# *From type 2 diabetes diagnosis to developing complications*

*a multi-country approach to understanding patients' journey*

## BACKGROUND

Overall, incidence and prevalence of Type 2 diabetes (T2D) have increased rapidly in the last decades (1, 2). Micro and macrovascular damage caused by T2D may induce the onset of chronic complications such as kidney disease, retinopathy, neuropathy, cardiovascular, and cerebrovascular disease (3-7). Although there has been extensive research in understanding these conditions independently in populations with T2D, little is known about their specific sequential occurrence in different countries and age groups.

## METHODS

A systematic evaluation of diverse healthcare data sources was performed leveraging the OMOP common data model and OHDSI tools. The study cohort included adult patients with incident T2D identified by diagnosis and treatment codes during the study period running between 2001 and 2019. At least one year of database history should be available before the first T2D diagnosis code in the database, which is considered the index event. Subsequently, we tracked the temporal sequence of occurrence of pre-specified conditions during their observation period. The conditions considered were Chronic kidney disease (CKD), diabetic retinopathy (DR), diabetic neuropathy (DNeu), cardiovascular disease (CVD), cerebrovascular disease (CeVD), heart failure (HF) and peripheral artery disease (PAD). Data sources included in the study are: MarketScan commercial claims and medicare (MS), Optum Claims, and IQVIA US Ambulatory EMR from the US, CPRD and IMRD-UK from the UK, LPD Belgium, LPD France, LPD Italy and DA Germany. Once the condition sequences were determined and tabulated, we used the Txpath tool to produce sunburst plots stratified by database, calendar year, and age category.

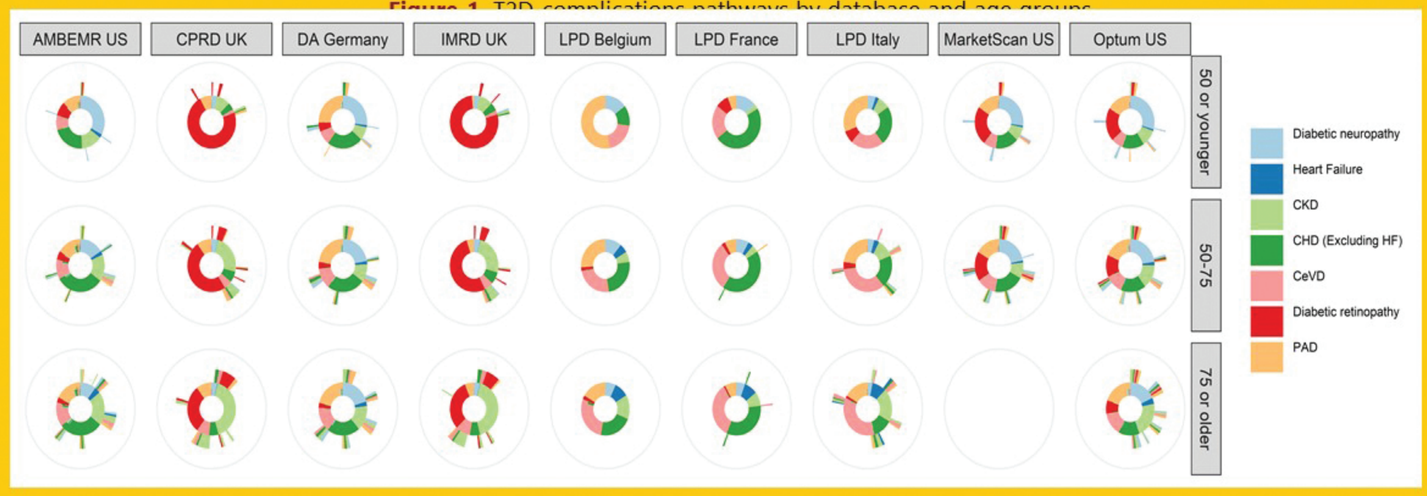


**Table 1.** Baseline characteristics of persons with type 2 diabetes and incidence rate of selected complications

| | DA Germany (n = 118504) | LPD Belgium (n = 10843) | LPD France (n = 74480) | LPD Italy (n = 36128) | IMRD UK (n = 180378) | AMBEMR US (n = 629335) | Marketscan (n = 859789) | CPRD UK (n = 170158) | Optum Claims (n = 430414) |
|---|---|---|---|---|---|---|---|---|---|
| **Age group, n (%)** | | | | | | | | | |
| 15 - 29 | 1114 (1) | 193 (1,8) | 583 (0,8) | 261 (0,7) | 1590 (0,8) | 7265 (1,1) | 8578 (2,4) | 546 (0,8) | 7816 (1,8) |
| 30 - 44 | 9426 (7,9) | 909 (8,3) | 5595 (7,5) | 2054 (5,8) | 9273 (10,6) | 62056 (9,9) | 181526 (21,1) | 17766 (10,5) | 48405 (15,9) |
| 45 - 59 | 38578 (32,6) | 2014 (30) | 23515 (31,6) | 5746 (26,5) | 63973 (35,5) | 206547 (32,8) | 501047 (58,4) | 59306 (34,9) | 160494 (37,4) |
| 60 - 74 | 47756 (40,2) | 4272 (39,4) | 31445 (42,2) | 15281 (42,3) | 69969 (38,7) | 275168 (43,7) | 157052 (18,3) | 66044 (38,8) | 144262 (33,5) |
| 75+ | 3199 (2,7) | 516 (4,7) | 2577 (3,5) | 2243 (6,2) | 4461 (2,4) | | | | |
| **Female, n (%)** | 54333 (45,8) | 5205 (48) | 32522 (43,7) | 16659 (46,1) | 77515 (43) | 314879 (50) | 394348 (45,9) | 73555 (43,2) | 194765 (45,3) |
| **Charlson comorbidity index, Mean (SD)** | 2,1 (1,6) | 1,6 (1) | 1,4 (0,8) | 1,9 (1,3) | 1,8 (1,2) | 1,7 (1,2) | 1,9 (1,4) | 1,6 (1,1) | 2,4 (2) |
| **Incidence rate of complications *** | | | | | | | | | |
| CeVD | 16.25 (15.95, 16.55) | 8.82 (7.9, 9.75) | 7.74 (7.37, 8.11) | 23.84 (23.01, 24.66) | 6.86 (6.71, 7.02) | 18.03 (17.87, 18.18) | 17.07 (16.91, 17.22) | 6.98 (6.81, 7.14) | 32.85 (32.54, 33.16) |
| CHD (Excluding HF) | 29.82 (29.37, 30.26) | 9.16 (8.21, 10.11) | 10.35 (9.92, 10.78) | 12.23 (11.65, 12.82) | 6.43 (6.28, 6.58) | 37.68 (37.44, 37.92) | 24.84 (24.65, 25.03) | 6.58 (6.42, 6.73) | 41.23 (40.87, 41.6) |
| CKD | 16.2 (15.91, 16.49) | 3.23 (2.68, 3.78) | 1.57 (1.41, 1.73) | 10.75 (10.23, 11.28) | 25.2 (24.9, 25.5) | 25.1 (24.91, 25.28) | 13.11 (12.98, 13.24) | 27.72 (27.4, 28.06) | 42.28 (41.92, 42.64) |
| Diabetic neuropathy | 25.68 (25.3, 26.06) | 3.67 (3.08, 4.25) | 2.01 (1.83, 2.2) | 2.86 (2.6, 3.13) | 3.77 (3.66, 3.88) | 20.25 (20.08, 20.41) | 29.2 (29, 29.4) | 3.99 (3.87, 4.11) | 53.39 (52.99, 53.78) |
| Diabetic retinopathy | 4.34 (4.19, 4.49) | 0.79 (0.52, 1.06) | 0.59 (0.49, 0.69) | 2.36 (2.12, 2.6) | 40.0 (39.6, 40.4) | 6.19 (6.1, 6.28) | 22.32 (22.14, 22.49) | 42.16 (41.7, 42.58) | 28 (27.72, 28.27) |
| Heart Failure | 2.97 (2.85, 3.09) | 2.45 (1.97, 2.93) | 1.31 (1.16, 1.46) | 4.2 (3.87, 4.53) | 0.2 (0.17, 0.22) | 5.43 (5.34, 5.51) | 2.05 (2, 2.1) | 0.26 (0.23, 0.29) | 8.56 (8.42, 8.71) |
| PAD | 27.35 (26.94, 27.75) | 9.21 (8.26, 10.17) | 2.09 (1.9, 2.28) | 13.88 (13.26, 14.49) | 4.97 (4.84, 5.1) | 20.33 (20.16, 20.5) | 22.75 (22.57, 22.93) | 10.55 (10.3, 10.75) | 50.61 (50.21, 51) |

* Rate per 1,000 person-years and 95% confidence Interval

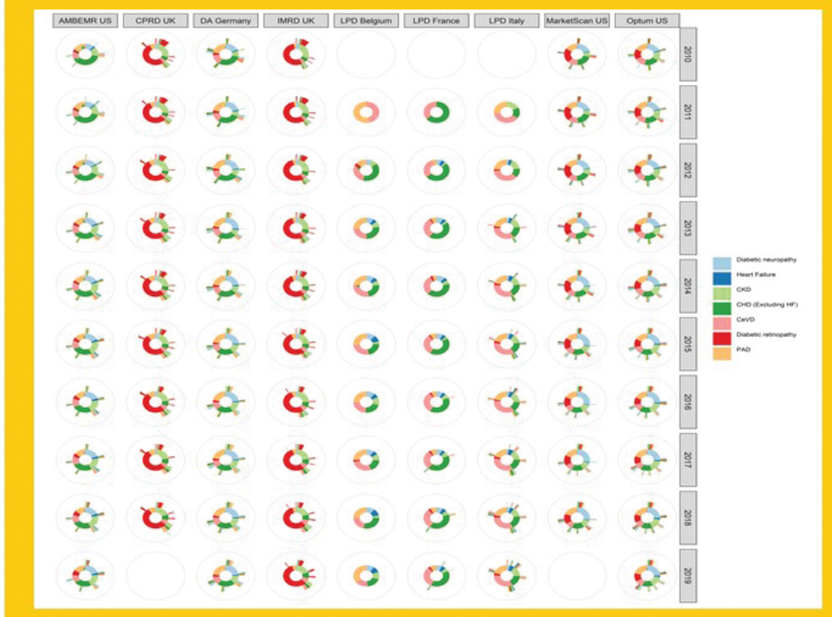



**Figure 2.** T2D complications pathways by database and calendar year (2010 – 2019)

## RESULTS

In total, 2,442,997 T2D patients were identified in the nine databases. Female proportion ranged from 43% in IMRD UK to 48% in LPD Belgium. For all databases except OPTUM and MS, more than half of the population were aged 60 years or more. For OPTUM, 45% of the population was 60 years or more and for MS, it was 40%. Populations had a median Charlson score at index of 1(IQR: 1-2) except for OPTUM and DA Germany where the score was 2 (IQR:1-3). We observed large differences in incidence of complications across databases. For example, CKD ranges from 1.57 cases per 1000 person-years in LPD FRANCE to 42.28 cases per 1000 person-years in OPTUM US. Our results did not detect often more than one complication in the patient journey, perhaps related to the length of follow-up or the setting of the data sources. UK EMR databases were more likely to detect a second condition in the sequence.

## CONCLUSIONS

Our results did not detect often more than one complication in the patient journey, perhaps related to the length of follow-up or the setting of the data sources. Combination of specialist and primary care databases may increase the likelihood of finding multiple complications per patient. We observed differences of T2D natural history in diverse populations from Europe and the US. DNeu and DR, the most frequent complications of T2D, seem more commonly diagnosed as the first complication in younger T2D patients compared to older ones. On the other hand, CKD as a first diagnosis seems more plausible in older groups, but it is seen also in patients aged 50 years or less. When comparing secular changes in calendar years in diagnostic schemes we see little variation. Of note, the irruption of novel antidiabetic treatments in the last decade has not resulted in an apparent reduction of the proportional incidence of CKD or CVD compared to DR or Dneu.


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