**Supplemental online material**

**Cost of macrovascular complications in people with diabetes from a public healthcare perspective: a retrospective database study in Brazil**

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**Supplementary Table S1**. Frequency of qualifying complications for study entry in patients with diabetes

|  |  |  |  |
| --- | --- | --- | --- |
| **Cohort**  | **Complication type**  | **Condition**  | **N (%)** |
| Overall (N=1668) | Macrovascular | Heart failure | 560 (33.6) |
| Stroke | 255 (15.3) |
| Atherosclerosis | 181 (10.9) |
| Acute MI | 174 (10.4) |
| Angina | 128 (7.7) |
| PVD | 93 (5.6) |
| Chronic IHD | 83 (5.0) |
| Cerebral infarction | 48 (2.9) |
| Cerebrovascular diseases | 45 (2.7) |
| Acute IHD | 43 (2.6) |
| Transient cerebral ischemia | 30 (1.8) |
| Other macrovascular | 18 (1.1) |
| Occlusion and stenosis | 10 (0.6) |
| Macrovascular (N=1193) | Macrovascular  | Heart failure | 459 (38.5) |
| Stroke | 189 (15.8) |
| Acute MI | 136 (11.4) |
| Atherosclerosis | 109 (9.1) |
| PVD | 65 (5.4) |
| Angina | 58 (4.9) |
| Chronic IHD | 41 (3.4) |
| Cerebral infarction | 36 (3.0) |
| Acute IHD | 31 (2.6) |
| Cerebrovascular diseases | 29 (2.4) |
| Transient cerebral ischemia | 21 (1.8) |
| Other macrovascular | 11 (0.9) |
| Occlusion and stenosis | 8 (0.7) |
| Macrovascular and microvascular (N=475) | Microvascular | Kidney disease | 297 (62.5) |
| Eye disease and diabetic retinopathy | 59 (12.4) |
| Other microvascular | 53 (11.2) |
| Diabetic foot including ulcer | 52 (10.9) |
| Neuropathy | 13 (2.7) |
| PVD | 1 (0.2) |

IHD, ischemic heart disease; MI, myocardial infarction; PVD, peripheral vascular disease

**Supplementary Table S2.** Demographic characteristics of patients with diabetes who experienced a macrovascular complication with or without a microvascular complication by federative unit

|  |  |  |  |
| --- | --- | --- | --- |
| **Location**  | **Macrovascular (N=1193)** | **Macrovascular and microvascular (N=475)** | **Overall study population (N=1668)** |
| *Midwest* |  |  |  |
| Distrito Federal | 12 (1.0) | 2 (0.4) | 14 (0.8) |
| Goiás | 7 (0.6) | 1 (0.2) | 8 (0.5) |
| Mato Grosso | 3 (0.3) | 2 (0.4) | 5 (0.3) |
| Mato Grosso do Sul | 0 (0.0) | 4 (0.8) | 4 (0.2) |
| *North* |  |  |  |
| Acre | 4 (0.3) | 0 (0.0) | 4 (0.2) |
| Rondônia | 4 (0.3) | 0 (0.0) | 4 (0.2) |
| Pará | 2 (0.2) | 2 (0.4) | 4 (0.2) |
| Roraima | 2 (0.2) | 1 (0.2) | 3 (0.2) |
| Tocantins | 1 (0.1) | 0 (0.0) | 1 (0.1) |
| Amapá | 1 (0.1) | 0 (0.0) | 1 (0.1) |
| *Northeast* |  |  |  |
| Bahia | 50 (4.2) | 5 (1.1) | 55 (3.3) |
| Maranhão | 23 (1.9) | 4 (0.8) | 27 (1.6) |
| Pernambuco | 7 (0.6) | 16 (3.4) | 23 (1.4) |
| Sergipe | 11 (0.9) | 1 (0.2) | 12 (0.7) |
| Rio Grande do Norte | 1 (0.1) | 10 (2.1) | 11 (0.7) |
| Piauí | 9 (0.8) | 1 (0.2) | 10 (0.6) |
| Alagoas | 1 (0.1) | 4 (0.8) | 5 (0.3) |
| Paraíba | 3 (0.3) | 2 (0.4) | 5 (0.3) |
| *South* |  |  |  |
| Santa Catarina | 52 (4.4) | 12 (2.5) | 64 (3.8) |
| Paraná | 33 (2.8) | 20 (4.2) | 53 (3.2) |
| Rio Grande do Sul | 14 (1.2) | 22 (4.6) | 36 (2.2) |
| *Southeast* |  |  |  |
| São Paulo | 761 (63.8) | 296 (62.3) | 1057 (63.4) |
| Rio de Janeiro | 93 (7.8) | 25 (5.3) | 118 (7.1) |
| Minas Gerais | 75 (6.3) | 41 (8.6) | 116 (7.0) |
| Espírito Santo | 24 (2.0) | 4 (0.8) | 28 (1.7) |

Data presented are n (%) or mean ± standard deviation. Cohorts were defined at the time of the qualifying complication by ICD-10 diagnosis codes as ‘macrovascular’ or ‘macrovascular and microvascular’ (i.e. both complication types) (full list available in **Table 1**). The month of the qualifying macrovascular complication was defined as the index date

ICD-10, International Classification of Diseases, 10th Revision

**Supplementary Table S3.** Demographic characteristics of patients with diabetes who experienced a macrovascular complication with or without a microvascular complication stratified by diabetes type

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Insulin dependent(N=468)** | **Non-insulin dependent(N=255)** | **Unspecified(N=945)** | **Overall study population****(N=1668)** |
| Location |  |  |  |  |
| *Midwest* | 9 (1.9) | 7 (2.7) | 15 (1.6) | 31 (1.9) |
| Distrito Federal | 0 (0.0) | 5 (2.0) | 9 (1.0) | 14 (0.8) |
| Goiás | 6 (1.3) | 0 (0.0) | 2 (0.2) | 8 (0.5) |
| Mato Grosso | 1 (0.2) | 2 (0.8) | 2 (0.2) | 5 (0.3) |
| Mato Grosso do Sul | 2 (0.4) | 0 (0.0) | 2 (0.2) | 4 (0.2) |
| *North* | 3 (0.6) | 2 (0.8) | 12 (1.3) | 17 (1.0) |
| Acre | 0 (0.0) | 0 (0.0) | 4 (0.4) | 4 (0.2) |
| Rondônia | 2 (0.4) | 1 (0.4) | 1 (0.1) | 4 (0.2) |
| Pará | 0 (0.0) | 1 (0.4) | 3 (0.3) | 4 (0.2) |
| Roraima | 0 (0.0) | 0 (0.0) | 3 (0.3) | 3 (0.2) |
| Tocantins | 1 (0.2) | 0 (0.0) | 0 (0.0) | 1 (0.1) |
| Amapá | 0 (0.0) | 0 (0.0) | 1 (0.1) | 1 (0.1) |
| *Northeast* | 35 (7.5) | 11 (4.3) | 102 (10.8) | 148 (8.9) |
| Bahia | 9 (1.9) | 4 (1.6) | 42 (4.4) | 55 (3.3) |
| Maranhão | 4 (0.9) | 1 (0.4) | 22 (2.3) | 27 (1.6) |
| Pernambuco | 7 (1.5) | 2 (0.8) | 14 (1.5) | 23 (1.4) |
| Sergipe | 1 (0.2) | 2 (0.8) | 9 (1.0) | 12 (0.7) |
| Rio Grande do Norte | 5 (1.1) | 1 (0.4) | 5 (0.5) | 11 (0.7) |
| Piauí | 6 (1.3) | 0 (0.0) | 4 (0.4) | 10 (0.6) |
| Alagoas | 2 (0.4) | 0 (0.0) | 3 (0.3) | 5 (0.3) |
| Paraíba | 1 (0.2) | 1 (0.4) | 3 (0.3) | 5 (0.3) |
| *South* | 40 (8.5) | 25 (9.8) | 88 (9.3) | 153 (9.2) |
| Santa Catarina | 9 (1.9) | 10 (3.9) | 45 (4.8) | 64 (3.8) |
| Paraná | 13 (2.8) | 7 (2.7) | 33 (3.5) | 53 (3.2) |
| Rio Grande do Sul | 18 (3.8) | 8 (3.1) | 10 (1.1) | 36 (2.2) |
| *Southeast* | 381 (81.4) | 210 (82.4) | 728 (77.0) | 1319 (79.1) |
| São Paulo | 289 (61.8) | 180 (70.6) | 588 (62.2) | 1057 (63.4) |
| Rio de Janeiro | 48 (10.3) | 15 (5.9) | 55 (5.8) | 118 (7.1) |
| Minas Gerais | 39 (8.3) | 14 (5.5) | 63 (6.7) | 116 (7.0) |
| Espírito Santo | 5 (1.1) | 1 (0.4) | 22 (2.3) | 28 (1.7) |
| Female | 240 (51.3) | 141 (55.3) | 531 (56.2) | 912 (54.7) |
| Age at index  | 58.6 ± 13.2 | 60.6 ± 12.3 | 59.6 ± 11.5 | 59.5 ± 12.2 |

Data presented are n (%) or mean ± standard deviation. Patients were stratified by diabetes type based on ICD-10 diagnosis codes (full list available in **Table 1**). The month of the qualifying macrovascular complication was defined as the index date

ICD-10, International Classification of Diseases, 10th Revision

**Supplementary Table S4.** Direct medical costs in patients with diabetes who experienced a macrovascular complication alone (A), or in conjunction with a microvascular complication (B), and in the overall study population (C), stratified by diabetes type

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Diabetes type** | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Insulin dependent (N=310) | Baseline –1 | 106 | 173.6 ± 192.9 | 101.8 (87.1; 195.1) | 1.5; 1126.2 | 136.4; 210.7 |
| Baseline | 216 | 244.0 ± 428.4 | 121.2 (86.7; 218.2) | 0.0; 3895.0 | 186.6; 301.5 |
| First year | 310 | 611.2 ± 876.6 | 266.9 (176.2; 688.2) | 10.1; 7073.9 | 513.2; 709.2 |
| Second year | 75 | 223.3 ± 236.6 | 123.5 (71.3; 317.2) | 1.8; 998.5 | 168.9; 277.8 |
| Third year | 65 | 302.0 ± 492.6 | 127.0 (34.3; 346.7) | 0.8; 3245.4 | 179.9; 424.0 |
| Non-insulin dependent (n=183) | Baseline –1 | 74 | 219.8 ± 317.2 | 102.6 (64.8; 208.5) | 0.0; 1779.2 | 146.3; 293.3 |
| Baseline | 127 | 270.6 ± 372.2 | 129.8 (90.7; 285.8) | 0.8; 2276.9 | 205.2; 336.0 |
| First year | 183 | 815.6 ± 1142.1 | 333.7 (184.7; 932.9) | 11.1; 9484.3 | 649.1; 982.2 |
| Second year | 50 | 369.8 ± 526.6 | 183.2 (69.5; 398.0) | 0.8; 2257.0 | 220.1; 519.5 |
| Third year | 47 | 164.1 ± 209.5 | 95.0 (29.4; 200.6) | 0.0; 913.3 | 102.6; 225.6 |
| Unspecified (N=700) | Baseline –1 | 276 | 176.0 ± 233.6 | 101.1 (90.7; 188.8) | 0.8; 2060.7 | 148.3; 203.7 |
| Baseline | 463 | 202.5 ± 315.9 | 109.4 (91.0; 205.0) | 1.3; 3045.0 | 173.6; 231.3 |
| First year | 700 | 507.9 ± 738.7 | 260.5 (176.2; 498.5) | 11.1; 7910.1 | 453.1; 562.7 |
| Second year | 173 | 281.4 ± 433.7 | 115.7 (85.2; 317.5) | 0.0; 3117.4 | 216.4; 346.5 |
| Third year | 138 | 274.6 ± 650.3 | 100.8 (33.2; 250.2) | 0.0; 6159.6 | 165.1; 384.0 |

**B**)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Diabetes type**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Insulin dependent (N=158) | Baseline –1 | 88 | 440.8 ± 1057.1 | 147.4 (84.9; 323.3) | 0.8; 7369.7 | 216.8; 664.8 |
| Baseline | 118 | 505.9 ± 992.3 | 208.4 (93.7; 424.5) | 3.0; 7549.7 | 325.0; 686.8 |
| First year | 158 | 2495.5 ± 2970.4 | 872.2 (327.6; 4213.8) | 10.1; 12,663.7 | 2028.8; 2962.3 |
| Second year | 123 | 2851.4 ± 4326.7 | 798.9 (160.8; 6143.1) | 8.1; 30,864.0 | 2079.1; 3623.7 |
| Third year | 115 | 1972.8 ± 2952.2 | 222.3 (91.0; 3100.0) | 0.0; 8991.2 | 1427.4; 2518.1 |
| Non-insulin dependent (N=72) | Baseline –1 | 40 | 374.9 ± 1011.8 | 136.0 (51.8; 267.5) | 0.8; 6395.2 | 51.3; 698.5 |
| Baseline | 66 | 376.6 ± 602.9 | 174.3 (99.2; 442.8) | 0.0; 4045.0 | 228.4; 524.8 |
| First year | 72 | 2812.3 ± 2931.3 | 1075.7 (365.8; 5405.6) | 26.0; 8958.4 | 2123.4; 3501.1 |
| Second year | 56 | 2774.9 ± 3368.6 | 720.2 (165.8; 6045.2) | 2.5; 12,265.8 | 1872.7; 3677.0 |
| Third year | 45 | 2396.3 ± 3078.6 | 334.2 (102.3; 5738.7) | 0.8; 7890.9 | 1471.4; 3321.2 |
| Unspecified (N=245) | Baseline –1 | 136 | 183.1 ± 205.0 | 113.5 (90.4; 201.7) | 0.0; 1151.2 | 148.3; 217.9 |
| Baseline | 189 | 411.3 ± 870.3 | 191.8 (93.0; 371.0) | 0.8; 7927.2 | 286.4; 536.2 |
| First year | 245 | 2351.6 ± 2881.3 | 694.0 (286.3; 4561.6) | 0.8; 9863.4 | 1989.0; 2714.2 |
| Second year | 197 | 2562.5 ± 3196.1 | 580.4 (129.0; 5712.3) | 0.0; 11,271.3 | 2113.4; 3011.6 |
| Third year | 173 | 2745.2 ± 3399.6 | 417.6 (117.2; 7037.6) | 0.0; 10,412.5 | 2235.0; 3255.4 |

**C)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Diabetes type**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Insulin dependent (N=468) | Baseline –1 | 194 | 294.8 ± 736.1 | 116.2 (85.5; 234.3) | 0.8; 7369.7 | 190.5; 399.0 |
| Baseline | 334 | 336.5 ± 692.9 | 136.2 (90.7; 301.2) | 0.0; 7549.7 | 261.9; 411.1 |
| First year | 468 | 1247.4 ± 2066.5 | 346.3 (186.3; 1172.4) | 10.1; 12,663.7 | 1059.6; 1435.1 |
| Second year | 198 | 1855.9 ± 3639.7 | 312.5 (97.3; 1089.2) | 1.8; 30,864.0 | 1345.8; 2366.0 |
| Third year | 180 | 1369.4 ± 2507.0 | 189.5 (82.6; 715.8) | 0.0; 8991.2 | 1000.7; 1738.2 |
| Non-insulin dependent (N=255)  | Baseline –1 | 114 | 274.2 ± 651.1 | 112.5 (61.1; 212.4) | 0.0; 6395.2 | 153.4; 395.0 |
| Baseline | 193 | 306.8 ± 465.3 | 136.6 (90.7; 340.7) | 0.0; 4045.0 | 240.8; 372.9 |
| First year | 255 | 1379.4 ± 2036.5 | 477.1 (201.4; 1478.4) | 11.1; 9484.3 | 1128.2; 1630.5 |
| Second year | 106 | 1640.4 ± 2743.8 | 326.7 (91.0; 1645.8) | 0.8; 12,265.8 | 1112.0; 2168.8 |
| Third year | 92 | 1255.9 ± 2421.5 | 143.0 (39.1; 451.9) | 0.0; 7890.9 | 754.4; 1757.4 |
| Unspecified (N=945) | Baseline –1 | 412 | 178.3 ± 224.4 | 103.1 (90.7; 189.6) | 0.0; 2060.7 | 156.6; 200.1 |
| Baseline | 652 | 263.0 ± 546.4 | 123.1 (91.0; 245.7) | 0.8; 7927.2 | 221.0; 305.0 |
| First year | 945 | 985.9 ± 1789.8 | 313.2 (181.4; 721.2) | 0.8; 9863.4 | 871.6; 1100.1 |
| Second year | 370 | 1496.0 ± 2610.1 | 238.4 (95.0; 993.1) | 0.0; 11,271.3 | 1229.1; 1762.8 |
| Third year | 311 | 1648.9 ± 2848.0 | 184.5 (82.2; 898.7) | 0.0; 10,412.5 | 1331.1; 1966.7 |

Data presented are direct medical costs in 2019 United States dollars. Baseline corresponds to the year prior to the qualifying complication, while baseline –1 refers to the year prior to baseline (i.e. between 1–2 years prior to the qualifying complication). First, second and third year refer to the respective year after the qualifying complication. Patients were stratified by diabetes type based on ICD-10 diagnosis codes (full list available in **Table 1**)

CI, confidence interval; n, number of patients that contributed to data point; ICD-10, International Classification of Diseases, 10th Revision;

IQR, interquartile range; SD, standard deviation

**Supplementary Table S5.** Direct medical costs in patients with diabetes who experienced a macrovascular complication alone (A), or in conjunction with a microvascular complication (B), stratified by gender

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Gender**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Female (N=692)  | Baseline –1 | 280 | 184.9 ± 260.5 | 101.3 (87.8; 188.8) | 0.0; 2060.7 | 154.2; 215.5 |
| Baseline  | 472 | 213.7 ± 331.4 | 119.5 (90.7; 226.6) | 0.0; 3895.0 | 183.7; 243.6 |
| First year | 692 | 550.9 ± 795.7 | 267.1 (178.2; 545.7) | 11.1; 9484.3 | 491.5; 610.3 |
| Second year | 183 | 249.9 ± 336.1 | 115.4 (63.6; 319.3) | 0.0; 2142.8 | 200.9; 298.9 |
| Third year | 156 | 201.7 ± 350.0 | 94.0 (23.9; 243.7) | 0.0; 3245.4 | 146.4; 257.1 |
| Male (N=501)  | Baseline –1 | 176 | 178.8 ± 206.2 | 100.7 (88.5; 192.0) | 0.8; 1170.8 | 148.1; 209.5 |
| Baseline  | 334 | 239.4 ± 394.2 | 111.4 (90.7; 214.9) | 0.8; 3045.0 | 197.0; 281.9 |
| First year | 501 | 624.8 ± 928.8 | 268.6 (176.2; 630.8) | 10.1; 7910.0 | 543.2; 706.3 |
| Second year | 115 | 332.2 ± 510.4 | 136.3 (91.0; 383.2) | 4.5; 3117.3 | 237.9; 426.4 |
| Third year | 94 | 359.1 ± 773.3 | 131.5 (77.9; 285.7) | 0.0; 6159.6 | 200.7; 517.5 |

**B)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Gender**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Female (N=220)  | Baseline –1 | 126 | 212.1 ± 395.2 | 113.2 (57.4; 191.1) | 0.0; 3856.2 | 142.4; 281.7 |
| Baseline | 178 | 417.9 ± 911.5 | 162.7 (90.7; 352.2) | 0.0; 7927.2 | 283.1; 552.7 |
| First year | 220 | 2365.1 ± 2882.1 | 736.6 (297.1; 3976.8) | 6.0; 12,663.7 | 1982.1; 2748.0 |
| Second year | 174 | 2539.0 ± 3274.7 | 487.1 (125.3; 5879.2) | 0.8; 14,105.2 | 2049.0; 3029.0 |
| Third year | 152 | 2386.6 ± 3223.4 | 251.3 (96.3; 6079.4) | 0.0; 10,412.5 | 1870.0; 2903.1 |
| Male (N=255)  | Baseline –1 | 138 | 376.6 ± 956.5 | 140.2 (90.7; 313.0) | 0.0; 7369.7 | 215.5; 537.6 |
| Baseline | 195 | 450.7 ± 834.1 | 206.6 (99.0; 431.3) | 0.0; 7549.7 | 332.9; 568.6 |
| First year | 255 | 2559.2 ± 2949.3 | 795.1 (352.6; 5096.2) | 0.8; 9345.2 | 2195.5; 2922.9 |
| Second year | 202 | 2817.6 ± 3898.3 | 735.2 (185.4; 5975.9) | 0.0; 30,864.0 | 2276.7; 3358.4 |
| Third year | 181 | 2468.9 ± 3223.4 | 440.0 (109.1; 5844.1) | 0.0; 9737.4 | 1996.1; 2941.6 |

Data presented are direct medical costs in 2019 United States dollars. Baseline corresponds to the year prior to the qualifying complication, while baseline –1 refers to the year prior to baseline (i.e. between 1–2 years prior to the qualifying complication). First, second and third year refer to the respective year after the qualifying complication

CI, confidence interval; n, number of patients that contributed to data point; IQR, interquartile range; SD, standard deviation

**Supplementary Table S6.** Direct medical costs in patients with diabetes who experienced a macrovascular complication with or without a microvascular complication and survived (A) or died (B) during the study period

**A)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cohort**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Macrovascular (N=916) | Baseline –1 | 340 | 173.2 ± 233.0 | 100.4 (82.5; 187.5) | 0.0; 2060.7 | 148.4; 198.1 |
| Baseline  | 606 | 209.9 ± 319.0 | 110.5 (90.7; 207.0) | 0.8; 3045.0 | 184.5; 235.4 |
| First year | 916 | 542.2 ± 768.8 | 258.6 (176.2; 523.4) | 10.1; 7910.0 | 492.4; 592.1 |
| Second year | 209 | 267.6 ± 427.8 | 114.7 (81.1; 284.3) | 0.0; 3117.4 | 209.2; 325.9 |
| Third year | 167 | 200.1 ± 358.6 | 95.0 (24.2; 215.5) | 0.0; 3208.8 | 145.4; 254.9 |
| Macrovascular and microvascular (N=251)  | Baseline –1 | 129 | 257.4 ± 668.8 | 100.6 (80.9; 227.8) | 0.0; 6395.2 | 140.9; 373.9 |
| Baseline  | 191 | 359.1 ± 658.6 | 172.1 (91.0; 318.7) | 0.0; 4565.4 | 265.1; 453.1 |
| First year | 251 | 2083.3 ± 2737.1 | 628.0 (262.5; 2792.1) | 0.8; 9038.0 | 1743.0; 2423.5 |
| Second year | 187 | 2256.7 ± 3134.0 | 421.6 (117.2; 4416.8) | 0.0; 14,105.2 | 1804.6; 2708.9 |
| Third year | 164 | 2346.8 ± 3280.4 | 216.7 (85.3; 6002.7) | 0.0; 10,412.5 | 1841.0; 2852.6 |
| Overall study population (N=1167)  | Baseline –1 | 469 | 196.4 ± 403.8 | 100.6 (80.9; 190.0) | 0.0; 6395.2 | 159.8; 233.0 |
| Baseline  | 797 | 245.7 ± 430.0 | 121.2 (90.7; 232.6) | 0.0; 4565.4 | 215.8; 275.6 |
| First year | 1167 | 873.7 ± 1572.1 | 284.3 (179.2; 728.6) | 0.8; 9038.0 | 783.4; 964.0 |
| Second year | 396 | 1206.9 ± 2389.6 | 195.6 (91.0; 589.7) | 0.0; 14,105.2 | 970.8; 1443.0 |
| Third year | 331 | 1263.7 ± 2556.5 | 131.0 (39.3; 465.6) | 0.0; 10,412.5 | 987.3; 1540.2 |

**B**)

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Cohort**  | **Time period** | **n** | **Mean** ± **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Macrovascular (N=277) | Baseline –1 | 116 | 209.8 ± 261.4 | 111.0 (90.7; 221.4) | 0.0; 1695.0 | 161.7; 257.8 |
| Baseline | 200 | 268.0 ± 456.9 | 127.4 (90.7; 251.3) | 0.0; 3895.0 | 204.3; 331.7 |
| First year | 277 | 713.2 ± 1082.3 | 318.8 (178.2; 717.2) | 11.1; 9484.3 | 585.2; 841.2 |
| Second year | 89 | 314.6 ± 377.1 | 190.0 (79.9; 437.7) | 0.0; 2000.2 | 235.1; 394.0 |
| Third year | 83 | 383.2 ± 802.8 | 139.4 (83.7; 378.6) | 0.0; 6159.6 | 207.9; 558.5 |
| Macrovascular and microvascular (N=224) | Baseline –1 | 135 | 336.9 ± 814.9 | 143.9 (90.7; 301.8) | 0.0; 7369.7 | 198.1; 475.6 |
| Baseline | 182 | 514.8 ± 1044.5 | 222.8 (99.0; 494.8) | 1.5; 7927.2 | 362.1; 667.6 |
| First year | 224 | 2901.8 ± 3054.5 | 1183.9 (380.5; 5913.8) | 6.0; 12,663.7 | 2499.6; 3304.0 |
| Second year | 189 | 3116.0 ± 4008.3 | 952.1 (184.0; 6597.3) | 0.0; 30,864.0 | 2540.8; 3691.1 |
| Third year | 169 | 2513.3 ± 3165.4 | 467.0 (130.8; 5738.7) | 3.0; 9070.8 | 2032.6; 2994.0 |
| Overall study population (N=501) | Baseline –1 | 251 | 278.1 ± 625.6 | 133.3 (90.7; 241.3) | 0.0; 7369.7 | 200.3; 355.9 |
| Baseline | 382 | 385.6 ± 801.6 | 173.0 (91.0; 359.0) | 0.0; 7927.2 | 304.9; 466.2 |
| First year | 501 | 1691.8 ± 2448.4 | 523.2 (224.3; 1723.5) | 6.0; 12,663.7 | 1476.8; 1906.7 |
| Second year | 278 | 2219.1 ± 3558.7 | 471.9 (115.7; 2445.0) | 0.0; 30,864.0 | 1799.0; 2639.3 |
| Third year | 252 | 1811.7 ± 2814.8 | 253.8 (99.0; 1774.2) | 0.0; 9070.8 | 1462.5; 2160.9 |

Data presented are direct medical costs in 2019 United States dollars. Baseline corresponds to the year prior to the qualifying complication, while baseline –1 refers to the year prior to baseline (i.e. between 1–2 years prior to the qualifying complication). First, second and third year refer to the respective year after the qualifying complication. Patients were defined as having died if the death took place in hospital or if the high complexity procedures authorization (APAC) profile was closed with a reason of death

CI, confidence interval; n, number of patients that contributed to data point; IQR, interquartile range; SD, standard deviation

**Supplementary Table S7.** Direct medical costs of the ten most frequent utilized medical procedures by patients with diabetes who experienced (A) a macrovascular complication alone or (B) in conjunction with a microvascular complication

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Procedure** | **n** | **Mean** **±** **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Treatment of diabetes mellitus | 734 | 329.2 ± 405.2 | 189.9 (97.0; 383.9) | 90.7; 4286.9 | 299.9; 358.6 |
| Treatment of cardiac insufficiency | 418 | 339.2 ± 455.6 | 197.2 (179.4; 286.3) | 176.2; 4733.7 | 295.4; 383.0 |
| Treatment of stroke (ischemic or acute hemorrhagic) | 220 | 293.4 ± 466.9 | 149.3 (124.7; 248.2) | 116.4; 4583.3 | 231.4; 355.5 |
| Complicated diabetic foot treatment | 208 | 225.0 ± 246.1 | 143.8 (86.9; 243.2) | 80.9; 1697.3 | 191.4; 258.7 |
| Amputation/finger disarticulation | 138 | 327.9 ± 812.3 | 136.3 (93.2; 276.3) | 85.2; 7446.9 | 191.1; 464.6 |
| Treatment of pneumonia or influenza  | 131 | 235.8 ± 236.0 | 163.6 (148.7; 220.8) | 146.7; 1928.6 | 195.0; 276.6 |
| Amputation/disarticulation of lower limbs | 126 | 743.8 ± 1126.5 | 359.9 (246.7; 585.7) | 224.8; 7386.1 | 545.2; 942.5 |
| Transthoracic echocardiography | 118 | 16.5 ± 10.2 | 10.1 (9.8; 19.9) | 9.8; 69.3 | 14.7; 18.4 |
| Tonometry | 116 | 3.9 ± 7.0 | 1.8 (0.8; 3.4) | 0.8; 61.5 | 2.6; 5.2 |
| Treatment of acute heart attack | 109 | 411.0 ± 408.4 | 232.1 (158.5; 510.1) | 148.2; 2440.2 | 333.5; 488.5 |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Procedure** | **n** | **Mean** **±** **SD** | **Median (IQR)** | **Minimum; maximum** | **95% CI** |
| Treatment of diabetes mellitus | 362 | 716.6 ± 1182.3 | 335.1 (146.9; 725.0) | 90.7; 12,071.7 | 594.4; 838.8 |
| Hemodialysis (≥3 sessions per week) | 217 | 18,097.2 ± 13,166.2 | 15,784.6 (7044.9; 27,465.4) | 90.2; 51,263.8 | 16,335.5; 19,858.8 |
| Complicated diabetic foot treatment | 198 | 339.9 ± 556.4 | 183.6 (107.6; 371.4) | 80.9; 6572.4 | 261.9; 417.9 |
| Transthoracic echocardiography | 169 | 17.6 ± 11.8 | 10.1 (9.8; 20.2) | 9.8; 89.5 | 15.8; 19.4 |
| Preparation of arterial-venous fistula for hemodialysis | 143 | 219.2 ± 164.6 | 151.2 (124.5; 302.4) | 0.0; 907.2 | 192.0; 246.4 |
| Tonometry | 141 | 4.3 ± 5.4 | 2.3 (0.8; 5.3) | 0.0; 37.6 | 3.4; 5.2 |
| Amputation/finger disarticulation | 140 | 401.5 ± 972.8 | 174.4 (114.0; 348.0) | 7.1; 9084.4 | 239.0; 564.1 |
| Ferric hydroxide sacarate 100 mg injectable (5 mL vial) | 139 | 73.3 ± 138.3 | 38.1 (17.5; 73.8) | 0.0; 1286.0 | 50.1; 96.5 |
| Retinal mapping | 130 | 31.1 ± 37.6 | 18.1 (6.1; 42.3) | 6.1; 260.1 | 24.6; 37.6 |
| Bandage grade II with or without debridement | 130 | 75.2 ± 123.5 | 24.2 (16.1; 70.6) | 0.0; 737.6 | 53.7; 96.6 |

Data presented are direct medical costs in 2019 United States dollars over the study period, both before and after the qualifying complication(s). Costs were weighted by patient observation time using an annual general standardization. Procedures were defined as per the SUS table of procedures, medications and orthoses, prostheses and special materials [1]

CI, confidence interval; n, number of patients that contributed to data point; IQR, interquartile range; SD, standard deviation; SUS, Sistema Único de Saúde (the Brazilian public health system)

**Supplemental references**

1. DataSUS. The SUS table of procedures, medications and orthoses, prostheses and special materials (OPM) (SIGTAP) 2019 [Oct 2019]. Available from: <http://www.sgc.goias.gov.br/upload/links/arq_961_tabelacompleta.pdf>