarded.

[i] Values in micromole/L converted as 1 micromol/L = 88.57 g/dL. Values lower than 10 or greater than 6000 g/dL are discarded.

[j] Two values reported in mmol/L, eight in mg/dL, two in missing units. Since no conversion can be made, they are reported as if they all were in mg/mmol.

[k] Multi-response question. Denominators for % calculation exclude patients with missing value in the main category.

**Supplementary Table 5: Description of T2DM treatments including monotherapy or combinations (by LoT)**

| Type of drugs and ATC codes | Drug class | Values |
|---|---|---|
| ***Monotherapy or combinations used during 2nd LoT*** | | |
| **ATC codes [a]** | **Drug class** | **2nd LoT (N=352) [b]** |
| A10BH | DPP-4 inhibitors | 120 (34.1%) |
| A10BB | Sulphonylureas | 57 (16.2%) |
| A10AE | Long-acting insulins | 36 (10.2%) |
| A10BB + A10BH | Sulphonylureas + DPP-4 inhibitors | 16 (4.5%) |
| A10BA | Biguanides | 15 (4.3%) |
| A10AB + A10AE | Fast-acting insulins + long-acting insulins | 14 (4.0%) |
| A10AD | Intermediate or long-acting insulins combined with fast-acting | 14 (4.0%) |
| A10AB | Fast-acting insulins | 12 (3.4%) |
| A10AC | Intermediate-acting insulins | 11 (3.1%) |
| A10BJ | GLP-1 analogues | 8 (2.3%) |
| A10AE + A10BB | Long-acting insulins + sulphonylureas | 5 (1.4%) |
| A10AE + A10BH | Long-acting insulins + DPP-4 inhibitors | 5 (1.4%) |
| A10BA + A10BH | Biguanides + DPP-4 inhibitors | 4 (1.1%) |
| A10BK | SGLT2 inhibitors | 4 (1.1%) |
| Other regimens | | 31 (8.8%) |
| ***Monotherapy or combinations used during both 1st and 2nd LoT*** | | |
| **ATC codes [c]** | **Drug class** | **1st and 2nd LoT (N=352) [b]** |
| A10BA + A10BB, A10BH | Biguanides + sulphonylureas, DPP-4 inhibitors | 85 (24.1%) |
| A10BA, A10BB | Biguanides, sulphonylureas | 27 (7.7%) |
| A10BA, A10BH | Biguanides, DPP-4 inhibitors | 18 (5.1%) |
| A10BA + A10BB + A10BH, A10AE | Biguanides + sulphonylureas + DPP-4 inhibitors, long-acting insulins | 16 (4.5%) |
| A10BA + A10BB, A10BB | Biguanides + sulphonylureas, sulphonylureas | 16 (4.5%) |
| A10BA + A10BB, A10AE | Biguanides + sulphonylureas, long-acting insulins | 15 (4.3%) |
| A10BA, A10BB + A10BH | Biguanides, sulphonylureas + DPP-4 inhibitors | 8 (2.3%) |
| A10BA + A10BB, A10AD | Biguanides + sulphonylureas, premixed insulins | 7 (2.0%) |
| A10BA + A10BB + A10BH, A10BH | Biguanides + sulphonylureas + DPP-4 inhibitors, DPP-4 inhibitors | 6 (1.7%) |
| A10BA + A10BB, A10AB + A10AE | Biguanides + sulphonylureas, fast-acting insulins + long-acting insulins | 6 (1.7%) |

| | | |
|---|---|---|
| Other regimens | | 148 (42.0%) |

*ATC* anatomical therapeutic chemical, *DPP-4* dipeptidyl peptidase 4, *GLP-1* glucagon-like peptide-1, *LoT* line of therapy, *SGLT2* sodium-glucose co-transporter 2, *T2DM* type 2 diabetes mellitus.

[a] Only regimens present in at least 1% of patients with a 2nd LoT will be reported. Some T2DM treatments, present in a low number of patients, may be included only in 'Other regimens' because of this.

[b] Only for patients with a 1st and 2nd line of T2DM treatment (insulins and other blood glucoses lowering drugs).

[c] Only regimens present in at least 1.5% of patients with a 1st and 2nd LoT will be reported.

**Supplementary Table 6: Proportion of patients using other treatments and screening tests stratified by with or without CVD history at baseline**

| **Type of therapy** [a] | **Values, N (%)** |
|---|---|
| **Use of concomitant medications** | |
| **Patients without cardiovascular disease history, (N=598)** [b] | |
| Statins | 397 (66.4%) |
| Aspirin | 296 (49.5%) |
| ACE-I/ARB | 140 (23.4%) |
| **Patients with cardiovascular disease history, (N=35)** [b] | |
| Statins | 21 (60.0%) |
| Aspirin | 23 (65.7%) |
| ACE-I/ARB | 12 (34.3%) |
| **Screening tests and patient management proportions** | |
| **Screened for eye disease** | |
| Yes | 391 (61.3%) |
| No | 247 (38.7%) |
| **Screened for renal disease** | |
| Yes | 14 (2.2%) |
| No | 624 (97.8%) |
| **Received intensive insulin after MI** | |
| Yes | 0 (0.0%) |
| No | 2 (100.0%) |

*ACE-I* angiotensin converting enzyme inhibitor, *ARB* angiotensin receptor blocker, *CVD* cardiovascular disease, *MI* myocardial infarction.

[a] Multi-response variable.

[b] Patients with missing information excluded. Only treatments with valid start date included.

**Supplementary Table 7: Description of number and cost of screening tests during follow-up per-patient per year**

| **Parameters** | **Description** | **Overall (N=638)** |
|---|---|---|
| Presence of eye screening | Yes | 391 (61.3%) |
| | No | 247 (38.7%) |
| Frequency of eye screening [a] | N | 388 |
| | Mean (SD), (number/year) | 0.51 (0.29) |
| | Median [Q1, Q3], (number/year) | 0.493 [0.32, 0.602] |
| | (Range) | (0.095, 1.68) |
| | Missing (n) | 3 |
| Cost for eye screening [a,b] | N | 388 |
| | Mean (SD), (SAR/year) | 129.4 (73.6) |
| | Median [Q1, Q3], (SAR/year) | 125.2 [81.3, 153.0] |
| | (Range) | (24.1, 426.2) |
| | Missing (n) | 3 |
| Presence of foot care | Yes | 380 (59.6%) |
| | No | 258 (40.4%) |
| Frequency of foot care [a] | N | 379 |
| | Mean (SD), (number/year) | 0.686 (0.476) |
| | Median [Q1, Q3], (number/year) | 0.534 [0.235, 1.18] |
| | (Range) | (0.0941, 1.99) |
| | Missing (n) | 1 |
| Cost for foot care [a,c] | N | 379 |
| | Mean (SD), (SAR/year) | 514.5 (356.7) |
| | Median [Q1, Q3], (SAR/year) | 400.2 [176.2, 887.0] |
| | (Range) | (70.6, 1494.7) |
| | Missing (n) | 1 |
| Presence of MA testing | Yes | 13 (2.0%) |
| | No | 625 (98.0%) |
| Frequency of MA test [a] | N | 13 |
| | Mean (SD), (number/year) | 0.137 (0.0226) |
| | Median [Q1, Q3], (number/year) | 0.128 [0.118, 0.154] |
| | (Range) | (0.103, 0.168) |
| | Missing (n) | 0 |

| | | |
|---|---|---|
| Cost for MA test [a,d] | N | 13 |
| | Mean (SD), (SAR/year) | 21.9 (3.62) |
| | Median [Q1, Q3], (SAR/year) | 20.5 [19.0, 24.7] |
| | (Range) | (16.4, 26.9) |
| | Missing (n) | 0 |
| Presence of GRP | Yes | 5 (0.8%) |
| | No | 633 (99.2%) |
| Frequency of GRP test [a] | N | 5 |
| | Mean (SD), (number/year) | 0.147 (0.0242) |
| | Median [Q1, Q3], (number/year) | 0.154 [0.128, 0.168] |
| | (Range) | (0.115, 0.168) |
| | Missing (n) | 0 |
| Cost for GRP test [a,e] | N | 5 |
| | Mean (SD), (SAR/year) | 5.87 (0.968) |
| | Median [Q1, Q3], (SAR/year) | 6.16 [5.13, 6.73] |
| | (Range) | (4.6, 6.73) |
| | Missing (n) | 0 |
| Presence of electrocardiogram | Yes | 91 (14.3%) |
| | No | 547 (85.7%) |
| Frequency of electrocardiogram [a] | N | 91 |
| | Mean (SD), (number/year) | 0.153 (0.0792) |
| | Median [Q1, Q3], (number/year) | 0.12 [0.118, 0.142] |
| | (Range) | (0.0922, 0.501) |
| | Missing (n) | 0 |
| Cost for electrocardiogram [a,f] | N | 91 |
| | Mean (SD), (SAR/year) | 22.9 (11.9) |
| | Median [Q1, Q3], (SAR/year) | 18.0 [17.8, 21.3] |
| | (Range) | (13.8, 75.1) |
| | Missing (n) | 0 |
| Presence of other screening | Yes | 3 (0.5%) |
| | No | 635 (99.5%) |
| Frequency of other screening [a] | N | 2 |
| | Mean (SD), (number/year) | 0.146 (0.0066) |

| | | |
|---|---|---|
| | Median [Q1, Q3], (number/year) | 0.146 [0.143, 0.148] |
| | (Range) | (0.141, 0.15) |
| | Missing (n) | 1 |

*GRP* gross renal proteinuria, *MA* microalbuminuria, *N* Total number of patients with available data, *Q1* quartile 1, *Q3* quartile 3, *SAR* Saudi Arabian Riyal, *SD* standard deviation.

[a] Patients not having this type of screening, are not included.

[b] Cost of eye screening estimated as 254 SAR.

[c] Cost of foot care estimated as 750 SAR.

[d] Cost of MA test estimated as 160 SAR.

[e] Cost of GRP test estimated as 40 SAR.

[f] Cost of electrocardiogram estimated as 150 SAR.

**Supplementary Table 8: Annual treatment cost (SAR) inputs of the most common 1st LoT for T2DM**

| Regimen, ATC codes | Drugs | Annual drug cost | SMBG cost [a] | Total annual costs |
|---|---|---|---|---|
| Regimen 1: A10BA + A10BB | Biguanides + sulphonylureas | 468.83 | - | 468.83 |
| Regimen 2: A10BA | Biguanides | 350.24 | - | 350.24 |
| Regimen 3: A10BA + A10BB + A10BH | Biguanides + sulphonylureas + DPP-4 inhibitors | 4,486.58 | - | 4,486.58 |
| Regimen 4: A10AB + A10AE | Fast-acting insulins + long-acting insulins | 2,408.59 | 1,976.73 | 4,385.32 |
| Regimen 5: A10BA + A10BH | Biguanides + DPP-4 inhibitors | 4,367.99 | - | 4,367.99 |
| Regimen 6: A10AD + A10BA | Premixed insulins + biguanides | 1,606.70 | 1,976.73 | 3,583.44 |
| Regimen 7: A10AB + A10AE + A10BA | Fast-acting insulins + long-acting insulins + biguanides | 2,758.83 | 1,976.73 | 4,735.56 |
| Regimen 8: A10AE | Long-acting insulins | 1,267.86 | 658.91 | 1,926.77 |

*ATC* anatomical therapeutic chemical, *DPP-4* dipeptidyl peptidase 4, *LoT* line of therapy, *SAR* Saudi Arabian Riyal, *SMBG* self-monitoring blood glucose, *T2DM* type 2 diabetes mellitus.

[a] Including cost of blood glucose test strip and lancets.

**Supplementary Table 9: Predicted event rates of T2DM-related complications per 1000 patient-years calculated with CDM**

| Event rate per 1000 patient-years | Regimens | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** |
| **Renal disease** | | | | | | | | |
| MA | 12.48 | 8.69 | 9.97 | 16.49 | 12.24 | 22.73 | 17.73 | 16.72 |
| GRP | 2.67 | 1.33 | 1.68 | 4.74 | 2.71 | 9.80 | 5.76 | 4.69 |
| ESRD | 0.43 | 0.16 | 0.23 | 1.02 | 0.46 | 3.19 | 1.39 | 0.99 |
| **Cardiovascular disease** | | | | | | | | |
| PVD | 6.13 | 4.99 | 5.22 | 7.38 | 5.77 | 9.80 | 7.14 | 6.97 |
| HF | 6.36 | 6.69 | 6.10 | 7.35 | 6.86 | 10.17 | 8.25 | 7.19 |
| Angina | 8.45 | 7.03 | 7.63 | 8.98 | 6.54 | 9.85 | 9.32 | 9.90 |
| Stroke | 4.17 | 3.73 | 3.75 | 4.56 | 4.02 | 5.07 | 4.25 | 4.65 |
| **Ocular disease** | | | | | | | | |
| BDR | 13.74 | 9.76 | 11.09 | 17.45 | 13.54 | 23.64 | 18.68 | 18.12 |
| PDR | 2.69 | 1.36 | 1.73 | 4.33 | 2.72 | 8.13 | 4.95 | 4.55 |
| ME | 11.36 | 7.91 | 8.99 | 14.66 | 11.17 | 20.46 | 15.72 | 15.18 |
| SVL | 6.27 | 4.10 | 4.86 | 8.58 | 6.21 | 12.71 | 9.33 | 9.30 |
| Cataract | 5.83 | 4.92 | 5.29 | 6.62 | 5.74 | 8.37 | 7.05 | 6.56 |
| **Ulcer/amputation/neuropathy** | | | | | | | | |
| Ulcer | 1.45 | 1.49 | 1.38 | 1.70 | 1.51 | 2.49 | 2.04 | 1.77 |
| Recurrent ulcer | 1.35 | 1.38 | 1.29 | 1.56 | 1.39 | 2.20 | 1.83 | 1.61 |
| 1st Amputation | 0.38 | 0.38 | 0.36 | 0.47 | 0.39 | 0.71 | 0.54 | 0.48 |
| 2nd Amputation | 0.14 | 0.12 | 0.13 | 0.17 | 0.14 | 0.25 | 0.20 | 0.17 |
| Neuropathy | 28.04 | 24.09 | 25.36 | 30.80 | 27.85 | 35.68 | 31.85 | 30.67 |
| **Hypoglycaemia** | | | | | | | | |
| NSHE | 34.58 | 0.00 | 183.96 | 3152.18 | 149.35 | 1,323.90 | 2,988.84 | 3,434.65 |
| SHE1 | 34.50 | 0.00 | 34.61 | 21.65 | 11.53 | 5.39 | 15.94 | 10.41 |
| SHE2 | 1.76 | 0.00 | 3.15 | 2.22 | 1.50 | 0.36 | 1.52 | 0.95 |

*CDM* Core Diabetes Model, *BDR* background diabetic retinopathy, *ESRD* end-stage renal disease, *GRP* gross renal proteinuria, *HF* heart failure, *MA* microalbuminuria, *ME* macular oedema, *NSHE* non-severe hypoglycaemia, *PDR* proliferative diabetic retinopathy, *PVD* peripheral vascular disease, *SHE1* severe hypoglycaemia (requiring non-medical assistance), *SHE2* severe hypoglycaemia (requiring medical assistance), *SVL* severe visual loss, *T2DM* type 2 diabetes mellitus.
Regimen 1: A10BA + A10BB = Biguanides + Sulphonylureas.
Regimen 2: A10BA = Biguanides.
Regimen 3: A10BA + A10BB + A10BH = Biguanides + Sulphonylureas + DPP-4 inhibitors.
Regimen 4: A10AB + A10AE = Fast-acting insulins + Long-acting insulins.
Regimen 5: A10BA + A10BH = Biguanides + DPP-4 inhibitors.
Regimen 6: A10AD + A10BA = Premixed insulins + Biguanides.
Regimen 7: A10AB + A10AE + A10BA = Fast-acting insulins + Long-acting insulins + Biguanides.
Regimen 8: A10AE = Long-acting insulins.

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