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REVIEW
Obesity Comorbidities / Policy

The burden of type 2 diabetes mellitus in states of the European Union and United Kingdom at the national and subnational levels: A systematic review

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Summary

Type 2 diabetes mellitus (T2D) is a highly prevalent disease worldwide, with an equally increased expenditure associated with it. We aimed to longitudinally evaluate the epidemiologic and economic burden of T2D in the current member states of the European Union and the United Kingdom (EU-28). The present systematic review is registered on PROSPERO (CRD42020219894), and it followed the PRISMA guidelines. Eligibility criteria comprised original observational studies in English reporting economic and epidemiological data for T2D in member states of the EU-28. Methodological assessment was performed with the Joanna Briggs Institute (JBI) Critical Appraisal Tools. The search retrieved 2253 titles and abstracts. After study selection, 41 studies were included in the epidemiologic analysis and 25 in the economic analysis. Economic and epidemiologic studies covered only 15 member states with reported data between 1970 and 2017, resulting in an incomplete picture. For children in particular, limited information is available. The prevalence, incidence, mortality, and expenditure of the T2D population have increased across the decades in member states. Therefore, policies should aim to prevent or reduce the burden of T2D in the EU and consequently mitigate the expenditure on T2D.

KEYWORDS
burden, European Union, systematic review, type 2 diabetes mellitus

1 | INTRODUCTION

Type 2 diabetes mellitus (T2D) is a complex metabolic disorder with a gradually increasing incidence worldwide, even between age groups below 30–40 years.[1] The disease is clinically characterized by a hyperglycemic state due to a progressive loss or dysfunction of β-cell mass. The etiology and causal association of the onset of T2D can involve genetic, behavioral, and environmental factors, such as physical inactivity, unhealthy diet, obesity, family history, age, and even race.[2] Individuals with T2D are highly susceptible to a wide number of chronic complications, such as neuropathy, nephropathy, retinopathy, cardiovascular disease, peripheral artery disease, dental disease, and reduced resistance to infection.[3] By 2021, it is estimated that at least one third to one half of people suffering from T2D worldwide were unaware of their disease.[4,5]

Evidence suggests that sex-specific T2D age-standardized prevalence has increased in all member states of European Union

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(EU) between 1990 and 2019.[6] As reversal of the disease is unlikely once it has occurred, prevention is of paramount importance.[7] T2D, as a significant cause of increased morbidity and mortality, results in a heavy economic burden in terms of healthcare expenditures. Individuals with T2D are prone to experiencing a negative impact on their productivity due to their disease, which not only affects the individual with T2D but also society and the national economy.[8] The economic burden of T2D is high due to the high demand on healthcare resources, including costs for medicines and outpatient, inpatient, and diagnostic services. It is also relevant to consider a wider range of indirect costs, such as monetary losses, including opportunity costs (death, disability, incapacitation), transportation expenses, accommodation, nutritional costs, social productivity losses and income losses.[9]

More than 48 million individuals in the EU were estimated to have T2D in 2019, representing 9.9% of the population.[10] Although in the EU the health sector has divided competences—the EU and its member states share powers and responsibilities—under Article 168 of the Treaty on the Functioning of the European Union (TFEU), EU member states are primarily responsible for the health services they provide to their citizens.[11] Following the St Vincent Declaration, there were initiatives in the EU to focus on DM, but these initiatives have failed.[12] The new initiative from 2021 entitled "The Blueprint for Action in the Diabetes in the European Union" is considered a building block for the activities of DM advocacy groups.[13] The EU, as an organization, has the power to provide economic support, such as funding for prevention and research to decrease the burden of this disease in the member states.[14] However, despite the public health measures implemented by the EU and its member states, all the member states show rising prevalence rates of T2D.[6] In fact, according to Global Burden of Disease (GBD) estimates, T2D stands out from the group of noncommunicable diseases (NCDs), as the burden of disease caused by T2D is increasing compared with other major NCD burdens.[15]

The institutions of the EU produce quantitative or qualitative measures to have comparable and reliable data on health and health-related behavior, diseases, and national health systems, for example, by the European Core Health Indicators or results from the European Health Interview Survey (EHIS). Despite the importance of T2D, the majority of data collections report overall outcomes of diabetes mellitus (DM) including T2D as one of the types.[16] Furthermore, policies and initiatives often do not distinguish between types.[13]

This overarching diabetes concept makes it challenging to collect epidemiological, economic, health, and policy data on the T2D population. In addition, most available data are limited to mortality and morbidity data, which do not adequately cover T2D, especially at the subnational level, which is rarely collected. Evidence shows that effective health policies require data collection and analysis with a subnational focus, rather than just a national one.[17]

Currently, there is a lack of systematic reviews regarding economic evaluation and epidemiological measures such as prevalence, incidence, and mortality associated with T2D in all countries of the EU and United Kingdom (EU-28). The lack of evidence implies that data from different countries and regions cannot be compared. This hampers the identification of good practices in prevention and the development of effective health policies tailored to each region or country. Accordingly, the aim is to demonstrate the economic disease burden, prevalence, incidence, and mortality associated with T2D in EU-28 member states through the systematic collection and analysis of epidemiological and economic data.

2 | MATERIAL AND METHODS

2.1 | Protocol and registration

The present systematic review was conducted in September 2020 following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.[18,19] The search was performed after the protocol was accepted on the International Prospective Register of Systematic Reviews (PROSPERO) with the following identification number: CRD42020219894.

2.2 | Research question

Considering that we aimed to assess data on the epidemiological data and economic burden of T2D, two different frameworks were used to develop the research questions. The framework frequently used to analyze incidence and prevalence is CoCoPop[20,21]:

- Condition (Co): T2D.
- Context (Co): Epidemiological data of incidence, prevalence, and mortality.
- Population (Pop): Individuals of any age living in the EU-28 member states, including the current 27 member states and United Kingdom.

For conducting economic evaluation, the PICOC framework was the first choice for systematic reviews in line with the literature[20]:

- Population (P): Individuals of any age with T2D.
- Intervention (I): Not applicable.
- Comparators (C): Not applicable.
- Outcomes (O): Direct costs as diagnosis, treatment and hospitalization expenditures and indirect costs associated with the economic burden of disease.
- Context (C): EU-28 member states, including the current 27 member states and UK.

Thus, our research questions were as follows:

1. What is the prevalence, incidence, and mortality of T2D in EU-28 member states?
2. What are the direct costs of diagnosis, treatment, hospitalization expenditures, and indirect costs associated with the economic burden of disease of individuals with T2D living in EU-28 member states?

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2.3 | Eligibility criteria

Studies were eligible for the present systematic review if they met the following inclusion criteria: (a) Studies in which the full text was published in the English language; (b) original research; (c) studies assessing data on individuals with T2D; (d) studies including individuals living in the EU-27 member states or the United Kingdom; (e) prospective observational studies, such as cohort and case–control nested within cohort studies, and economic studies; and (f) studies assessing prevalence, incidence, mortality, or cost-of-illness of T2D. The eligibility assessment followed this order of inclusion criteria during title and abstract assessment and for full-text analysis. Studies were excluded if they met the following exclusion criteria: (a) Studies such as RCTs, quasi-RCTs, crossover trials, controlled before and after studies, interrupted time series (ITS) studies, nonexperimental studies, studies of simulation models, case reports, series of cases, literature reviews, nonoriginal studies, expert opinions, and letters; (b) studies in which the data regarding T2D were merged with data on different types of diabetes or studies in which the type of diabetes was not explicitly reported; (c) studies in which the data between member states of the EU were merged within themselves; and (d) studies focused primarily on any topic other than T2D disease.

2.4 | Search strategy, study selection, and data extraction

An extensive search was performed in August 2020 by the first reviewer in the following electronic databases: MEDLINE via PubMed, EMBASE, and CINAHL Plus. Additionally, the list of references from the identified relevant articles was screened. A search strategy was created and adapted for each of the databases. The search strategy was based on the CoCoPop and PICOC frameworks, and the most appropriate MeSH terms and Boolean operators were used: (((“Germany”) OR “Belgium”) OR “Croatia”) OR “Netherlands”) OR “Italy”) OR “Hungary”) OR “Slovakia”) OR “Slovenia”) OR “Bulgaria”) OR “Spain”) OR “Denmark”) OR “Finland”) OR “Romania”) OR “Poland”) OR “Sweden”) OR “Greece”) OR “Ireland”) OR “Czech Republic”) OR “Luxembourg”) OR “Cyprus”) OR “Malta”) OR “Lithuania”) OR “Estonia”) OR “Latvia”) OR “Portugal”) OR “Austria”) OR “United Kingdom”)) AND ((((((((“Prevalence”) OR (“Incidence”)) AND (“diabetes mellitus, type 2”))) OR ((“diabetes mellitus, type 2/economics”) OR ((cost of illness) AND (“diabetes mellitus, type 2”))))) AND (cohort studies). Appendix S1 shows the adapted search strategy of each electronic database and the number of studies retrieved in each database.

The title and abstracts from the studies found in the databases were downloaded and imported to an EndNote 20 (*The EndNote Team*, *Clarivate*, *Philadelphia-USA*) library so that duplicate removal could be performed. Then, a master file containing the titles and abstracts of the studies was created. Five trained reviewers participated in the study selection process in pairs, with the fifth reviewer resolving any disagreements. A pilot screening of 30 studies was performed with the five reviewers in a calibration process, in which all the reviewers screened the same papers. Then, Cohen's kappa coefficient was used to assess the interrater reliability, and a meeting was held to discuss any disagreements and standardize the screening process. After the calibration process, the master file was then divided into six sections containing an equal number of studies. Each pair of reviewers was responsible for screening three sections, and disagreement meetings were held with the whole group. Eligibility criteria groups were generated in the EndNote file in the following order: (a) English language studies, (b) original research, (c) studies on the EU population, (d) studies on individuals with T2D, (e) cohort studies, and (f) studies assessing the economic burden or epidemiological measures of T2D. The reviewer selected “Include,” “Exclude,” or “Unclear” for each study. If the “Excluded” option was selected, the screening process ended for the study; otherwise, the screening process followed as mentioned. After all sections were screened, the full text of the studies included in the last group (f) were retrieved, downloaded, and imported to an EndNote file. If the full text was not available in a database, library, or website, the study was excluded from the systematic review.

The full-text screening followed the same methods of the title and abstract phases. A calibration was performed by the five reviewers with five papers, and a meeting to standardize the screening process was held. The eligibility criteria groups were placed in the same order; however, the “Unclear” option was excluded from the file. Another EndNote file was created containing all the included studies after an extensive screening process. Two online forms were created (Forms Office, Microsoft) so the data extraction could be accomplished by the reviewers in pairs; these forms were based on the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis.[22] One form was used to extract epidemiological measures, and the other form was used for economic burden data. Both forms had questions regarding the study characteristics (first author, publication year, country of the research, database or data source, and ethics approval), study methods (aims of the study, country, setting, study design, and follow-up), and sample characteristics (size, groups, age range, gender, methods of diagnostic, and/or definitions of T2D). The epidemiological form had specific questions regarding the type of measure analyzed in all the follow-up periods' prevalence, incidence, and mortality. Studies were considered to be population based if the selected sample included the entire population of a country or region. This means that all individuals in a given region who met the inclusion criteria were eligible to participate in the study.[23] The economic form was composed of questions related to the type of cost, currency, and prices related to T2D expenditures. All the data inserted into the forms were converted into an Excel file after the disagreement meetings.

2.5 | Methodological quality assessment and data analysis

The methodological quality assessment was carried out after all the studies had their data extracted. The JBI Critical Appraisal Tools for

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economic evaluations and for cohort studies were used for the quality assessment.[24] The forms were filled out by pairs of reviewers, and disagreements were resolved in meetings with the fifth reviewer. Both the checklist for cohort studies and that for economic evaluation contain 11 questions. However, the research group defined a few questions as highly critical domains to promote more accurate quality assessment of the cohort and economic studies: Items 3, 7, and 8 and items 3, 5, and 10, respectively. Additionally, the JBI critical appraisal checklist for studies reporting prevalence data was also used to assess the studies reporting prevalence and incidence.[25] Studies were considered to have low methodological quality if the following answers were provided for critical domain questions: Two "no" responses, one "no" response and one "unclear" response, or two "unclear" responses. Studies were also considered to have low methodological quality if the following answers were provided for noncritical domain questions: one "unclear" response and two or more "no" responses. High methodological quality was determined if the studies had a maximum of one "no" response or two "unclear" responses on noncritical domain questions.[24,26]

After data extraction regarding epidemiologic and economic measures, a few strategies to standardize and enable comparison within studies were taken. For prevalence, incidence, and mortality, the preferred measure was percentage. In cases in which the study reported the number of cases instead of the percentage, a calculation was performed to convert the data (see Equation 1 below). This strategy was also used in papers reporting the number of cases per year without the number of populations; in those cases, the population by year was extracted from EUROSTAT, and the percentage was calculated. Other studies reported rates per 1000 (see Equation 2a), 10,000 (see Equation 2b), or 100,000 (see Equation 2c); in those cases, another calculation strategy was taken. Epidemiologic measures were not presented in percentages in the final table if the rate was too small to be converted. Extracted data regarding prevalence, incidence, and mortality are gathered in Table S1.

$$\% = \frac{(number\ of\ cases \times 100)}{Population\ in\ a\ certain\ year} \tag{1}$$

$$\% = (x\ rate\ per\ 1000) \times 0.1 \tag{2a}$$

$$\% = (x\ rate\ per\ 10\,000) \times 0.01 \tag{2b}$$

$$\% = (x\ rate\ per\ 100\,000) \times 0.001 \tag{2c}$$

Economic studies report many different types of expenditure data. For this reason, all costs related to individuals with T2D are presented in Table S2 regardless of the type. To make further comparisons possible, five types of costs were either calculated or directly extracted: Mean annual direct cost, mean annual indirect cost, mean annual total cost, gross annual direct cost, and gross annual indirect cost. Direct costs were calculated based on the expenditure directly attributable to healthcare for the patient. Indirect costs were considered if the expenditure was related to anything other than patient care. Total costs were the sum of both of the above-cited types of costs.[27] After extracting, merging, or calculating direct, indirect, or total costs, all of them were adjusted for inflation for the year 2021 (Euro €). In cases of studies reporting semiannual means twice a year, they were summed to allow annual conversion. If costs were presented for only one semester of the year, they were multiplied by two to estimate the annual mean. Gross costs are reported as the mean cost of illness by person on a sample extrapolated to the whole population, and they were only included if the original study reported it.[28]

The interrater reliability rate for each phase of the study was calculated with Cohen's kappa coefficient (κ) in SPSS (IBM SPSS Statistics for Windows, version 25 [IBM Corp., Armonk, N.Y., USA]). Review Manager 5.3 (The Cochrane Collaboration, Copenhagen, Denmark) was used for methodological quality assessment synthesis. Although heterogeneity between studies prevented a meta-analysis, the economic burden and epidemiological measures for each country were summarized to facilitate further analysis.

3 | RESULTS

3.1 | Literature search and study selection

The literature search in the databases retrieved 1983 titles and abstracts, while records identified through other sources retrieved 270 titles. A total of 474 of these studies were found to be duplicates, and they were excluded accordingly. Next, the reviewers proceeded to analyze the 1779 titles and abstracts, and 1441 of these were excluded based on the eligibility criteria. In the next phase, 338 full texts were analyzed by the reviewers considering the inclusion and exclusion criteria for epidemiological or economic studies. Ultimately, 41 studies were included in the epidemiological analysis, and 25 studies were included in the economic analysis, with eight studies included in both evaluations (Figure 1). Cohen's kappa coefficient was used to assess the agreement rate between the two reviewers throughout all the methodological phases, and the rate was 0.83, which is considered "strong agreement."[29]

3.2 | Study characteristics and methodological assessment

All 41 studies included in the epidemiological analysis were published between 1991[30] and 2020.[31,32] The included studies reported data from 12 different countries, with the number of papers from each country as follows: Austria—2,[33,34] Denmark—4,[32,35–37] France—4,[31,36–38] Finland—1,[39] Germany—9,[8,38,40–46] Hungary—1,[47] Belgium—1,[38] Italy—4,[38,48–50] the Netherlands—2,[38,51] Spain—3,[38,52,53] Sweden—5,[30,38,54–56] and United Kingdom—14[38,57–69] (Figure 2). Some papers reported data on more than one country. The data source from which each study retrieved epidemiological data was highly heterogeneous within the publications, and most of the data were collected in databases, previous studies, or clinical/laboratory

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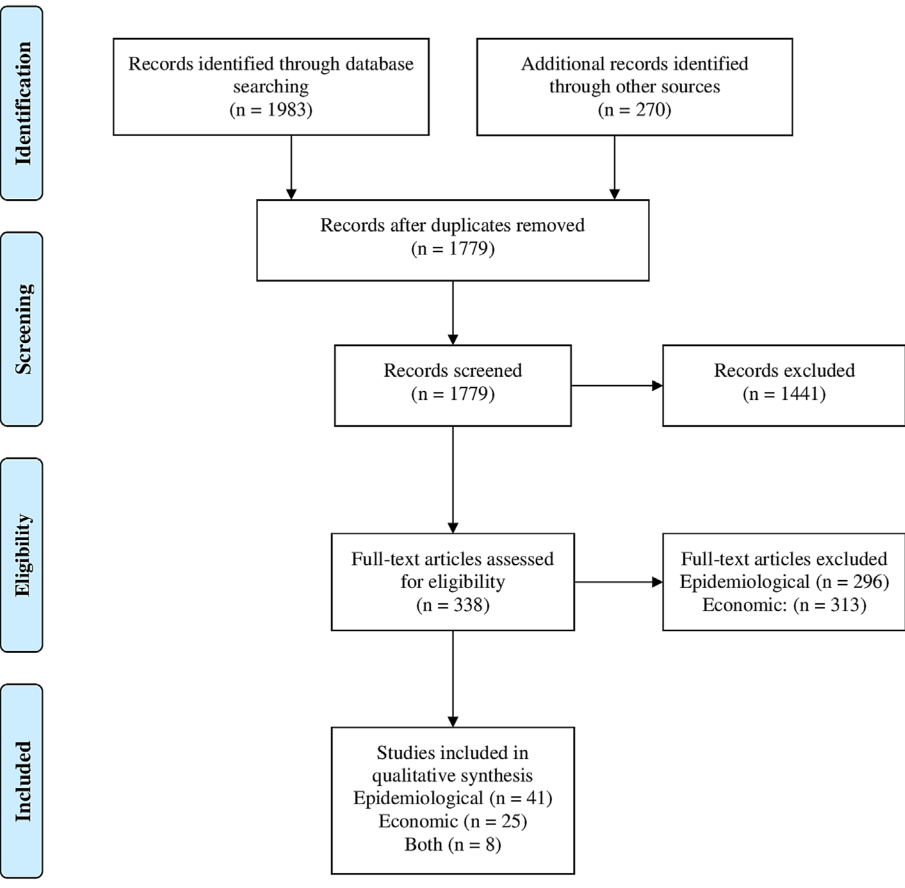

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) with description of the study selection process.

	Sweden	UK	Belgium	France	Germany	Italy	Netherlands	Spain	Austria	Denmark	Finland	Hungary	Total by year
1991	1												1
1995	1	1											2
2002	1	1	1	1	1	1	1	1					8
2003							1		1				2
2005						1							1
2006		1											1
2007		2								1			3
2008	1	1											2
2009		2			1				1				4
2011		1		1		1		1		1			5
2012		1		1	1					1			4
2013		1			1						1		3
2014					1			1					2
2015	1				2								3
2017		2			2	1							5
2018		1											1
2020				1						1		1	3
Total by country	5	14	1	4	9	4	2	3	2	4	1	1	50

FIGURE 2 Included studies reporting epidemiologic data from member states, with the number of papers from each country.

settings. A few examples of settings and databases cited in the papers were as follows: Hospitals,[35,52,56,69] social security systems,[43] primary care centers,[52,55] clinical centers/practices,[49,56,57,59,66] health information network,[44,68] laboratories,[35,50] national health systems,[31,32,34,35,49] health insurance systems,[8,39,46,47,56] surveys,[30,44] and research datalinks.[33,38,39,48,54,58,60,61,63,65,67] Secondary data

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analysis based on the following databases was published: AOK,[41] CPRD,[61,65,67] RECAP-DM,[55] SHIP,[44] EMIS,[68] CARLA,[44,45] DHS,[44] HNR,[44] KORA,[40,44] EPIC,[57,64] Ely,[59,62] Inter99,[36,37] D.E.S.I.R,[36,37] ACG,[48] Asturias,[53] ZODIAC,[51] BPSU,[58] and CODE-2.[38] Information related to ethical approval was also assessed; 18 studies did not have ethical approval or did not consider it to be necessary,[31,32,34–38,42,43,45–50,56,63,69] five studies were unclear regarding whether the protocol was approved,[8,40,52,65,66] and 18 reported the actual ethical approval by a formal committee.[30,33,39,41,44,51,53–55,57–62,64,67,68] The methodological quality assessment demonstrated that 37 studies were classified as "high quality,"[8,30–33,35–37,40–62,64–69] one study as "moderate quality,"[34] and three studies as "low quality."[38,39,63] Overall, 90.47% of the included papers on epidemiological analyses were classified as "high quality" (Table S3). Additional information about the methodological assessment of prevalence and incidence studies can be found in Table S4.

The economic analysis included 25 studies published between 2001[70] and 2019.[71,72] The member states for which the studies reported data were as follows: Belgium—1,[38] France—4,[38,71,73,74] Germany—7,[38,42,43,46,74–76] Greece—4,[74,75,77,78] Italy—3,[38,48,79] Netherlands—3,[38,72,80] Poland—1,[81] Spain—6,[38,52,74,75,82,83] Sweden—4,[38,43,75,84] Ireland—1,[85] and UK—5.[38,66,70,74,86] A few studies were conducted in more than one country. The number of papers in each country is cited above after the name of the country (Figure 3). Different sources of data were reported in the included studies for cost analysis; a few examples are as follows: hospitals,[52,85] social security systems,[43] primary care centers,[55,84] clinical centers/practices,[66,70] endocrinology clinics,[79,83] health information network,[86] national health systems,[75,81] health insurance systems,[46,73,81] statistical office,[81] national surveys,[38] and research datalinks.[48,82] A few studies did not report the data source, or it was not applicable.[42,76,78,80] Similarly, the economic studies reported secondary data from other study sources: VEKTIS,[72] SNDS,[71] ZODIAC,[72] RECAP-DM,[55] ROSE,[84] INSTIGATE,[74,75,77] TREAT,[75] CODE-2,[38,70] and CODEIRE.[85] Since the analysis was a cost evaluation, most of the studies did not have, or need, ethical approval ($n = 14$).[38,42,43,46,48,52,71–73,79–81,83,86] However, six studies reported that they were officially approved by an ethics committee,[55,70,74,78,84,85] and five studies left this topic unclear through the text.[66,75–77,82] Unlike the previous analysis, the economic quality methodological assessment showed that only 36% of the economic studies were evaluated as "high quality." The analysis indicated nine studies to be "high quality,"[48,52,71,73,76,81,82,85,86] one to be "moderate quality,"[77] and 15 to be "low quality"[38,42,43,46,55,66,70,72,74,75,78–80,83,84] (Table S5).

3.3 | Study findings from the epidemiologic evaluations

3.3.1 | Studies reporting prevalence

In the United Kingdom, the study with longest follow-up reported nationwide prevalence of T2D, in a population of all ages, ranging from 1.32% in 1991 to 3.05% in 2004 and 4.54% in 2013.[65] Similarly, in a smaller population of individuals above 16 years old, the prevalence of T2D was very similar, going from 3.80% for males and 2.68% for females in 2004 to 6.25% for males and 4.37% for females in 2014.[61] Subnationally, in Tayside (Scotland), the prevalence of T2D in a "low quality" population-based study matched very closely the national percentages: 1.49% in 1993 to 3.12% in 2004.[63] A nationwide population-based study from Denmark reported prevalence of T2D from 1996 to 2017, ranging from 1.16% for males and 1.17% for

	UK	Ireland	Netherlands	Sweden	Belgium	France	Germany	Italy	Spain	Greece	Poland	Total by year
2001	1											1
2002	1		2	1	1	1	1	1	1			9
2006		1						1	1			3
2008				1								1
2010	1											1
2012	2					1	2		1	1		7
2013				1			1		1	2		5
2014									1		1	2
2015				1			2			1		4
2016									1			1
2017							1	1				2
2018						1						1
2019			1			1						2
Total by country	5	1	3	4	1	4	7	3	6	4	1	39

FIGURE 3 Included studies reporting economic data from different member states, with the number of papers from each country.

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females, to 4.83% for males and 3.90% for females, respectively.[32] Subnationally, between 2000 and 2003, accounting only the population within 40–70 years old of the County of Aarhus, the prevalence was higher: 3.73%.[35] For Italy, a single population-based study reported prevalence percentage; in this study, the T2D prevalence of adult individuals only for Verona was 5% in 2012.[48] According to a nationwide population-based study in Germany, the prevalence of T2D was 9.8% in 2010.[46] The German region with highest prevalence percentage was the East region with 9.33% in 2002–2006, and the lowest was the South with 3.32% in 1999–2001.[44] In France, a much higher prevalence was found in a study analyzing individuals above 45 years in the National Health Data System—the prevalence of T2D for males was 11.5% in 2010 and 12.1% in 2017; for females, it was 7.9% and 8.1% in the same years.[31] In a population of 2 million individuals under 18 years old in Hungary, the prevalence of T2D ranged from 19.85 per 100,000 in 2001 to 22.15 per 100,000 in 2016.[47]

In 1999, the prevalence percentage of T2D in a nationwide population of adults above 30 years old was 1.7% in the Netherlands, 2.2% in France, 3% in Italy, and 3.3% in Belgium.[38] In Spain, a similar tendency was found, since a smaller prevalence of 3.9% was reported in 1999[38] and an increased percentage of 14% was found only for Barcelona (Badalona) later in 2010.[52] In Sweden, the lowest prevalence percentage was found in Vetlanda Municipality in 1987[56] and the highest was 3.6% being reported nationally for 1999.[38] In Germany, the prevalence of T2D in a non-population-based study was 6.8% in 2005[43] and 4.2% similar study.[38] Prevalence measures reported in studies are shown in Table 1.

3.3.2 | Studies reporting incidence

The incidence of T2D in the United Kingdom, for individuals of all ages, ranged from 0.16% in 1991 to 0.38% in 2003.[67] Between 2004 and 2010, two studies evaluated incidence of T2D in the UK population. One study reported values 0.41%–0.36% (males-females) in 2004 and 0.53%–0.49% (males-females) for 2010,[67] while the other study showed an incidence of 0.52%–0.38% (males-females) in 2004 and 0.51%–0.34% (males-females) in 2010.[61] Subnationally, the lowest incidence percentage in the United Kingdom was 0.19% which occurred in Tayside (Scotland) in 1993.[63] The highest percentage was 2.46% found between 1993 and 2004 in adults (40–78 years) in Norwich (Norfolk, England).[64] In Germany, the only nationwide analysis included 8787 individuals (45–74 years) and the incidence percentage was 5.9% in a mean follow-up between 2.2 and 7.1 years considering a baseline at 1997–2006. The same study reported the lowest incidence of T2D in Germany, being 3.7% in the West region.[44] A long follow-up study in Västerbotten County (Sweden), with an average 10-year follow-up between 1990 and 2013, reported a T2D incidence of 7%, based on a sample of 32,120 people (aged 35 to 55 years).[54] In a population-based study in Denmark, the incidence of T2D was 0.21% in 1996, 0.22% in 2000, and 0.32% in 2016.[32] In the Netherlands, the incidence percentage was the same as in Denmark in 2000: 0.22%.[51] In northern Spain, the incidence of T2D was 6.98% between 1998/1999 and 2004/2005, in a 630 sample of people (aged 30–75 years).[53] The lowest incidence rates were found in Turin (northern Italy), for adults (aged 30–49 years) in 1999, 2000, and 2001, 50.7, 41.1, and 58.0 per 100,000, respectively.[49] Both Austrian studies analyzed a nationwide sample of people under 15 years old. The incidence between 1999 and 2001 was 0.25 per 100,000 (eight cases) in a "moderate methodological quality" study[34]; however, in the other study (high quality), the incidences in 1999, 2000, and 2002 were respectively: 0.14, 0.28, and 0.42 per 100,000.[33] In the United Kingdom, the incidence of T2D for people under 17 years old in 2015 was 0.72 per 100,000.[58] For children and adolescents in Hungary, the incidence of T2D was much higher between 2001 and 2016: 8.35 and 5.06 per 100,000 in 2016.[47]

The highest regional percentage was 10.5%, found in Southern Germany between 2001–2008 in a sample of 887 individuals (55–74 years) from a non-population-based study.[40] The highest follow-up between studies was 34 years in Finland (Helsinki), and the incidence percentage was 9.43% in a sample of 1145 males[39]; however, the study was assessed as a "low quality" study regarding its methodology and it was not population based. The oldest study was also performed in Sweden (Uppsala) with the same 10-year average follow-up; the incidence percentage for 1860 males was 4.13%.[30] In France, the incidence of the disease was 2.4% in a sample of 3784 people (aged 30–65 years) in the 1994–1996 baseline study and 6-year follow-up.[36,37] Incidence measures reported in studies can be found in Table 2.

3.3.3 | Studies reporting mortality

In Germany, a population-based study reported a mortality percentage of 16% in 2010 within 64.9 million people.[8] In Tayside (UK), a "low quality" population-based study reported the mortality per individual with T2D was 6.9% in 1993 and 5.39% in 2003.[63]

Another German study comprised a sample of 19,888 individuals, and the mortality was 7.17% in a 3-year follow-up between 2005 and 2007.[42] In Cambridgeshire (UK), the mortality among people aged 40–65 was 6% between 1991–1998 and 8% between 2000–2008.[59] Mortality measures reported in studies are shown in Table 3.

3.3.4 | Study findings from the economic analysis

In Belgium, the estimated total gross direct cost of T2D in 1998 was €1.62 billion, estimated on the basis of an annual average of €4842.97 per person per year in a "low quality" study.[38] However, a "high quality" study in Poland assessed direct costs for the T2D population, except for drugs and primary care; it was estimated at €31.87 million in 2004 and rose to €61.35 million in 2009.[81]

In France, a "low quality" study estimated total direct costs of €5.85 billion per year for T2D population between 1997 and 1999[38]; a "high level" study reported an increased amount of €9.2 billion for 2013.[73] The mean direct cost for T2D individuals in France was €4503.45 in 1998.[38] In 2006, two studies reported the annual direct

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TABLE 1 Prevalence data of EU member states and subnational regions.

Country	Region/City	1978	1980	1987	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
UK	24 British towns	1.20%		12.10%												
	Norwich						3.30%									
	Tayside (Scotland)						1.49%	1.58%	1.68%	1.78%	1.89%	2.03%	2.14%	2.32%	2.53%	2.72%
	Nationwide				1.32% (1.30–1.34)	1.43% (1.41–1.45)	1.51% (1.49–1.53)	1.59% (1.57–1.61)	1.67% (1.65–1.69)	1.76% (1.74–1.78)	1.82% (1.80–1.83)	1.93% (1.91–1.94)	2–2.04% (2.02–2.06)	2.18% (2.16–2.19)	2.39% (2.37–2.40)	2.61% (2.60–2.63)
Hungary	Nationwide														19.85°	23.69°
Denmark	Nationwide									1.16–1.17%	1.29–1.27%	1.41–1.36%	1.54–1.45%	1.68–1.56%	1.81–1.66%	1.94–1.74%
	County of Aarhus													3.73%		
Italy	Nationwide												3%			
	ULSS20 Verona in Italy															
France	Nationwide												2.20%			
Germany	Nationwide												4.20%			
	East															9.33%
	Northeast										8.10%					
	West													5.60%		
	South												3.32%			
Sweden	Vetlanda Municipality			1.33%												
	Nationwide												3.60%			
	Uppsala County													2.30%	2.47%	2.56%
Belgium	Nationwide												3.30%			
Netherlands	Nationwide											2.16% (2.13–2.28)	2.83%			
													1.70%			
Spain	Nationwide												3.90%			
	Badalona (Barcelona)															

° - Rate per 100,000

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TABLE 1 Prevalence data of EU member states and subnational regions.

Country	Region/City	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
UK	24 British towns	12.10%														
	Norwich															
	Tayside (Scotland)	2.91%	3.12%													
	Nationwide		3.80% (3.77–3.83) –2.68% (2.66–2.70)	4.19% (4.16–4.22) –2.97% (2.95–2.99)	4.70% (4.67–4.73) –3.34% (3.32–3.37)	5.00% (4.97–5.04) –3.56% (3.54–3.59)	5.26% (5.23–5.29) –3.73% (3.70–3.75)	5.52% (5.49–5.56) –3.90% (3.87–3.93)	5.80% (5.76–5.83) –4.07% (4.04–4.10)	6.01% (5.98–6.05) –4.22% (4.19–4.25)	6.13% (6.09–6.16) –4.28% (4.25–4.31)	6.21% (6.17–6.25) –4.31% (4.28–4.34)	6.25% (6.21–6.29) –4.37% (4.33–4.40)			
		2.83% (2.82–2.85)	3.05% (3.04–3.07)	3.26% (3.24–3.28)	3.47% (3.45–3.48)	3.64% (3.62–3.66)	3.83% (3.81–3.84)	3.99% (3.98–4.01)	4.18% (4.16–4.19)	4.34% (4.32–4.36)	4.46% (4.44–4.48)	4.54% (4.52–4.56)				
Hungary	Nationwide	29.08°	33.23°	35.23°	36°	34.15°	32.15°	30.62°	29.54°	28.15°	26.77°	27.23°	25.69°	23.54°	22.15°	
Denmark	Nationwide	2.11–1.90%	2.31–2.06%	2.52–2.23%	2.68–2.34%	2.83–2.43%	2.99–2.54%	3.19–2.68%	3.41–2.82%	3.66–2.98%	4.04–3.3%	4.3–3.51%	4.46–3.64%	4.59–3.73%	4.7–3.81%	4.83–3.90%
	County of Aarhus	3.73%														
Italy	Nationwide															
	ULSS20 Verona in Italy										5%					
France	Nationwide								11.5–7.9%	11.7–8.0%	11.9–8.1%	11.9–8.1%	12.1–8.2%	12.2–8.2%	12.2–8.2%	12.1–8.1%
Germany	Nationwide			6.80%		8.20%			9.80%							
	East	9.33%														
	Northeast															
	West	8.38%														
	South															
Sweden	Vetlanda Municipality															
	Nationwide															
	Uppsala County	2.67%	2.72%													
Belgium	Nationwide															
Netherlands	Nationwide															
Spain	Nationwide															
	Badalona (Barcelona)								14% (13.7–14.2)							

° - Rate per 100,000

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TABLE 2 Incidence data of EU member states and subnational regions.

Country	Region/City	1970	1974	1978	1980	1987	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
UK	Leicester					0.29%												
	Cambridgeshire						0.73% (0.57–0.94)											
	Norfolk Region									1.30%								
	Tayside (Scotland)									0.19%	0.19%	0.21%	0.19%	0.22%	0.23%	0.26%	0.29%	0.32%
	England and Wales									3.06%								
	Norwich									2.46%								
	Exeter																	
	Nationwide							0.16%	0.17%	0.17%	0.16%	0.19%	0.19%	0.21%	0.25%	0.28%	0.37%	0.43%
Hungary	Nationwide																	8.35[a]
Finland	Helsinki		9.43%															
Denmark	Copenhagen															2.80%		
	Nationwide												0.21%	0.20%	0.22%	0.23%	0.22%	0.22%
France	Nationwide										2.40%							
Sweden	Uppsala	4.13%																
	Västerbotten County						7% (6.56 to 7.13)											
Austria	Nationwide															0.25[a]		
	Nationwide															0.14[a] (0.03–0.44)	0.28[a] (0.10–0.64)	0.42[a] (0.18–0.82)
Italy	Turin															50.7[a] (45.5–56.5)	41.1[a] (36.6–46.3)	58[a] (54.7–61.5)
	Desio								2.20%									
Germany	Lower Saxony																	
	East																	
	Northeast													6.50%				
	West																3.7–5.9%	
	South															6.30%		
	Nationwide																5.90%	
	Southern																	10.50%
	Halle																	
Spain	Principality of Asturias (Northern)														6.98% (4.5–12.71)			
Netherlands	Nationwide															0.22% (0.22–0.22)		

[a]Rate per 100,000.

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TABLE 2 Incidence data of EU member states and subnational regions.

Country	Region/City	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
UK	Leicester															
	Cambridgeshire															
	Norfolk Region															
	Tayside (Scotland)	0.33%	0.34%	0.38%												
	England and Wales															
	Norwich	2.46%														
	Exeter							1.65%	2.23%	2.06%						
	Nationwide	0.45%	0.38%	0.39%	0.38%	0.38%	0.44%	0.48%	0.53%	0.52%						
				0.52% (0.51–0.53) –0.38% (0.37–0.39)	0.49% (0.48–0.50) –0.36% (0.35.- 0.37)	0.64% (0.63–0.65) –0.46% (0.45–0.47)	0.49% (0.48–0.50) –0.35% (0.34–0.36)	0.49% (0.48–0.50) –0.34% (0.33–0.35)	0.52% (0.50–0.53) –0.35% (0.34–0.36)	0.51% (0.50–0.52) –0.34% (0.33–0.35)	0.47% (0.46–0.48) –0.33% (0.32–0.34)	0.48% (0.47–0.49) –0.34% (0.33–0.34)	0.51% (0.50–0.52) –0.35% (0.35–0.36)	0.42% (0.41–0.43) –0.31% (0.30–0.32)	0.72[a]	
Hungary	Nationwide	6.38[a]	7.8[a]	8.24[a]	7.55[a]	7.07[a]	5.17[a]	4.91[a]	4.91[a]	6.2[a]	5.32[a]	5.98[a]	6.85[a]	4.77[a]	4.62[a]	5.06[a]
Finland	Helsinki	9.43%														
Denmark	Copenhagen	2.80%														
	Nationwide	0.28%	0.31%	0.31%	0.27%	0.26%	0.28%	0.31%	0.33%	0.37%	0.51%	0.40%	0.32%	0.30%	0.31%	0.32%
France	Nationwide	2.40%														
Sweden	Uppsala															
	Västerbotten County	7% (6.56 to 7.13)														
Austria	Nationwide															
	Nationwide	0.55[a] (0.27–0.99)	0.2[a] (0.06–0.53)	0.07[a] (0.01–0.32)	0.21[a] (0.06–0.55)	0.15[a] (0.02–0.43)	0.34[a] (0.14–0.72)									
Italy	Turin															
	Desio	2.20%														
Germany	Lower Saxony				5.24%											
	East	6.40%														
	Northeast															
	West	3.7–5.9%														
	South															
	Nationwide	5.90%														
	Southern	10.50%														
	Halle			4.45%												
Spain	Principality of Asturias (Northern)	6.98% (4.5–12.71)														
Netherlands	Nationwide															

[a]Rate per 100,000.

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TABLE 3 Mortality data of EU member states and subnational regions.

Country	Region/City	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2005	2007	2008	2010
Germany	Nationwide												7.17%			16%
UK	Tayside (Scotland)	6.9%	6.67%	7.05%	6.32%	5.15%	5.68%	5.47%	4.92%	4.81%	4.77%	5.39%				
	Cambridgeshire	6%							8%							

cost that ranged from €2474.97 in a “high quality” study[71] to €3492.6 in a “low quality” study.[74] Similarly in 2013, two “high quality” studies reported different costs, the mean annual direct costs were €4915.06 in one study[71] and another one reported €7055.91.[73] The mean indirect costs in France were €702.51 in 2006 and €491.48 in 2015. The total costs amounted €5593.66 in 2008 and €5935.45 in 2015.[71]

For the T2D population in Germany, a “low-quality” study estimated an annual direct cost of €1.83 billion between 1996 and 1998.[38] In 2010, the gross direct costs increased to €32.8 billion in one “high quality” study[76] and €38.5 in another (low quality).[46] The annual mean direct costs per person for Germany were €5255.98 between 1996–1998 in one study (low quality),[38] decreasing to €3977.5 in a “low quality” study in 2003, including only hospital and drug costs.[42] Additionally, two “low quality studies” reported direct annual cost per person in Germany in 2006, being €2394 in one study[74] compared with €2955.76 in another.[43] In a sample including T2D insured by the German statutory health insurance system, in a “high quality” study the direct costs per person were €5955.5 in 2010[76] and another “low quality” study reported €5065.53 for the same year.[46]

All four studies reporting cost analyses in Greece reported only the direct annual mean expenditure for people with T2D and they were considered from “low” to “moderate” quality. Three studies used the same baseline sample of the Greek T2D population from the INSTIGATE database (2005–2008). In their first and second years, the sample presented mean costs of €1331.53 and €1205.68, respectively.[74,75,77] One of these studies also used the TREAT database (2007–2010), and reported an annual cost was €1440.1.[75] Another study had a different follow-up from 2001 to 2011 with an annual mean cost of €7712.05.[78]

In Italy, a “low quality” study estimated annual direct expenditure at €7.6 billion, based on an annual average of €4396.15 per person.[38] Regionally, in northern Italy, another “low quality” study reported the indirect costs per person to be €2715 between 2001 and 2002 in Portogruaro[79] and the mean direct costs, including hospitalization, outpatient care, and medications, were €3639.2 for 2012 in Verona in a “high quality” study.[48]

According to a nationwide study in Spain, the annual direct expenditure was €2.88 billion, and the mean per patient was €1918.08 in 1998–1999.[38] Two studies reported the costs of individuals with T2D initiating insulin therapy (INSTIGATE),[74] with one reporting the costs for the first semester and the second for the entire year.[75] One study had an annual mean direct cost of €2765.18 in 2006[74] and decreased to €2041.7 in another study (2005–2008).[75]

The highest costs found regionally in Spain were from Cadiz in 1999, where the mean direct, indirect, and total costs were €3719.06, €2678.88, and €6397.94, respectively.[83]

In 1998, the Netherlands had a gross direct annual expenditure of €627 million based on the cost per patient of €2891.08 in one study[80] and €652 million extrapolated from €2685.31 in another one.[38] For the same year, the indirect costs based on productivity lost and travel costs were estimated to be €58.6 million.[80] Between 2008 and 2011, the annual direct mean per patient was €5047.02 for the northern region of the Netherlands.[72] Nationally, in Sweden for the period between 1993–1996, the annual mean gross direct expenditure in billions was estimated to be €1.08, which was estimated based in the mean direct cost per patient of €3865.56.[38] A study estimated a direct annual cost to be €4537.18 in 2001, decreasing to €3330.34 in 2009[84] and €1795.2 in 2010 in a study comprising individuals starting insulin therapy between 2007 and 2010.[75] In Uppsala (Sweden), the annual mean for direct costs was €4391.17 in the period between 2000 and 2004.[55] All studies reporting costs for the Netherlands and Sweden had a “low quality” methodological assessment.

In the United Kingdom between 1994 and 1995, the direct costs amounted to an annual mean of €3.83 billion and a per patient mean of €3254.12.[38] In 1998, the direct costs for Bradford, Jersey, and Salford (UK) were €2800.66.[70] Comprising only costs for primary care and prescriptions, the direct costs per patient were €895.69 in 1997 and €1316.62 in 2007 in a “high quality” study.[86] In another study (low quality), the mean annual direct cost per patient was €1925.66 only for 2006.[74] In a “high quality” study reporting cost data for Dublin and Cork (Ireland), the total expenditure for direct costs was €501.4 million, and the mean per patient was €3281.7 in 1999.[85] Economic findings reported in studies can be found in Table 4.

4 | DISCUSSION

Our unique systematic review based on 41 articles draws from 47 years of longitudinal data (1970–2017), including data on prevalence, incidence, and mortality and direct and indirect costs associated with T2D in the EU-28, such as hospitalization, drugs, complications, consultations, and blood glucose control emergencies. Research questions on the epidemiological and economic burden of T2D are discussed in the following six points.

First, data on T2D are generally incomplete, especially for data from Eastern European countries, despite the fact that a country-by-country search has been applied. No studies were identified mainly

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TABLE 4 Economic data of EU member states and subnational regions.

Country	Region	Type of cost	1994	1997	1998	1999	2000	2001	2002	2003	2004	2005
Belgium	Nationwide	Annual direct in billion			1.61							
		Annual direct (mean)			4842.97 (58.82–108648.67)							
France	Nationwide	Annual direct in billion			5.85							
		Annual direct (mean)			4503.45 (29.41–121581.81)							
		Annual indirect (mean)										
		Annual total (mean)										
Germany	Nationwide	Annual direct in billion			1.83							
		Annual direct (mean)			5255.98 (117.64–103128.38)					3977.5		2796.65
Greece	Nationwide	Annual direct (mean)						7712.05 (7080–8340)				
Italy	Verona (Northern)	Annual indirect (mean)										
	Nationwide	Annual direct in billion			7.60							
		Annual direct (mean)			4396.15 (33.82–119768.68)							
	Portogruaro	Annual direct (mean)							2715			
Netherlands	Nationwide	Annual indirect in million			58.6							
		Annual direct in million			627–652							
		Annual direct (mean)			2685.31 (42.64–99593.27) –2891.08							
	Northern	Annual direct (mean)										
Poland	Nationwide	Annual direct in million									31.87	34.84
Spain	Badalona (Barcelona)	Annual direct (mean)										
		Annual indirect (mean)										
		Annual total (mean)										
	Cadiz (Southern)	Annual direct (mean)				3719.06 (3171–4270)						
		Annual indirect (mean)										

(Continues)

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TABLE 4 (Continued)

Country	Region	Type of cost	1994	1997	1998	1999	2000	2001	2002	2003	2004	2005
						2678.88 (1928–3431)						
		Annual total (mean)				6397.94 (5187–7088)						
	Catalonia	Annual direct (mean)										
	Nationwide	Annual direct in billion			2.88							
		Annual direct (mean)			1918.08 (23.53–40681.68)							2041.7
Sweden	Nationwide	Annual direct (mean)			3865.56 (10.29–52379.59)			4537.18 (4455.43–4614.79)	2976.43 (2902.51–3050.88)	2967.63	3028.08	3032.48
		Annual direct in billion			1.08							
	Uppsala	Annual direct (mean)					4391.17 (4140–4640)					
Ireland	Dublin and Cork	Annual direct in billion				0.50						
		Annual direct (mean)				3281.7						
UK	Nationwide	Annual direct in billion	3.83									
		Annual direct (mean)	3254.13 (39.72–80475.31)	895.69	956.84–2800.66	1076.49	1131.68	1211.9	1305.85	1386.46	1414.08	1317.49

TABLE 4 Economic data of EU member states and subnational regions.

Country	Region	Type of cost	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Belgium	Nationwide	Annual direct in billion										
		Annual direct (mean)										
France	Nationwide	Annual direct in billion								9.2		
		Annual direct (mean)	2474.97–3492.6	2577.16	4913.03	4888.61	4898.88	4863.45	4879.01	4915.06–7055.91 (6920–7190)	5222.16	5443.97
		Annual indirect (mean)	702.51	658.31	680.63	677.37	631.89	583.57	558.35	527.08	512.93	491.48
		Annual total (mean)	3177.48	3235.47	5593.66	5565.98	5530.77	5447.02	5437.36	5442.14	5735.09	5935.45
Germany	Nationwide	Annual direct in billion					32.8–38.5					
		Annual direct (mean)	2394–2955.76	3196.46	2172.3	5829.41	5065.53–5955.5					
Greece	Nationwide	Annual direct (mean)	1331.53–1437.4	1205.68	1261.1		1440.1					
			7712.05 (7080–8340)									

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TABLE 4 (Continued)

Country	Region	Type of cost	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Italy	Verona (Northern)	Annual indirect (mean)							3639.2 (3540–3730)			
	Nationwide	Annual direct in billion										
		Annual direct (mean)										
	Portogruaro	Annual direct (mean)										
Netherlands	Nationwide	Annual indirect in million										
		Annual direct in million										
		Annual direct (mean)										
	Northern	Annual direct (mean)			5047.02 (4940–5160)							
Poland	Nationwide	Annual direct in million	41.35	43.31	61.5	61.35						
Spain	Badalona (Barcelona)	Annual direct (mean)						3550.17 (3476.2–3623.47)				
		Annual indirect (mean)						1349.72 (1160.57–1538.63)				
		Annual total (mean)						4899.89 (4691.72–5107.15)				
	Cadiz (Southern)	Annual direct (mean)										
		Annual indirect (mean)										
		Annual total (mean)										
	Catalonia	Annual direct (mean)						3503.67 (3454.14–3553.28)				
	Nationwide	Annual direct in billion										
		Annual direct (mean)	2765.18	2041.7								
Sweden	Nationwide	Annual direct (mean)	3056.66	3010.5	3192.95	3330.34 (3136.61–3521.26)	1795.2					
		Annual direct in billion										
	Uppsala	Annual direct (mean)										
Ireland	Dublin and Cork	Annual direct in billion										
		Annual direct (mean)										
UK	Nationwide	Annual direct in billion										
		Annual direct (mean)	1322.81–1925.66	1316.62								

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in Eastern European countries: Bulgaria, Croatia, Republic of Cyprus, Czech Republic, Estonia, Latvia, Lithuania, Luxembourg, Malta, Portugal, Romania, Slovakia, and Slovenia. Given the less favorable socioeconomic factors in Eastern European countries compared with Western Europeans,[87] it is likely that important adverse disease burden data were not identified. Moreover, there are no regularly published data for any country. Such incomplete picture therefore limits our ability to assess the burden of T2D in the EU-28 in a truly global way.

Second, prevalence and incidence were the most reported epidemiological measures from 15 countries reporting data on T2D. Over our study period, prevalence values for adults varied between 1.16% and 14%. A partially similar systematic review with meta-analysis investigated disparities in the T2D prevalence of different minority groups in Europe.[88] The study covered a 20-year period; however, contrary to our study, it did not compare the prevalence in different years. In the Netherlands, the study reported prevalence rates of T2D between 3.1% and 6.2%, which were higher than those in our study of 1.7%–2.83%. In Sweden, percentages had a broader range, at 1.7%–19%; in our study the range was 1.33%–3.6%. The prevalence in Denmark was 3.6% in the study and we found a range of 1.16%–4.83%.

Regarding subnational data availability, Germany was one of the few countries where the epidemiology of T2D was reported from different regions: The South, Lower Saxony, East, Northeast, West, and Halle. Many risk factors and etiologic factors have been associated with T2D onset. Differences between regions were reported in health-related attitudes, education, unemployment, income, and private home ownership.[44] This study found association between educational level and time to onset of T2D. Inverse association between lower educational level and risk of developing T2D was already presented from several European countries, and body mass index (BMI) is considered an important potential mediator in the relationship between educational level and T2D since the hazard ratio (HR) levels were increased when adjustments for BMI were made.[89] Furthermore, socioeconomic status, income, and regional deprivation are also associated with risk of T2D and obesity. A study performed in England reported that individuals with low socioeconomic status have a 2.59× greater risk of experiencing a diagnosis of T2D than individuals in higher socioeconomic levels.[90] The northeast part of Germany, which is a highly deprived area, had high T2D prevalence rates, while the southern part of Germany showed a low prevalence.[44] Another study in the United Kingdom proved that the prevalence, incidence, and mortality of T2D is higher in males, mainly when they are older and live in deprived areas.[61] A higher relative risk of T2D is often associated with populations with low economic levels and low-income countries,[91,92] but little is known about within-country variation across the EU-28, so these studies are very valuable.

Mortality was one of the least reported epidemiologic measures, with only four studies.[8,42,59,63] This would certainly deserve more attention; as a study found that 12.3% of multiple cause death certificates cited diabetes, but only 2.9% reported diabetes as an underlying cause of death.[93] Different standardized methods of assessing T2D mortality should be adopted by databases and studies since most diabetic patients' causes of death are currently attributed to comorbidities and severe complications.[93]

Third, the change in T2D over time is well tracked despite the scarcity of data: Prevalence, incidence, and mortality are increasing in all countries in which longitudinal comparisons were possible. Prevalence rates increased over the years in the United Kingdom, Denmark, Italy, France, Germany, Sweden, Netherlands, and Spain. Prevalence changes were most reported for the United Kingdom between 1978 and 2014 in our work, showing an increase from 1.20% to 4.37–6.25% by different studies. Evidence suggests that T2D prevalence is increasing not only in the EU,[6] which mostly reported from the Western countries,[11] but also globally.[94] Globally, diabetes prevalence has increased from 4.3%–5% to 7.9%–9% from 1980 until 2014. Over 34 years, none of the countries worldwide reported a decrease in diabetes prevalence.[95] This study found the lowest percentages in the population of northwestern European countries, in Switzerland, Austria, Denmark, Belgium, and the Netherlands.[95]

There were very few and diverging longitudinal data on incidence. Some countries reported increasing incidence across years (UK [Tayside], Denmark, Italy, and Austria), while the western part of Germany, the United Kingdom, and Hungary showed a decrease in incidence rates. The mixed pattern in the EU was already reported by Magliano et al.[96] Helsinki (Finland) remained a relatively low T2D incidence rate of 9.43% during 34 years of follow-up. However, their sample was all male, had a low risk of diabetes, a low obesity rate, a fasting plasma glucose level below 5 mmol/L, and the highest socioeconomic status.[39] A prospective study conducted in the United Kingdom reported that the increase in the incidence of T2D between 1984 and 2007 was indeed associated with BMI/adiposity, even though BMI explained only 26% of this increase. The remaining percentages should be associated with different factors, such as a lack of physical activity and dietary changes.[97] Predicting the onset of T2D in populations at risk can be an efficient method to apply prevention policies and decrease the incidence of diabetes. Countries including the United Kingdom and Germany use tools (i.e., Cambridge Diabetes Risk Score, German Diabetes Risk Score, and QDScore) to identify and predict not only the risk of diabetes onset but also undiagnosed hyperglycemia and metabolic syndromes.[45,57,68,98]

Fourth, there are no sufficient data on prevalence, incidence, and mortality in all age groups. Childhood T2D is surprisingly understudied, which makes it difficult to predict the adulthood T2D risk.[99] The paucity of literature on the epidemiology of T2D in children and adolescents might be explained by the fact that this type of diabetes accounts for less than 10% of all cases in most countries.[100] Data regarding the incidence and prevalence of T2D in children and adolescents were reported in four studies from the United Kingdom, Austria, and Hungary.[33,34,47,58] The incidence reportedly increased from 0.53 to 0.72 per 100,000 per year in the United Kingdom (2005 and 2015), mostly in girls and nonwhite populations. Interestingly, the sample in the United Kingdom comprised mostly obese children with a family history of diabetes.[58] In Austria, the incidence rate showed similar trends when compared with the United Kingdom since it increased

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from 0.14 to 0.34 per 100,000 (1999–2007).[33,34] Hungary demonstrated an inverse change in incidence rate, which decreased from 8.35 to 5.06 per 100,000 per year (2001–2016). However, the prevalence of T2D in children and adolescents increased from 19.85 to 22.15 per 100,000 in the same period,[47] which may be explained by the fact that the decrease in incidence is more than offset by the low number of deaths. However, some longitudinal data have reported different patterns in the prevalence and incidence of T2D in under-18s in different countries: no increase in prevalence in Denmark and Germany,[101,102] an increase in prevalence in the United Kingdom,[103] no increase in incidence in Australia,[104] and an increase in prevalence and incidence in the United States.[105,106] Despite the nonhomogeneous findings, it can be stated that changing behavioral patterns related to diet, physical activity, and childhood obesity increase the burden of T2D in Europe.[107]

Fifth, T2D-related expenditure is growing. Unfortunately, data specifically for T2D are often not available; for example, the total cost of DM can be reached from the Netherlands (2016), which was €6.8 billion.[108] The financial burden of noncommunicable diseases in the EU was evaluated in a systematic review, published in 2019.[109] Costs for T2D in this study excluded comorbidities but included complications. The systematic review only included three studies accounting for two countries (Germany and the Netherlands) regarding T2D expenditure. For Germany, direct costs were estimated at between €12,927 million and €17,637 million in 2010. For the Netherlands, the direct and indirect costs in 2016 were €1276 million and €3297 million respectively. Our study reported different results in different years: in Germany, the direct annual cost was €1.83 billion in 1998 and €32.8–38.5 billion in 2010. The Netherlands reported indirect costs of €58.6 million in 1998 and direct costs of €627–652 million. The study cited above concludes that more research on spending on non-communicable diseases in the EU should be carried out while implementing public health policies in order to reduce the economic burden.

Prices for indirect costs of DM can be higher than direct costs. Although this information is from a study where data on T1D, T2D, and complications were pooled, these results should be further investigated in future studies.[81] However, studies may report different data even from the same country. For example, there was a large difference in mean direct costs per person in 2013 between the two nationwide studies from France: €4915.06 versus €7055.91.[71,73] Such difference is probably related to the fact that the study with higher costs did not include people who died during the cohort and least severe cases of T2D.[73]

Sixth, T2D patients have higher treatment costs than patients without the disease. Costs attributable to T2D individuals can be 72.4% higher than the expenditure in nondiabetic individuals.[82] A good strategy to decrease costs in the diabetic population is to invest in lowering blood glucose[110] since the higher costs in T2D individuals can be proportionally associated with the duration of disease, presence of complications, and elevated HbA1c value.[52,72,83] In Poland, comparing 2004 to 2009, there was an increase of 36% in medical services costs related to T2D individuals. The costs for the treatment of diabetes complications were five times greater than those for hospital care and diabetes care only.[81] For this reason, European associations urge policies to prevent diabetes complications as a method to decrease costs for the T2D population.[13] The financial impact of diabetic individuals who fail to achieve satisfactory glycemic control can result in an increase of 59.5% in annual expenditures, including pharmaceutical costs, laboratories, diagnostic tests, and consultations.[111] Hospitalization costs tend to diminish after insulin initiation since hypoglycemic episodes, although more frequent, are less severe and are usually solved at home.[77]

Individuals with T2D receiving insulin therapy usually have higher costs associated with devices, hospitals and specialists.[72,112] Expenditures related to hospitalization and diagnostic and pharmacological treatment are often high due to chronic complications, such as cardiovascular problems.[48,83] Increased GP and drug costs can be found in T2D individuals who are not well controlled regarding their blood glucose.[72,113] Glycemic control, use of oral medication/insulin, and duration of T2D have a great impact on the total expenditure of this population. One included study found a much higher cost of €520 (not inflated) for individuals with uncontrolled T2D (HbA1c > 7.5%) compared with those with good glycemic control (HbA1c < 6.5%).[72,83] Evidence also shows the relationship of higher expenditure related to patients under insulin treatment when compared with oral medication or no pharmaceutical treatment[72,73,82,112] since they usually have higher levels of HbA1c and require intense treatment.[72]

The study limitations were mainly associated with heterogeneity and availability of data. The epidemiological data were highly heterogeneous, being collected from different data sources such as hospitals, surveys, or national databases. In fact, even the diagnosis of T2D was biased, considering that the samples of people with T2D included people identified through self-report and laboratory diagnosis, people starting insulin therapy, and also people hospitalized for the disease. In addition, differences in studies' age-related inclusion criteria made comparisons between studies or countries difficult. Furthermore, the units used to report incidence, prevalence, and mortality were also very diverse: Rate per 1000, rate per 100,000, percentage, or absolute numbers. Although 90% of the epidemiological studies had their methodology classified as "high quality" according to the JBI critical appraisal tool for cohort studies, it is imperative to mention that this tool does not take into consideration whether the study was a population-based or if they used representative samples. Population-based studies would provide more accurate data regarding the epidemiologic burden of T2D compared with studies with much smaller samples due to inevitably some degree of sampling bias. Comparisons between included studies could have led to unequal outcomes. In addition, the results of studies on a representative sample are not necessarily the most adequate for making decisions about the general population. More population-based studies on these fields are required, as it is not appropriate to base policy and economic decisions on population samples. Although calculations including quality of life are a very important part of the burden of disease studies, as only one study could be identified in our study period, which is far from sufficient to assess the situation in Europe, it is excluded from

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the analysis. The number of diabetes studies that take quality of life into account is low, as highlighted by other systematic reviews.[114]

The economic studies also used a number of different data sources; additionally, each took different elements into account to calculate indirect or direct costs, which made comparisons between studies inaccurate. In the included economic studies, different methods were applied to assess the total, gross, direct, and indirect costs. For this reason, comparison between studies or different regions became problematic, as underlined by other economic systematic reviews.[27] Additionally, a few studies analyzed the costs for patients in completely different phases of disease, for example, 6 months after insulin initiation or a sample with many years since T2D onset. Another bias in the comparison relates to the very different healthcare systems in EU countries, which precluded an accurate comparison of expenditure for T2D patients.

In the future, if homogeneous studies become available, it would be important to summarize the studies that appear in the form of a meta-analysis in addition to a systematic review.

On the other hand, the major strength in the present study is the novelty of being a recent and unique systematic review aiming to include all epidemiologic and economic burden data related to T2D in EU-28 countries. We report data on a wide range of measurements of T2D disease burden including prevalence, incidence, mortality, and costs (indirect, direct, total, and gross). Furthermore, the analyses included a 47-year follow-up period, which allowed to provide an overview of the longitudinal evolution of T2D. Additionally, this study beyond cross-country comparisons pays attention to regional data as well which enabled comparison with other regions or national data. Another strength of this study is related to the rigorous methodology used through the selection and the evaluation process.

5 | CONCLUSIONS

This systematic review assessed the epidemiological and economic burden data on T2D in 15 EU member states, including populations of all ages, in publications from 1970 to 2017. However, the existing published data are insufficient to provide a comprehensive picture of the burden and distribution of T2D in the EU-28 countries, especially among children. In most EU countries, the disease burden of T2D is increasing dramatically over time, as reflected in the increasing expenditure on this population as well. In the case of epidemiological indicators, variations within countries are as significant as those between countries. Incidence and prevalence are certainly increasing over the years. The absence of data on mortality rates prevented us from generating trustworthy assumptions. Despite the measurement heterogeneity on direct and indirect costs, total costs of T2D have clearly been increasing in the EU-28 countries over the years. More well-designed, population-based disease burden studies are needed across the EU-28 to build a coherent picture. In addition, studies are needed on what policy changes might reduce the burden of T2D in the EU-28, in particular approaches to reduce expenditure on the disease and its complications.

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CONFLICT OF INTEREST STATEMENT

No conflict of interest statement.

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REFERENCES

1. Schwarz PE, Muylle F, Valensi P, Hall M. The European perspective of diabetes prevention. *Horm Metab Res*. 2008;40(8):511-514. doi:10.1055/s-2008-1081501
2. American Diabetes Association. Classification and diagnosis of diabetes: standards of medical care in diabetes—2021. *Diabetes Care*. 2021;44(Supplement_1):S15-S33. doi:10.2337/dc21-s002
3. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of diabetes 2017. *J Diabetes Res*. 2018;2018:3086167. doi:10.1155/2018/3086167
4. Ceriello A, Devalk HW, Guerci B, et al. The burden of type 2 diabetes in Europe: current and future aspects of insulin treatment from patient and healthcare spending perspectives. *Diabetes Res Clin Pract*. 2020;161:108053. doi:10.1016/j.diabres.2020.108053
5. International Diabetes Federation. *IDF Diabetes Atlas*. 10th ed. Belgium; 2021. Available at: https://www.diabetesatlas.org
6. Goodall R, Alazawi A, Hughes W, et al. Trends in type 2 diabetes mellitus disease burden in European Union countries between 1990 and 2019. *Sci Rep*. 2021;11(1):15356. doi:10.1038/s41598-021-94807-z
7. Hallberg SJ, Gershuni VM, Hazbun TL, Athinarayanan SJ. Reversing type 2 diabetes: a narrative review of the evidence. *Nutrients*. 2019;11(4):766. doi:10.3390/nu11040766
8. Jacobs E, Hoyer A, Brinks R, Kuss O, Rathmann W. Burden of mortality attributable to diagnosed diabetes: a nationwide analysis based on claims data from 65 million people in Germany. *Diabetes Care*. 2017;40(12):1703-1709. doi:10.2337/dc17-0954
9. Hu H, Sawhney M, Shi L, et al. A systematic review of the direct economic burden of type 2 diabetes in China. *Diab Ther*. 2015;6(1):7-16. doi:10.1007/s13300-015-0096-0
10. Global Burden of Disease Collaborative Network, Global Burden of Disease Study 2019 (GBD 2019) Results (Institute for Health Metrics and Evaluation – IHME). 2022 Accessed 18 October 2022. https://vizhub.healthdata.org/gbd-results/
11. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al KJ. Epidemiology of type 2 diabetes—global burden of disease and forecasted trends. *J Epidemiol Global Health*. 2019;10(1):107-111. doi:10.2991/jegh.k.191028.001
12. European Parliament. Addressing the EU diabetes epidemic. Accessed May 17, 2022. https://www.europarl.europa.eu/doceo/document/TA-7-2012-0082_EN.html
13. MEPs Mobilising for Diabetes. Blueprint for Action on Diabetes in the European Union by 2030. In: Greybe LDaK, 2021. Accessed 2022, May 17. https://www.mepinterestgroupdiabetes.eu/wp-content/uploads/2021/03/MMD-BLUEPRINT-FOR-ACTION-ON-DIABETES.pdf
14. European Commission. *Non-Communicable Diseases Overview*. European Commission. Accessed 27 March 2021.

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15. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet*. 2020;396(10258):1204-1222. doi:10.1016/S0140-6736(20)30925-9
16. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119
17. Schipf S, Werner A, Tamayo T, et al. Regional differences in the prevalence of known type 2 diabetes mellitus in 45-74 years old individuals: results from six population-based studies in Germany (DIAB-CORE Consortium). *Diabet Med*. 2012;29(7):e88-e95. doi:10.1111/j.1464-5491.2012.03578.x
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *J Clin Epidemiol*. 2021;134:178-189. doi:10.1016/j.jclinepi.2021.03.001
19. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097. doi:10.1371/journal.pmed.1000097
20. Munn Z, Stern C, Aromataris E, Lockwood C, Jordan Z. What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. *BMC Med Res Methodol*. 2018;18(1):5. doi:10.1186/s12874-017-0468-4
21. Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc*. 2015;13(3):147-153. doi:10.1097/xeb.0000000000000054
22. Munn Z, Tufanaru C, Aromataris E. JBI's systematic reviews: data extraction and synthesis. *AJN A J Nursing*. 2014;114(7):49-54. doi:10.1097/01.NAJ.0000451683.66447.89
23. Lieb R. Population-based study. 2012. doi:10.1007/978-1-4419-1005-9_45
24. Moola S, Munn Z, Tufanaru C, et al. Chapter 7: systematic reviews of etiology and risk. In: *Joanna Briggs Institute Reviewer's Manual*. Vol.5. The Joanna Briggs Institute; 2017.
25. Joanna Briggs Institute. *JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data*. University of Adelaide; 2017.
26. de Lima AKA, Dos Santos JA, Stefani CM, de Lima AA, Damé-Teixeira N. Diabetes mellitus and poor glycemic control increase the occurrence of coronal and root caries: a systematic review and meta-analysis. *Clin Oral Investig*. 2020;24(11):3801-3812. doi:10.1007/s00784-020-03531-x
27. Afroz A, Alramadan MJ, Hossain MN, et al. Cost-of-illness of type 2 diabetes mellitus in low and lower-middle income countries: a systematic review. *BMC Health Serv Res*. 2018;18(1):972. doi:10.1186/s12913-018-3772-8
28. O'Sullivan R, Murphy A, O'Caoimh R, et al. Economic (gross cost) analysis of systematically implementing a programme of advance care planning in three Irish nursing homes. *BMC Res Notes*. 2016;9(1):237. doi:10.1186/s13104-016-2048-9
29. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)*. 2012;22(3):276-282. doi:10.11613/BM.2012.031
30. Skarfors ET, Selinus KI, Lithell HO. Risk factors for developing non-insulin dependent diabetes: a 10 year follow up of men in Uppsala. *BMJ*. 1991;303(6805):755-760. doi:10.1136/bmj.303.6805.755
31. Fuentes S, Mandereau-Bruno L, Regnault N, et al. Is the type 2 diabetes epidemic plateauing in France? A nationwide population-based study. *Diabetes Metab*. 2020;46(6):472-479. doi:10.1016/j.diabet.2019.12.006
32. Carstensen B, Rønn PF, Jørgensen ME. Prevalence, incidence and mortality of type 1 and type 2 diabetes in Denmark 1996–2016. *BMJ Open Diabetes Res Care*. 2020;8(1):e001071. doi:10.1136/bmjdrc-2019-001071
33. Schober E, Waldhoer T, Rami B, Hofer S. Incidence and time trend of type 1 and type 2 diabetes in Austrian children 1999-2007. *J Pediatr*. 2009;155(2):190-193. doi:10.1016/j.jpeds.2009.03.010
34. Rami B, Schober E, Nachbauer E, Waldhör T. Type 2 diabetes mellitus is rare but not absent in children under 15 years of age in Austria. *Eur J Pediatr*. 2003;162(12):850-852. doi:10.1007/s00431-003-1323-7
35. Kristensen JK, Bak JF, Wittrup I, Lauritzen T. Diabetes prevalence and quality of diabetes care among Lebanese or Turkish immigrants compared to a native Danish population. *Prim Care Diabetes*. 2007;1(3):159-165. doi:10.1016/j.pcd.2007.07.007
36. Soulimane S, Simon D, Shaw J, et al. HbA1c, fasting plasma glucose and the prediction of diabetes: Inter99, AusDiab and D.E.S.I.R. *Diabetes Res Clin Pract*. Jun 2012;96(3):392-399. doi:10.1016/j.diabres.2011.06.003
37. Soulimane S, Simon D, Shaw JE, et al. Comparing incident diabetes as defined by fasting plasma glucose or by HbA(1c). The AusDiab, Inter99 and DESIR studies. *Diabet Med*. 2011;28(11):1311-1318. doi:10.1111/j.1464-5491.2011.03403.x
38. Jönsson B. Revealing the cost of type II diabetes in Europe. *Diabetologia*. 2002;45(7):S5-S12. doi:10.1007/s00125-002-0858-x
39. Strandberg AY, Pienimäki T, Pitkälä KH, Tilvis RS, Salomaa VV, Strandberg TE. Comparison of normal fasting and one-hour glucose levels as predictors of future diabetes during a 34-year follow-up. *Ann Med*. 2013;45(4):336-340. doi:10.3109/07853890.2013.785233
40. Rathmann W, Strassburger K, Heier M, et al. Incidence of type 2 diabetes in the elderly German population and the effect of clinical and lifestyle risk factors: KORA S4/F4 cohort study. *Diabet Med*. 2009;26(12):1212-1219. doi:10.1111/j.1464-5491.2009.02863.x
41. Muschik D, Icks A, Tetzlaff J, Epping J, Eberhard S, Geyer S. Morbidity compression, morbidity expansion, or dynamic equilibrium? The time trend of AOK-insured patients with type 2 diabetes in Lower Saxony, Germany. *J Public Health*. 2017;25(1):19-28. doi:10.1007/s10389-016-0756-1
42. Drabik A, Büscher G, Thomas K, Graf C, Müller D, Stock S. Patients with type 2 diabetes benefit from primary care-based disease management: a propensity score matched survival time analysis. *Popul Health Manag*. 2012;15(4):241-247. doi:10.1089/pop.2011.0063
43. Sittig DT, Friedel H, Wasem J. Prevalence and treatment costs of type 2 diabetes in Germany and the effects of social and demographical differences. *Eur J Health Econ*. 2015;16(3):305-311. doi:10.1007/s10198-014-0575-7
44. Schipf S, Ittermann T, Tamayo T, et al. Regional differences in the incidence of self-reported type 2 diabetes in Germany: results from five population-based studies in Germany (DIAB-CORE Consortium). *J Epidemiol Community Health*. 2014;68(11):1088-1095. doi:10.1136/jech-2014-203998
45. Hartwig S, Kuss O, Tiller D, et al. Validation of the German Diabetes Risk Score within a population-based representative cohort. *Diabet Med*. 2013;30(9):1047-1053. doi:10.1111/dme.12216
46. Müller N, Heller T, Freitag MH, et al. Healthcare utilization of people with type 2 diabetes in Germany: an analysis based on health insurance data. *Diabet Med*. 2015;32(7):951-957. doi:10.1111/dme.12747
47. Barkai L, Kiss Z, Rokszin G, et al. Changes in the incidence and prevalence of type 1 and type 2 diabetes among 2 million children and adolescents in Hungary between 2001 and 2016—a nationwide population-based study. *Arch Med Sci*. 2020;16(1):34-41. doi:10.5114/aoms.2019.88406
48. Demurtas J, Alba N, Rigon G, Nesoti MV, Bovo C, Vaona A. Epidemiological trends and direct costs of diabetes in a Northern Italy area:

1467789x, 2023, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/obr.13593 by University Of Debrecen, Wiley Online Library on [08/09/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2012 health administrative records analysis LHT n. 20 Verona. *Prim Care Diabetes*. 2017;11(6):570-576. doi:10.1016/j.pcd.2017.06.001
49. Bruno G, Runzo C, Cavallo-Perin P, et al. Incidence of type 1 and type 2 diabetes in adults aged 30-49 years: the population-based registry in the province of Turin, Italy. *Diabetes Care*. 2005;28(11):2613-2619. doi:10.2337/diacare.28.11.2613
50. Brambilla P, La Valle E, Falbo R, et al. Normal fasting plasma glucose and risk of type 2 diabetes. *Diabetes Care*. 2011;34(6):1372-1374. doi:10.2337/dc10-2263
51. Ubink-Veltmaat LJ, Bilo HJ, Groenier KH, Houweling ST, Rischen RO, Meyboom-de JB. Prevalence, incidence and mortality of type 2 diabetes mellitus revisited: a prospective population-based study in the Netherlands (ZODIAC-1). *Eur J Epidemiol*. 2003;18(8):793-800. doi:10.1023/a:1025369623365
52. Sicras-Mainar A, Navarro-Artieda R, Ibáñez-Nolla J. Clinical and economic characteristics associated with type 2 diabetes. *Rev Clin Esp (Barc)*. 2014;214(3):121-130. doi:10.1016/j.rce.2013.11.002
53. Valdés S, Botas P, Delgado E, Alvarez F, Díaz-Cadórniga F. HbA (1c) in the prediction of type 2 diabetes compared with fasting and 2-h post-challenge plasma glucose: the Asturias study (1998-2005). *Diabetes Metab*. 2011;37(1):27-32. doi:10.1016/j.diabet.2010.07.002
54. Long GH, Johansson I, Rolandsson O, et al. Healthy behaviours and 10-year incidence of diabetes: a population cohort study. *Prev Med*. 2015;71:121-127. doi:10.1016/j.ypmed.2014.12.013
55. Ringborg A, Martinell M, Stålhammar J, Yin DD, Lindgren P. Resource use and costs of type 2 diabetes in Sweden—estimates from population-based register data. *Int J Clin Pract*. 2008;62(5):708-716. doi:10.1111/j.1742-1241.2008.01716.x
56. Persson U. The indirect costs of morbidity in type II diabetic patients. *Pharmacoeconomics*. 1995;8(Suppl 1):28-32. doi:10.2165/00019053-199500081-00007
57. Rahman M, Simmons RK, Harding AH, Wareham NJ, Griffin SJ. A simple risk score identifies individuals at high risk of developing type 2 diabetes: a prospective cohort study. *Fam Pract*. 2008;25(3):191-196. doi:10.1093/fampra/cmn024
58. Candler TP, Mahmoud O, Lynn RM, Majbar AA, Barrett TG, Shield JPH. Continuing rise of type 2 diabetes incidence in children and young people in the UK. *Diabet Med*. 2018;35(6):737-744. doi:10.1111/dme.13609
59. Simmons RK, Rahman M, Jakes RW, et al. Effect of population screening for type 2 diabetes on mortality: long-term follow-up of the Ely cohort. *Diabetologia*. 2011;54(2):312-319. doi:10.1007/s00125-010-1949-8
60. Thomas MC, Hardoon SL, Papacosta AO, et al. Evidence of an accelerating increase in prevalence of diagnosed type 2 diabetes in British men, 1978-2005. *Diabet Med*. 2009;26(8):766-772. doi:10.1111/j.1464-5491.2009.02768.x
61. Zghebi SS, Steinke DT, Carr MJ, Rutter MK, Emsley RA, Ashcroft DM. Examining trends in type 2 diabetes incidence, prevalence and mortality in the UK between 2004 and 2014. *Diabetes Obes Metab*. 2017;19(11):1537-1545. doi:10.1111/dom.12964
62. Forouhi NG, Luan J, Hennings S, Wareham NJ. Incidence of type 2 diabetes in England and its association with baseline impaired fasting glucose: the Ely study 1990-2000. *Diabet Med*. 2007;24(2):200-207. doi:10.1111/j.1464-5491.2007.02068.x
63. Evans JM, Barnett KN, Ogston SA, Morris AD. Increasing prevalence of type 2 diabetes in a Scottish population: effect of increasing incidence or decreasing mortality? *Diabetologia*. 2007;50(4):729-732. doi:10.1007/s00125-006-0585-9
64. Harding AH, Griffin SJ, Wareham NJ. Population impact of strategies for identifying groups at high risk of type 2 diabetes. *Prev Med*. 2006;42(5):364-368. doi:10.1016/j.ypmed.2006.01.013
65. Holden SE, Jenkins-Jones S, Morgan CL, Peters JR, Schernthaner G, Currie CJ. Prevalence, glucose control and relative survival of people with type 2 diabetes in the UK from 1991 to 2013. *Diabet Med*. 2017;34(6):770-780. doi:10.1111/dme.13332
66. Pereira Gray DJ, Evans PH, Wright C, Langley P. The cost of diagnosing type 2 diabetes mellitus by clinical opportunistic screening in general practice. *Diabet Med*. 2012;29(7):863-868. doi:10.1111/j.1464-5491.2012.03607.x
67. Holden SH, Barnett AH, Peters JR, et al. The incidence of type 2 diabetes in the United Kingdom from 1991 to 2010. *Diabetes Obes Metab*. 2013;15(9):844-852. doi:10.1111/dom.12123
68. Hippisley-Cox J, Coupland C, Robson J, Sheikh A, Brindle P. Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. *BMJ*. 2009;338:b880. doi:10.1136/bmj.b880
69. Muzulu S, Jagger C, McNally P, Burden A. Does the time of diagnosis of type 2 diabetes have a seasonal variation? *Pract Diabetes Int*. 1995;12(4):170-171. doi:10.1002/pdi.1960120409
70. Williams R, Baxter H, Bottomley J, et al. CODE-2† UK: our contribution to a European study of the costs of type 2 diabetes. *Practical Diabetes International*. 2001;18(7):235-238. doi:10.1002/pdi.238
71. Baudot FO, Aguadé AS, Barnay T, Gastaldi-Ménager C, Fagot-Campagna A. Impact of type 2 diabetes on health expenditure: estimation based on individual administrative data. *Eur J Health Econ*. 2019;20(5):657-668. doi:10.1007/s10198-018-1024-9
72. Rodríguez-Sánchez B, Feenstra TL, Bilo HJ, Alessie R. Costs of people with diabetes in relation to average glucose control: an empirical approach controlling for year of onset cohorts. *Eur J Health Econ*. 2019;20(7):989-1000. doi:10.1007/s10198-019-01072-z
73. Charbonnel B, Simon D, Dallongeville J, et al. Direct medical costs of type 2 diabetes in France: an insurance claims database analysis. *Pharmacoecon Open*. 2018;2(2):209-219. doi:10.1007/s41669-017-0050-3
74. Jones S, Castell C, Goday A, et al. Increase in direct diabetes-related costs and resource use in the 6 months following initiation of insulin in patients with type 2 diabetes in five European countries: data from the INSTIGATE study. *Clinicoecon Outcomes Res*. 2012;4:383-393. doi:10.2147/ceor.S36148
75. Brismar K, Benroubi M, Nicolay C, Schmitt H, Giaconia J, Reaney M. Evaluation of insulin initiation on resource utilization and direct costs of treatment over 12 months in patients with type 2 diabetes in Europe: results from INSTIGATE and TREAT observational studies. *J Med Econ*. 2013;16(8):1022-1035. doi:10.3111/13696998.2013.812040
76. Jacobs E, Hoyer A, Brinks R, Icks A, Kuß O, Rathmann W. Healthcare costs of type 2 diabetes in Germany. *Diabet Med*. 2017;34(6):855-861. doi:10.1111/dme.13336
77. Aloumanis K, Benroubi M, Sourmeli S, Drossinos V. Clinical outcomes and costs for patients with type 2 diabetes mellitus initiating insulin therapy in Greece: two-year experience from the INSTIGATE study. *Prim Care Diabetes*. 2013;7(3):235-242. doi:10.1016/j.pcd.2013.04.001
78. Migdalis I, Rombopoulos G, Hatzikou M, Manes C, Kypraios N, Tentolouris N. The cost of managing type 2 diabetes mellitus in Greece: a retrospective analysis of 10-year patient level data "the HERCULES study". *Int J Endocrinol*. 2015;2015:520759. doi:10.1155/2015/520759
79. Morsanutto A, Berto P, Lopatriello S, et al. Major complications have an impact on total annual medical cost of diabetes: results of a database analysis. *J Diabetes Complications*. 2006;20(3):163-169. doi:10.1016/j.jdiacomp.2005.06.011
80. Redekop WK, Koopmanschap MA, Rutten GE, Wolffenbuttel BH, Stolk RP, Niessen LW. Resource consumption and costs in Dutch patients with type 2 diabetes mellitus. Results from 29 general

1467789x, 2023, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/obr.13593 by University Of Debrecen, Wiley Online Library on [08/09/2023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

practices. *Diabet Med*. 2002;19(3):246-253. doi:10.1046/j.1464-5491.2002.00654.x
81. Leśniowska J, Schubert A, Wojna M, Skrzekowska-Baran I, Fedyna M. Costs of diabetes and its complications in Poland. *Eur J Health Econ*. 2014;15(6):653-660. doi:10.1007/s10198-013-0513-0
82. Mata-Cases M, Casajuana M, Franch-Nadal J, et al. Direct medical costs attributable to type 2 diabetes mellitus: a population-based study in Catalonia, Spain. *Eur J Health Econ*. 2016;17(8):1001-1010. doi:10.1007/s10198-015-0742-5
83. Ballesta M, Carral F, Olveira G, Girón JA, Aguilar M. Economic cost associated with type II diabetes in Spanish patients. *Eur J Health Econ*. 2006;7(4):270-275. doi:10.1007/s10198-006-0367-9
84. Sabale U, Bodegård J, Sundström J, et al. Healthcare utilization and costs following newly diagnosed type-2 diabetes in Sweden: a follow-up of 38,956 patients in a clinical practice setting. *Prim Care Diabetes*. 2015;9(5):330-337. doi:10.1016/j.pcd.2015.01.001
85. Nolan JJ, O'Halloran D, McKenna TJ, Firth R, Redmond S. The cost of treating type 2 diabetes (CODEIRE). *Ir Med J*. 2006;99(10):307-310.
86. Currie CJ, Gale EA, Poole CD. Estimation of primary care treatment costs and treatment efficacy for people with type 1 and type 2 diabetes in the United Kingdom from 1997 to 2007*. *Diabet Med*. 2010;27(8):938-948. doi:10.1111/j.1464-5491.2010.03040.x
87. Jutz R. Health inequalities in Eastern Europe. Does the role of the welfare regime differ from Western Europe? *Soc Sci Med*. 2020;267:113357. doi:10.1016/j.socscimed.2020.113357
88. Meeks KA, Freitas-Da-Silva D, Adeyemo A, et al. Disparities in type 2 diabetes prevalence among ethnic minority groups resident in Europe: a systematic review and meta-analysis. *Intern Emerg Med*. 2016;11(3):327-340. doi:10.1007/s11739-015-1302-9
89. Sacerdote C, Ricceri F, Rolandsson O, et al. Lower educational level is a predictor of incident type 2 diabetes in European countries: the EPIC-InterAct study. *Int J Epidemiol*. 2012;41(4):1162-1173. doi:10.1093/ije/dys091
90. Stringhini S, Zaninotto P, Kumari M, Kivimäki M, Batty GD. Life-course socioeconomic status and type 2 diabetes: the role of chronic inflammation in the English Longitudinal Study of Ageing. *Sci Rep*. 2016;6(1):24780. doi:10.1038/srep24780
91. Kolb H, Martin S. Environmental/lifestyle factors in the pathogenesis and prevention of type 2 diabetes. *BMC Med*. 2017;15(1):131. doi:10.1186/s12916-017-0901-x
92. Connolly V, Unwin N, Sherriff P, Bilous R, Kelly W. Diabetes prevalence and socioeconomic status: a population based study showing increased prevalence of type 2 diabetes mellitus in deprived areas. *J Epidemiol Community Health*. 2000;54(3):173-177. doi:10.1136/jech.54.3.173
93. Fedeli U, Zoppini G, Goldoni CA, Avossa F, Mastrangelo G, Saugo M. Multiple causes of death analysis of chronic diseases: the example of diabetes. *Popul Health Metr*. 2015;13(1):21. doi:10.1186/s12963-015-0056-y
94. Alzaid A, Ladrón de Guevara P, Beillat M, Lehner Martin V, Atanasov P. Burden of disease and costs associated with type 2 diabetes in emerging and established markets: systematic review analyses. *Expert Rev Pharmacoecon Outcomes Res*. 2021;21(4):785-798. doi:10.1080/14737167.2020.1782748
95. Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4.4 million participants. *Lancet*. 2016;387(10027):1513-1530. doi:10.1016/s0140-6736(16)00618-8
96. Magliano DJ, Islam RM, Barr ELM, et al. Trends in incidence of total or type 2 diabetes: systematic review. *BMJ*. 2019;366:l5003. doi:10.1136/bmj.l5003
97. Hardoon SL, Morris RW, Thomas MC, Wannamethee SG, Lennon LT, Whincup PH. Is the recent rise in type 2 diabetes incidence from 1984 to 2007 explained by the trend in increasing BMI?: evidence from a prospective study of British men. *Diabetes Care*. 2010;33(7):1494-1496. doi:10.2337/dc09-2295
98. Schulze MB, Hoffmann K, Boeing H, et al. An accurate risk score based on anthropometric, dietary, and lifestyle factors to predict the development of type 2 diabetes. *Diabetes Care*. 2007;30(3):510-515. doi:10.2337/dc06-2089
99. Hudda MT, Aarestrup J, Owen CG, et al. Association of childhood fat mass and weight with adult-onset type 2 diabetes in Denmark. *JAMA Netw Open*. 2021;4(4):e218524. doi:10.1001/jamanetworkopen.2021.8524
100. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. *Pediatr Diabetes*. 2009;10:3-12. doi:10.1111/j.1399-5448.2009.00568.x
101. Neu A, Feldhahn L, Ehehalt S, Hub R, Ranke MB. Type 2 diabetes mellitus in children and adolescents is still a rare disease in Germany: a population-based assessment of the prevalence of type 2 diabetes and MODY in patients aged 0-20 years. *Pediatr Diabetes*. 2009;10(7):468-473. doi:10.1111/j.1399-5448.2009.00528.x
102. Oester IM, Kloppenborg JT, Olsen BS, Johannesen J. Type 2 diabetes mellitus in Danish children and adolescents in 2014. *Pediatr Diabetes*. 2016;17(5):368-373. doi:10.1111/pedi.12291
103. Hsia Y, Neubert AC, Rani F, Viner RM, Hindmarsh PC, Wong IC. An increase in the prevalence of type 1 and 2 diabetes in children and adolescents: results from prescription data from a UK general practice database. *Br J Clin Pharmacol*. 2009;67(2):242-249. doi:10.1111/j.1365-2125.2008.03347.x
104. Tran F, Stone M, Huang CY, et al. Population-based incidence of diabetes in Australian youth aged 10-18 yr: increase in type 1 diabetes but not type 2 diabetes. *Pediatr Diabetes*. 2014;15(8):585-590. doi:10.1111/pedi.12131
105. Mayer-Davis EJ, Dabelea D, Lawrence JM. Incidence trends of type 1 and type 2 diabetes among youths, 2002–2012. *N Engl J Med*. 2017;377(3):301. doi:10.1056/NEJMc1706291
106. Dabelea D, Mayer-Davis EJ, Saydah S, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. *Jama*. 2014;311(17):1778-1786. doi:10.1001/jama.2014.3201
107. Kiess W, Böttner A, Raile K, et al. Type 2 diabetes mellitus in children and adolescents: a review from a European perspective. *Horm Res*. 2003;59(Suppl 1):77-84. doi:10.1159/000067829
108. Peters ML, Huisman EL, Schoonen M, Wolffenbuttel BHR. The current total economic burden of diabetes mellitus in the Netherlands. *Neth J Med*. 2017;75(7):281-297.
109. Vandenberghe D, Albrecht J. The financial burden of non-communicable diseases in the European Union: a systematic review. *Eur J Public Health*. 2020;30(4):833-839. doi:10.1093/eurpub/ckz073
110. Giorda CB, Manicardi V, Diago CJ. The impact of diabetes mellitus on healthcare costs in Italy. *Expert Rev Pharmacoecon Outcomes Res*. 2011;11(6):709-719. doi:10.1586/erp.11.78
111. Athanasakis K, Ollandezos M, Angeli A, Gregoriou A, Geitona M, Kyriopoulos J. Estimating the direct cost of type 2 diabetes in Greece: the effects of blood glucose regulation on patient cost. *Diabet Med*. 2010;27(6):679-684. doi:10.1111/j.1464-5491.2010.03004.x
112. Brandle M, Zhou H, Smith BR, et al. The direct medical cost of type 2 diabetes. *Diabetes Care*. 2003;26(8):2300-2304. doi:10.2337/diacare.26.8.2300
113. Mevissen MRJ, Geurten RJ, Hendriks SH, Elissen A, van Dijk PR, Bilo HJG. Distribution of care expenditures for men and women with type 2 diabetes treated in primary care in the Netherlands: a case-control study (ZODIAC-59). *BMJ Open*. 2022;12(2):e052592. doi:10.1136/bmjopen-2021-052592

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114. Charalampous P, Gorasso V, Plass D, et al. Burden of non-communicable disease studies in Europe: a systematic review of data sources and methodological choices. *Eur J Public Health*. 2022; 32(2):289-296. doi:10.1093/eurpub/ckab218

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