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Article type : Original Article

The global burden of atopic dermatitis: lessons from the GBD Study - 1990 to 2017

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Conflict of Interest: CF is Chief Investigator of the UK National Institute for Health Research-funded TREAT (ISRCTN15837754) and SOFTER (Clinicaltrials.gov: NCT03270566) trials as well as the UK-Irish Atopic eczema Systemic Therapy Register (A-STAR; ISRCTN11210918). He and SML are Principle Investigators in the European Union Horizon 2020 IMI2-funded BIOMAP Consortium (grant number 821511). His department has also received funding from Sanofi-Genzyme

for skin microbiome work. RD served as a medical consultant to Altus Labs from July 2018 to July 2020, and he directs a big data dermatology research fellowship with independently awarded and administrated competitive grant funds provided to his department by Pfizer Pharmaceuticals (grant numbers 41064185 and 58858477).

Funding: SML is supported by a Wellcome Senior Research Fellowship in Clinical Science (205039/Z/16/Z). CF is supported by the NIHR Biomedical Research Centre at Guy's & St Thomas' NHS Foundation Trust and King's College London.

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What's already known about this topic?

- Atopic dermatitis (AD) is a common skin condition affecting around 20% of children and up to 10% of adults in high income countries.
- However, there is a sparsity of studies that have taken a truly global approach, in particular among adult populations.

What does this study add?

- We provide the first global map of the burden of AD across age groups, including disability-adjusted life years (DALYs).
- This ranks AD 15th among non-fatal diseases overall and top among skin diseases.
- The burden of AD has remained stable between 1990-2017, with the highest prevalence rate seen during early childhood and a second raise from middle age.

Abstract

The Global Burden of Disease (GBD) Study provides an annually updated resource to study disease-related morbidity and mortality worldwide. Here we present the burden estimates for atopic dermatitis (AD), including data from inception of the GBD project in 1990 until 2017.

Atopic dermatitis (AD) ranks 15th among all non-fatal diseases and has the highest disease burden among skin diseases as measured by disability-adjusted life years (DALYs). Overall, the global DALY rate for AD in 1990 was 120.83 (65.37-201.04) and remained similar in 2017 at 123.31 (66.79-205.17) in 2017. The 3 countries with the highest DALY rates of AD were Sweden (326.91 [177.70-547.39]), the United Kingdom (284.15 [154.81-477.66]), and Iceland (276.98 [149.02-464.91]), whereas Uzbekistan (85.14 [45.23-144.49]), Armenia (85.12 [45.83-142.94]) and Tajikistan (85.11 [46.06-143.20]) ranked lowest. The global prevalence rate of AD has remained stable from 1990 to 2017. However, the distribution of AD by age groups shows a bimodal curve with the highest peak in early childhood, decreasing in prevalence amongst young adults and a second peak in middle-aged and older populations. We also found a moderate positive correlation between a country's Gross Domestic Product (GDP) and disease burden.

GBD data confirms the substantial worldwide burden of AD, which has remained stable since 1990 but shows significant geographical variation. Lifestyle factors, partially linked to affluence, are likely important disease drivers. However, the GBD methodology needs to be developed further to incorporate environmental risk factors, such as UV exposure, to better understand the geographical and age-related variation in disease burden.

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin condition affecting around 20% of children[1,2] and up to 10% of adults in high income countries.[3,4,5,6] The pathogenesis is complex involving genetic susceptibility, impaired skin barrier function, dysfunctional cell-mediated immunity, and environmental and life-style factors.[7,8] AD is also associated with sleep disruption, mainly due to pruritus, decreased work productivity[9] as well as depression and anxiety, which all carry additional health and economic burden for patients and their families.[10]

Assessing the economic burden of AD is complex as it consists of costs for medical care, non-medical care and indirect costs (e.g. loss of education and workdays). The degree to which medical costs are an individual (out-of-pocket) burden or a collective one, depends largely on the health care system. This diversity is reflected in the studies on this subject. Firstly, two studies from the USA reported direct and indirect costs totalling about $US 3300 per person per year (pppy) for children[11] and adults in 2013.[12] Three European studies reported out-of-pocket costs for medical care as $US 1500 pppy for Italian children (2016),[13] € 351 for French adults (2018)[14] and € 927 for adults with moderate-to-severe AD in nine European-countries (2018).[15] In the latter study, for German patients costs were higher for AD than for psoriasis and rheumatoid arthritis (€ 941, € 224 and € 628 respectively).[15] Similar cost estimates have been published for AD in Singapore[16], the Asia Pacific region, Thailand, South Korea and Vietnam.[17] Understandably, cost increases with disease severity.[12,14,16]

Burden of disease can also be expressed in terms of Disability-Adjusted Life Years (DALY), a measure for the difference between living a life in perfect health and living with a disease. DALYs are calculated as Years Lost due to Disability (YLD) plus the Years of Life Lost (YLL). In other words, one DALY equals one year lost to illness, disability, or premature death within a given population. In non-fatal diseases such as AD, DALYs are measured predominantly by YLDs. The Global Burden of Disease (GBD) Institute for Health Metrics and Evaluation (IHME) measures, compares and reports health loss from disease through the use of DALYs. This study presents data from the GBD on AD by geographic location from 1990 to 2017 to better understand the global burden of this common skin disease.

Material and methods

A comprehensive description of the methodology used by GBD can be found in previous studies.[18,19] In this publication, we report the burden of AD by prevalence rates and DALYs (the sum of YLDs and YLLs). These results are estimated for 21 age groups, both sexes, and 195 countries and territories from 1990 to 2017. We report rates as age-standardised rates as per the World Health Organization world population age structure. All values are presented with 95% uncertainty intervals (UI), which estimate the distribution based on all data and input parameters including all sources. Values presented as rates indicate the value per 100,000 persons and for both sexes, unless otherwise specified, as per GBD standard approaches. Disability weights measures the relative valuations of health states, defined as an individual level of functioning within a set of health domains. For skin diseases weights encompass physical disfigurement, itch, and pain. The descriptions for disfigurement assessed in the disability weight surveys include psychological morbidity attributable to each skin disease. The values range between 0 (full health) and 1 (states equivalent to death) and were generated through expert consensus.[20] The severity associated with AD is split into three levels: mild, moderate and severe (Table S2). Data sources were obtained from a systematic search of the global scientific literature using PubMed and Google Scholar as well as through claims submitted to USA commercial health insurance companies. The prevalence estimates from these epidemiological studies were input into DisMod-MR 2.1, a Bayesian meta-regression tool, to estimate prevalence by age, sex, year, and geography (subnational, country, region, super-region) for AD.

For electronic health record data, AD was defined by ICD-10 code L20. Prevalence data for AD was derived from 195 countries and territories grouped in 21 regions and GBD super regions. A complete list of data sources used for estimation can be found using the Global Health Data Exchange online interactive tool (https://vizhub.healthdata.org/gbd-compare/). Inpatient data were not included. Study-level covariates were used to adjust prevalence estimates from the Medical Expenditure Panel Survey (MEPS)[21], US claims data from the USA for 2000, 2010, and 2012; self-reported data; and administrative data toward data based on clinical examination. In order to improve regional and global estimates, we set the minimum coefficient of variation was set at 0.4 and restricted location random effects for Paraguay, Sweden, and England were restricted to [-0.25, 0.25], [-0.25, 0.25], and

[-0.5, 0.5] respectively. A time window of ten years was used to determine which data points were used for a particular year of fit.[19]

The Gross Domestic Product (GDP) for each country was obtained through The Word Bank national account data (http://data.worldbank.org). The linear correlation between GDP and either DALY rate or prevalence rate was calculated using Pearson's correlation coefficient. A p value <0.05 was considered statistically significant. The analyses were performed using Prism, GraphPad (CA, USA).

Results

Out of 359 diseases and injuries analyzed by the GBD 2017, AD was responsible for 0.36% of the total DALYs. This ranked AD 59th among all GBD diseases and injuries in age-standardised global DALYs rate, below measles and above cirrhosis/other chronic liver diseases due to alcohol use. Among all non-fatal diseases, AD had the 15th highest age-standardised global DALYs rate. Furthermore, AD represented the highest age-standardised DALYs rate out of all skin diseases in 2017 123.31 (66.79-205.17), followed by psoriasis 70.01 (49.71-92.45), urticaria 67.45 (44.82-95.37), scabies 60 (33.18-97.8), and fungal skin diseases 54.86 (21.82-114.22). In 2017, the global prevalence rate of AD was 2,689.85 per 100,000 persons (2,535.20-2,860.85). The global DALYs rates for AD were stable between 1990 and 2017 (120.83 (65.37-201.04) versus 123.31 (66.79-205.17) respectively). The global age-standardised prevalence rates of AD have also remained stable between 1990 and 2017 (Figure 3). The prevalence of AD is highest in the paediatric population, decreasing in prevalence amongst young adults, only to increase again within the middle-aged and older adult population (Figure 2B).

There were notable differences in prevalence between countries (Figure 1), with a moderate positive correlation between DALY rates, prevalence rates and GDP, Pearson's r=0.458, p<0.001 and Pearson's r=0.452, p<0.001 respectively (Figure 2A and Supplemental Figure 2B).

Of the 195 countries, the five countries with the highest age-standardised DALY rates per 100.000 persons related to AD in 2017 were Sweden (326.91 [177.70-547.39]), the United Kingdom (284.15 [154.81-477.66]), Iceland (276.98 [149.02-464.91]), Finland (263.57 [143.55-442.67]) and Denmark (254.63 [137.41-423.97]). The five countries with the lowest age-standardised DALY rates due to AD in 2017, were Uzbekistan (85.14 [45.23-144.49]), Armenia (85.12 [45.83-142.94]), Tajikistan (85.11 [46.06-143.20]), China (82.10 [44.21-138.01]) and Kazakhstan (80.91 [43.62-136.33]).

In 2017, the five world regions with the highest age-standardised DALY rates of AD were Andean Latin American (225.02 [123.17–380.50]), Commonwealth High Income (203.44 [110.64-338.03]), Southern Sub-Saharan Africa (200.38 [108.73-335.68]), Central Sub-Saharan Africa (195.42 [104.55-324.49]), and Eastern Sub-Saharan Africa (189.54 [101.60-319.53]). In 2017, the

five world regions with the lowest age-standardised DALY rate were South-East Asia Region (90.26 [48.93-149.98]), East Asian & Pacific – WB (90.03 [48.82-150.47]), Western Pacific Region (87.51 [47.37-146.72]), Central Asia (83.73 [44.92-140.67]), and East Asia (66.52 [35.98-111.28]) (Table 1).

Discussion

AD has the highest DALY burden of all skin diseases and ranks 15th among all non-fatal diseases globally, with five European countries ranking top in age-standardised DALYs: Sweden, the United Kingdom, Iceland, Finland and Denmark. The global burden of AD expressed in DALYs remained stable during the data collection period from 1990 to 2017. While the disease prevalence rate is highest during early childhood, there was a second raise from middle age. In addition, we found a moderate positive correlation between a country's GDP and AD burden.

Key strengths of the GBD data set include its global reach, annually updated systematic data collection and disease burden estimates. However, the use of many different data sources invariably leads to pooling of data from studies that have used different methodologies and may have used different definitions of AD. The environmental factors that drive differences in disease burden between populations are difficult to determine with the GBD methodology. Furthermore, large prevalence studies commonly use questionnaire tools, which tend to overestimate the true disease burden, compared to standardised skin examination by a trained investigator (which may underestimate AD as it relies on the presence of AD at the time of examination).[22] There is also a risk of disease misclassification using questionnaires, partly because there are a number of pruritic skin conditions, including scabies, that might be reported as AD instead or vice versa.

Misclassification might also have contributed to the high regional AD burden seen in Andean Latin America and some African settings, as well as the high burden in European countries. However, high disease prevalence for AD has previously been noted in paediatric and adult populations for South America and Africa.[2,23]

We report that the highest AD prevalence is in children with a subsequent decline in prevalence and a further increase in prevalence in middle and older aged adults, which may be due to a gradual decline in water holding properties of the skin barrier in older age. These observations are consistent with reports from UK primary care data, a UK birth cohort and a survey of US adults. Interpretations discussed in the recent literature are that adult AD may be more common than previously believed, and likely includes both persisting or recurring disease from childhood and new onset adult AD; further research is required to better characterise adult AD.[6,24,25]

These is limited research on the association between disease burden and GDP; previous reports are consistent with our estimates, however these associations were not as strong as we had expected.[26] However, GDP is only a crude surrogate measure of lifestyle and other environmental factors linked with per capita income and AD development, such as air pollution, antibiotic prescribing, hygiene measures, dietary factors, and obesity.[27] We are only starting to understand how such environmental factors interact with the skin and gut microbiomes as well as host cell interactions at the level of the skin barrier.[28]

Where do we go from here? It will be important to develop the GBD methodology further, for instance by better estimates of prevalence and harmonised definitions, and efforts to map UV and air pollution exposure against burden of disease. These efforts will be particularly important to interpret effects of climate change. It is important to note that the burden of AD does not include commonly seen co-morbidities, such as food and respiratory allergies as well as psychiatric diseases (anxiety and depression).[29] Combining these associated diseases with AD burden estimates would help reflect the patient burden more closely. Further large population-based studies are needed to fill the remaining gaps on the burden of AD outside of Europe and North America, in particular in adult populations.

Acknowledgement: This review article is part of a special BJD issue on the globalburden of skin diseases

Figure legends

Figure 1. The global age-standardised prevalence of AD in both sexes per 100,000 persons (blue areas indicated low prevalence and red areas indicate high prevalence) [source: Global Burden of Disease project 2017 data, Institute for Health Metrics and Evaluation, University of Washington, Seattle, US].

Figure 2. Scatter-plot showing Disability-Adjusted Life Years (DALY) vs. Gross Domestic Product (GDP) per capita per country. Correlation measured by Pearson's $r = 0.458$, $p<0.001$.

Figure 3. The global prevalence of AD per 100,000 in both sexes by year (A) and by age group (B) (bars indicate 95% UI).

Figure S1. Age standardised DALY rates for AD rate per 100 000 by sex and region (in descending order of DALY rates) (bars indicate 95% UI).

Figure S2. A scatter-plot showing prevalence rate vs. GDP per capita per country. Correlation measured by Pearson's $r = 0.452$, $p<0.001$.

Tables legends

Table 1. Age-standardised disability-adjusted life-years (DALYs) rate and prevalence of atopic dermatitis (AD) in 2017 by region arranged in descending DALY rates.

Table S1. AD age-standardised, disability-adjusted life-years (DALYs) rate, percentage change of DALYs rate from 1990 to 2017, prevalence rate, percentage change of prevalence rate from 1990 to 2017, by country.

Table S2. Disability weight of AD.

Table 1. Age-standardised disability-adjusted life-years (DALYs) rate, prevalence rate (per 100,000 persons) of atopic dermatitis in 2017 by region arranged in descending order of DALY rates.

Highest Atopic Dermatitis DALYs Rate (per 100,000) in 2017		
Region	**Age-Standardized DALYs (Rate)**	**Age-Standardized Prevalence (Rate)**
Andean Latin America	220.33 (120.50 – 371.95)	4,994.46 (4,643.99 – 5,398.06)
High-Income North America	211.66 (112.83 – 371.95)	4,804.48 (4,679.04 – 4,940.71)
High-income Asia Pacific	209.28 (113.36 – 352.20)	4,736.96 (4,498.68 – 4,990.90)
Western Europe	205.01 (110.97 – 345.06)	4,653.22 (4,442.40 – 4,875.78)
Southern Sub-Saharan Africa	192.90 (104.62 – 322.15)	4,393.62 (4,098.34 – 4,694.45)
Australasia	182.01 (98.76 – 304.27)	4,134.02 (3,935.00 – 4,342.40)
Southern Latin America	171.52 (93.18 – 287.40)	3,893.80 (3,693.19 – 4,093.80)
Caribbean	168.93 (90.47 – 283.28)	3,839.09 (3,522.23 – 4,143.99)
Central Sub-Saharan Africa	154.60 (82.24 – 254.75)	3,548.69 (3,229.41 – 3,857.21)
Eastern Sub-Saharan Africa	152.60 (82.40 – 256.55)	3,484.67 (3,174.21 – 3,821.27)
Oceania	133.17 (70.96 – 220.19)	3,046.52 (2,787.22 – 3,317.61)
Central Latin America	131.25 (71.11 – 220.86)	2,971.89 (2,799.16 – 3,171.96)
Southeast Asia	127.59 (68.88 – 213.37)	2,895.82 (2,698.48 – 3,112.31)
North Africa and Middle East	124.36 (68.02 – 206. 89)	2,845.40 (2,593.14 – 3,142.09)

Western Sub-Saharan Africa	120.31 (65.50 – 200.67)	2,761.56 (2,497.67 – 2,059.05)
Tropical Latin America	118.75 (63.69 – 199.33)	2,701.59 (2,596.65 – 2,817.17)
Central Europe	116.56 (63.27 – 194.24)	2,655.57 (2,462.25 – 2,869.34)
Eastern Europe	111.57 (60.69 – 186.41)	2,543.25 (2,413.29 – 2,691.37)
South Asia	92.27 (49.84 – 153.36)	2,110.27 (1,988.94 – 2,243.68)
Central Asia	84.16 (45.11 – 141.48)	1,915.48 (1,738.21 – 2,095.11)
East Asia	82.56 (44.37 – 138.91)	1,866.03 (1,785.56 – 1,948.44)

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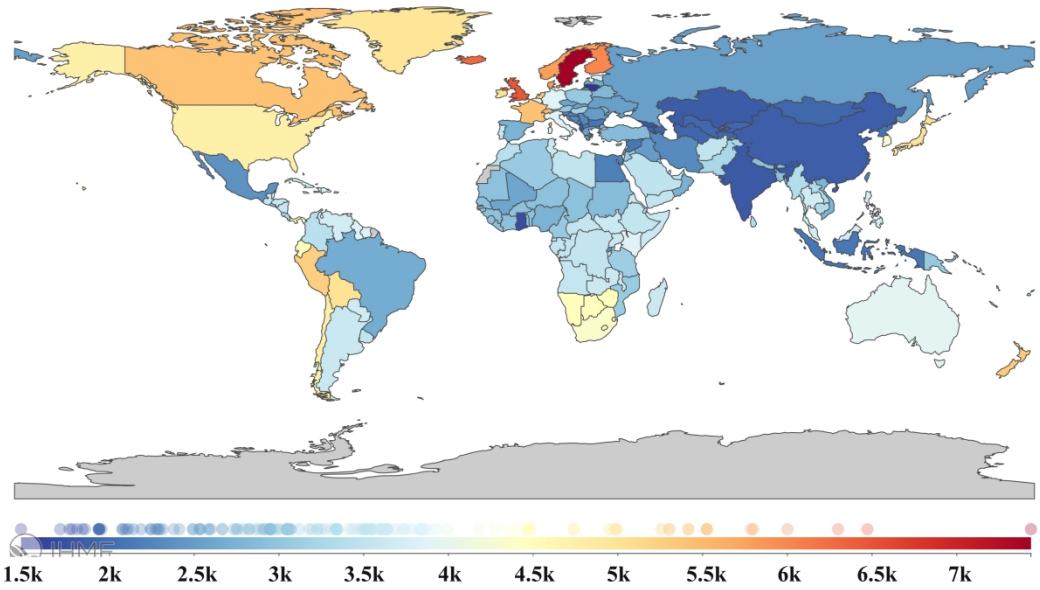

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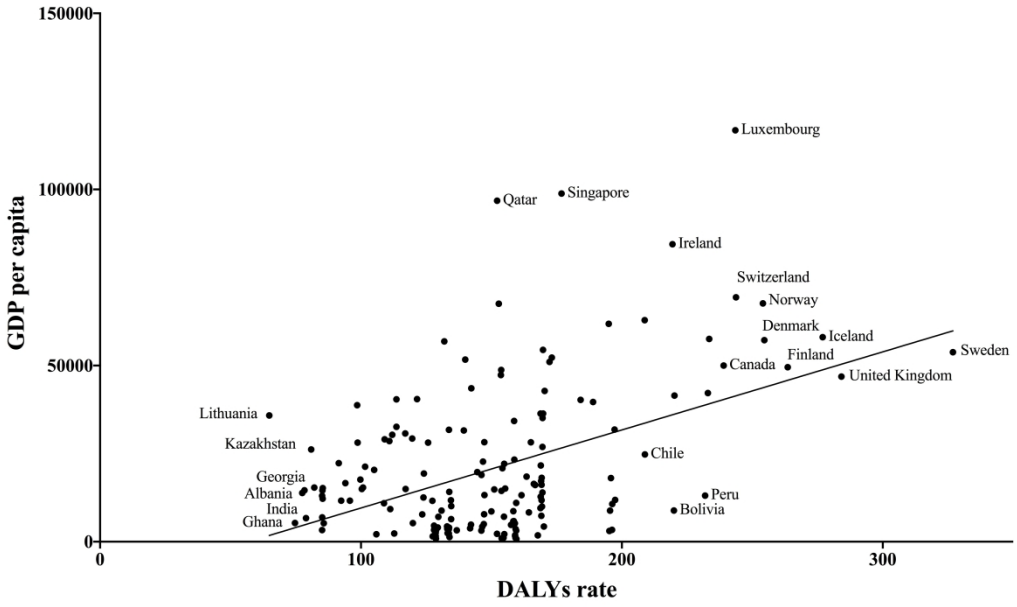

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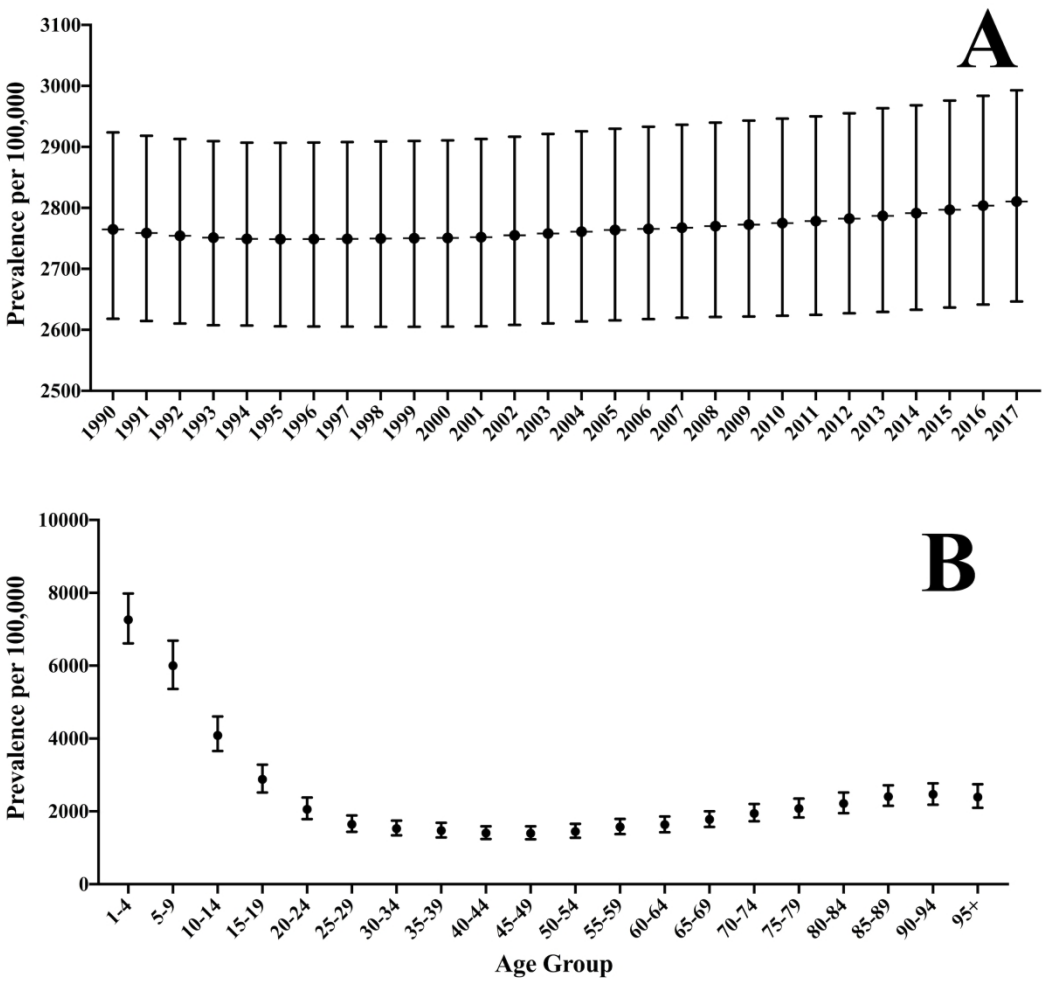

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