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Review

The prevalence of diabetes mellitus in Kazakhstan: A systematic review and meta-analysis

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Abstract. *Background and aim:* Accurately determining the prevalence of diabetes mellitus (DM) in Kazakhstan has posed challenges due to discrepancies in reported figures. This study seeks to elucidate the annual trends in diabetes mellitus prevalence in Kazakhstan based on the systematic review of the published literature. *Methods:* A comprehensive search was conducted in five electronic literature databases: PubMed, Web of Science, ScienceDirect, Academic Search Complete, and Google Scholar. After including initial studies, we conducted a reference search to obtain additional information. *Results:* Five articles met the criteria for inclusion in the systematic review. After reference search of the included articles, we added the MedInfo registry into the meta-analysis and eliminated duplicate data from the pooled prevalence estimation. Constant upward trend was observed in DM prevalence. The pooled mean DM prevalence in 2004 was 832.24 per 100,000 individuals, with significant heterogeneity observed across studies. For 2021, the pooled mean prevalence was 3743.92 per 100,000 individuals. Meta-regression revealed a significant association between DM prevalence and the male population. Sensitivity analysis identified data from 2021 as influential, contributing to publication bias. *Conclusions:* The study highlights an increasing trend in DM prevalence in Kazakhstan from 2004 to 2021. Gender-specific interventions may be warranted based on the association between DM prevalence and male populations. These findings underscore the need for enhanced methodologies in epidemiological studies to inform targeted public health strategies and healthcare policies addressing DM in Kazakhstan. (www.actabiomedica.it)

Key words: diabetes mellitus, Kazakhstan, prevalence, systematic review, meta-analysis

Introduction

The escalating prevalence of diabetes mellitus (DM) presents a critical global health challenge, with approximately 529 million individuals living with DM worldwide as of 2023 (1). An analysis of the global burden of diabetes projects future growth to 693 million by 2045 (2), accompanied by an escalating economic cost of diabetes mellitus worldwide (3,4). The epidemiology of diabetes mellitus is influenced by a multitude of factors including genetic predisposition, lifestyle choices, socioeconomic status, access to healthcare, and cultural dietary habits, leading to an increasing burden of the disease in populations previously considered low-risk (5). Kazakhstan has experienced rapid urbanization and significant lifestyle changes, contributing to the rising prevalence of DM in the region (6,7). As of 2020, the urban population has surpassed the rural population, and further increases are predicted (7). Kazakhstan has experienced significant socio-economic

development (8,9), coinciding with a transition toward sedentary lifestyles, adoption of unhealthy dietary habits, and a notable escalation in obesity prevalence (10,11). The overall prevalence of insufficient physical activity among DM patients is above 60% (12). As a result, Kazakhstan is grappling with the burden of diabetes, presenting substantial health and economic challenges (6,7). A recent investigation into macrovascular complications among individuals with diabetes mellitus (DM) found that while the cumulative incidence of acute myocardial infarctions and stroke aligns with international estimates, there is a notably higher incidence of lower limb amputations (13). This elevated risk of amputations places DM patients in Kazakhstan at increased mortality risk, particularly in the presence of cardiovascular complications. Concurrently, another study identified a downward trend in the incidence of disabilities attributed to myocardial infarction, cerebral circulation disorders, vision loss, and nephropathy in the city of Almaty, which exhibits the most unfavorable prevalence of DM patients in the country (14). Although numerous studies have examined the prevalence of DM in Kazakhstan, accurately determining prevalence rates has presented challenges, resulting in notable discrepancies in reported figures across various contexts. Conducting a systematic review and meta-analysis can help reconcile the variability in existing literature, thereby yielding a more precise estimate of DM prevalence. By aggregating data from published studies conducted in Kazakhstan, this study seeks to elucidate the annual trends in diabetes mellitus prevalence. Furthermore, we endeavor to investigate potential sources of heterogeneity through meta-regression analysis and sensitivity analysis. Through this research, we aim to provide a more comprehensive understanding of diabetes mellitus prevalence in Kazakhstan, elucidating its distribution across different time periods. Consequently, our findings are expected to furnish valuable insights for informing public health interventions and healthcare planning strategies.

Materials and Methods

The study protocol is registered with the PROSPERO International prospective register of systematic reviews (15)(ID: CRD42024488443).

Search strategy

A search in the PROSPERO database aimed to identify any registrations of comparable studies, but none were found. Following this, a comprehensive search was conducted in five prominent electronic literature databases: PubMed, Web of Science, ScienceDirect, Academic Search Complete, and Google Scholar. The search spanned from January 15, 2023, to March 27, 2024. The search strategy incorporated the following keywords: "diabetes," "diabetes mellitus," "Kazakhstan," and "prevalence." The complete strategy is detailed in the supplementary materials (Table S1). After including initial studies, we conducted a reference search to obtain additional information.

Eligibility criteria

Methodologically, the literature screening and synthesis adhered to the recommendations outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (16). The inclusion criteria for study selection comprised: (a) studies reporting data on the prevalence of diabetes mellitus among patients in Kazakhstan; (b) studies providing prevalence data based on registry sources; (c) full-text publications in English from peer-reviewed journals or publicly available patient data registry information. Exclusion criteria encompassed: (a) cross-sectional or cohort studies involving population samples; (b) studies exclusively focusing on type 1 diabetes, type 2 diabetes, or gestational diabetes; (c) studies containing duplicate data; (d) editorials, commentaries, and reviews.

Selection of studies and data extraction

After identifying the publications, we conducted deduplication and performed initial screening based on titles and abstracts, followed by a thorough evaluation of eligibility through full-text examination. During this process, publications were excluded according to predetermined criteria. Adhering to the PRISMA guidelines, two independent authors then extracted relevant data from the full-text articles using a standardized form. The extracted information encompassed details such as the name of the first author, publication

year, population size of the country or city, prevalence of diabetes mellitus at the country or city level, registry name, assessment year, number of male individuals in the population, and city name if the study was conducted at a subnational level.

Risk of bias

The risk of bias (quality) of the included studies was assessed using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist (17). The checklist consisted of ten questions, addressing aspects like study objectives, methodology, research design, recruitment approach, data collection methods, researcher-participant relationships, ethical considerations, data analysis, research findings, and overall value. Each criterion received a rating of 'yes' (scored as 1) when adequately described, 'no' (scored as 0) when absent, and 'can't tell' (scored as 0.5) when unclear or incomplete. Total scores ranged from 0 to 10, with a score of at least 7 indicating satisfactory quality.

Statistical analysis

Using subgroup analysis, the pooled mean prevalence of diabetes mellitus per year, along with 95% confidence intervals (95% CI), was calculated using a random-effects model for meta-analysis in RStudio software (18). Heterogeneity across studies was assessed using the I^2-statistic. Sensitivity analysis was carried out to identify any studies that significantly influenced the pooled prevalence estimates. Additionally, meta-regression analyses were performed to assess the effect of the gender. Publication bias was evaluated through visual inspection of a drapery plot and statistical analysis using Egger's test, examining potential asymmetry in the distribution of study results.

Results

A comprehensive search across PubMed, Web of Science, ScienceDirect, Academic Search Complete, and Google Scholar databases resulted in 551 records. After initial screening, 395 non-duplicative records remained, of which 63 full-text articles were evaluated. Ultimately, five articles met the criteria for inclusion in the systematic review. After conducting the reference search of the included articles, we incorporated the data from the MedInfo registry into the meta-analysis and eliminated duplicate data from the pooled prevalence estimation for the year 2016. The study selection process is illustrated in Figure 1 (16). Studies that appeared to meet the inclusion criteria but were excluded: studies containing information on type 1 or type 2 diabetes prevalence only (19–22); Almaty (a city in Kazakhstan) registry data only (23). The study selection process is illustrated in Figure 1 (16).

Methods of studies

The Ministry of National Economy data was the primary population data source utilized across most studies. Diabetes mellitus prevalence data were sourced from various entities, including MedInfo Statistical Data, The Public Foundation "Kazakhstan Society for the Study of Diabetes" (KSSD), The Ministry of Health Form 15 on the number of diabetes cases, The Ministry of Health of RK, the DM patients Dispensary Registration Database (D-registration), and the Unified National Electronic Health System (UNEHS) of Kazakhstan. Years included in the analysis start from 2004 and conclude with 2021. The summary of the included articles and sources is presented in Table 1.

The risk of bias assessment

The risk of bias assessment results are presented in Table 2. All of the studies had a CASP score 7 and above.

Prevalence rate and dynamics of the diabetes mellitus in Kazakhstan

Figure 2 provides a summary of the yearly prevalence rate of diabetes mellitus per 100 000 population. Significant variations in prevalence estimates were observed across all assessment years, indicating a consistent upward trend. According to the results obtained from the random effects model, the pooled mean prevalence of diabetes mellitus was 832.24 per 100,000 individuals (95% CI [692.88 - 999.35])

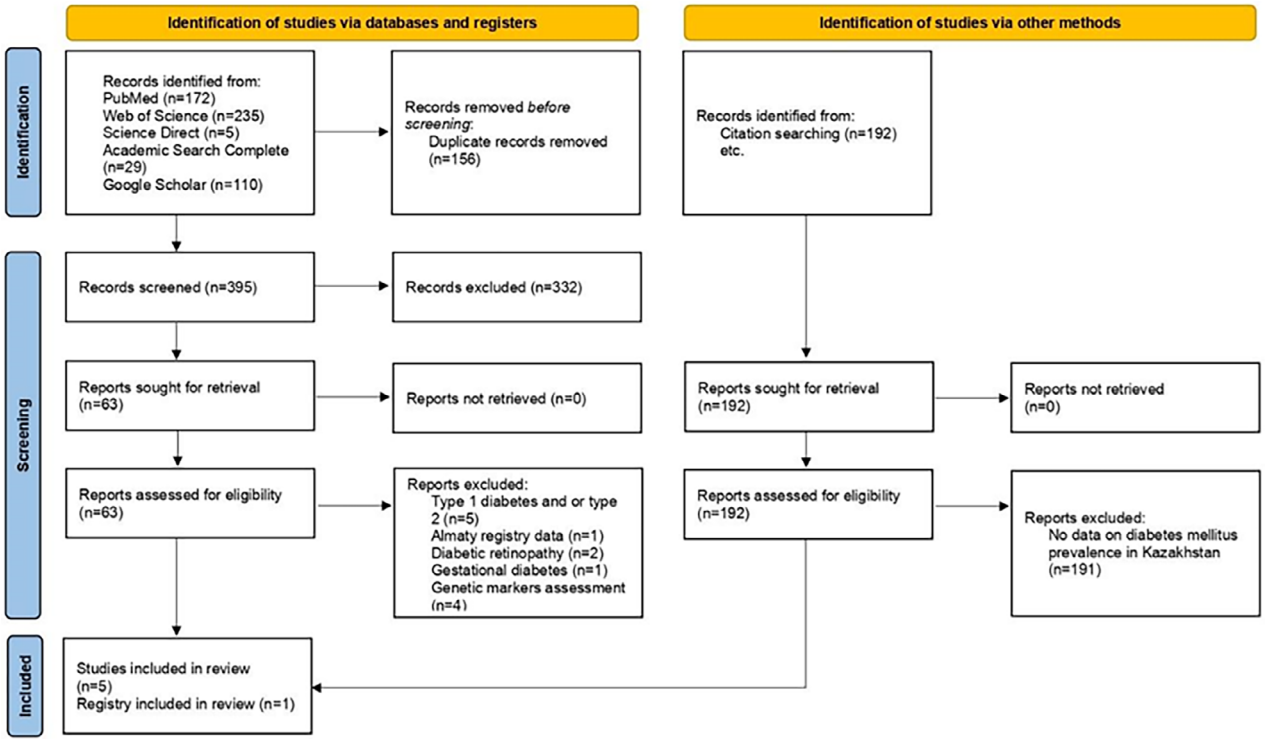

Figure 1. PRISMA flow chart of study selection (16).

Table 1. Summary of Included Articles and Sources.

First author, year	Population data source	Diabetes data source	Years included
Sikhayeva, 2018 (24)	MedInfo Statistical Data	MedInfo Statistical Data	2016
Mukasheva, 2019 (25)	The Committee on Statistics of the Ministry of National Economy of RK	The Public Foundation "Kazakhstan Society for the Study of Diabetes"	2004-2018
Beissova, 2022 (26)	The Ministry of National Economy	the Ministry of Health, Form No. 15	2018-2021
Mukasheva, 2022 (27)	The Committee on Statistics of the Ministry of National Economy of RK	The Ministry of Health of RK, the DM patients Dispensary Registration Database (D-registration)	2009-2019
Alimbayev, 2023 (28)	The Committee on Statistics of the Ministry of National Economy of RK	Unified National Electronic Health System (UNEHS) of Kazakhstan	2016-2019
MedInfo (29)	MedInfo Statistical Data	MedInfo Statistical Data	2004-2018

*Only data for 2016 was published in the article.
Abbreviation: RK: Republic of Public Health.

in 2004. However, the test for heterogeneity revealed substantial heterogeneity (I^2=100%, Q(df=1)=1784.65, p-value=0), suggesting diverse prevalence rates among the studies. Notably, for 2021, only one registry provided data, showing a pooled mean prevalence of 3743.92 per 100,000 individuals (95% CI [3735.42 - 3852.44]). Figure 3 illustrates the annual dynamics of diabetes prevalence from 2004 to 2021.

Table 2. CASP risk of bias assessment**.**

Author, year	Aim	Methodology	Design	Recruitment	Data collection	Relationship	Ethical	Data analysis	Finding	Values	Score
Sikhayeva, 2018	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	7.5
Mukasheva, 2019	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	7.5
Beissova, 2022	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	7.5
Mukasheva, 2022	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	7.5
Alimbayev, 2023	Yes	Yes	No	Can't tell	Yes	No	Yes	Yes	Yes	Yes	7.5
MedInfo	Yes	Can't tell	No	Can't tell	Yes	Yes	Yes	Yes	Yes	Yes	7

Abbreviation: CASP: Critical Appraisal Skills Programme.

Meta-Regression results

Random-effects multivariate meta-regressions were employed to investigate the sources of heterogeneity. Meta-regression analysis based on the number of male populations revealed a statistically significant association between the number of males in the population, and the prevalence of diabetes mellitus ($p < 0.0001$). The results of the meta-regression analysis are depicted in Figure 4.

Sensitivity analysis

A sensitivity analysis was conducted by sequentially excluding individual studies to assess the robustness of the pooled estimate. The results indicated persistent heterogeneity, with the pooled prevalence estimate significantly impacted by the high prevalence of diabetes mellitus reported in 2021, as shown in Form 15 (refer to supplemental materials Figure S1). Furthermore, a leave-one-out analysis identified the Form 15 data for the year 2021 as the most influential input, with its results presented in Figure S2.

Publication bias assessment

Upon visual inspection of the drapery plot (Figure S3), we observe an asymmetry, suggesting an asymmetrical distribution of study results around the estimated effect size. This finding was further confirmed by Egger's test for publication bias, which yielded significant results ($p < 0.0001$).

Discussion

The systematic review and meta-analysis aimed to investigate the prevalence dynamics of diabetes mellitus in Kazakhstan, providing valuable insights for public health interventions and healthcare planning. The findings revealed significant variations in prevalence estimates across different assessment years, indicating an overall upward trend in diabetes prevalence. We observe a consistent upward trend commencing from 2004. Moreover, in 2021, the prevalence of diabetes nearly doubled compared to 2020 and increased by a factor of 4.5 compared to 2004. This suggests a growing burden of diabetes in Kazakhstan, consistent with the global trend of increasing diabetes prevalence and projections of further escalation. Furthermore, the literature extensively discusses a bidirectional relationship between diabetes and coronavirus disease 2019 (COVID-19) (30–32), with diabetes being among the most common comorbidities in patients with COVID-19 that could explain the presence of publication bias and the heavy influence of these numbers on the pooled estimate results (33–35). The observed heterogeneity in diabetes prevalence estimates warrants further investigation into potential contributing factors. Although not the primary focus of our study, we have observed

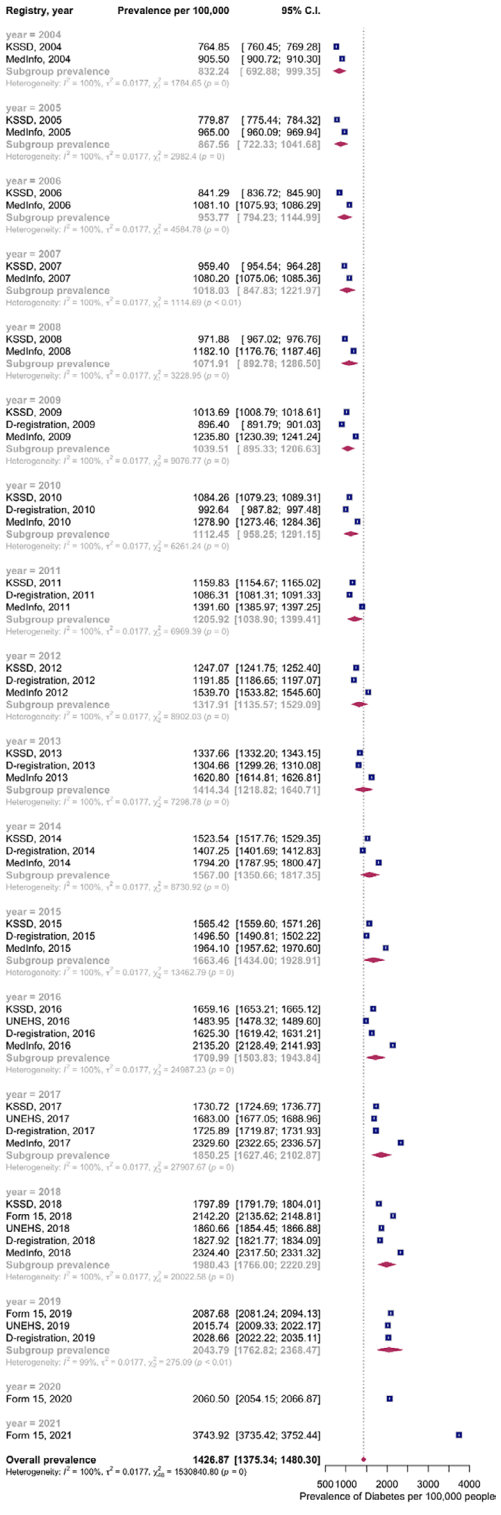

Figure 2. Subgroup analysis of the diabetes mellitus prevalence in Kazakhstan based on the year of assessment.

Abbreviations: C.I.: confidence interval; KSSD: Kazakhstan Society for the Study of Diabetes; UNEHS: Unified National Electronic Health System.

variability in diabetes mellitus prevalence depending on the registry from which the data was obtained for every year included in the analysis. One of the ways to explain this variability could be defining and understanding the data sources for the registry. For example, Gusmanov and colleagues have highlighted confounding by indication as a significant limitation in utilizing UNEHS for epidemiological studies (36). This limitation stems from the nature of UNEHS, which aggregates claims data obtained from healthcare providers in Kazakhstan. Our meta-regression analysis identified a significant association between the prevalence of diabetes mellitus and the male population, highlighting the need for gender-specific interventions and tailored healthcare strategies (37). The therapeutic outcomes in chronic diseases are shaped by a multifaceted interplay of biological, environmental, and social factors, underscoring the intricate interaction between these elements in both genders. The limitations of this study should be acknowledged. Firstly, the inclusion of only English-language publications from peer-reviewed journals or publicly available patient data registry information may introduce language and publication bias, potentially omitting relevant studies published in Russian or Kazakh languages or in non-peer-reviewed sources. Secondly, while efforts were made to adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for study selection and synthesis, there remains the possibility of selection bias inherent in the literature search and screening process. Thirdly, the reliance on registry data for prevalence estimates may introduce inherent biases, such as underreporting or misclassification of diabetes cases, which could impact the accuracy as discussed in a previous paragraph. Additionally, the heterogeneity observed across studies, particularly in registry sources, may limit the comparability of the pooled prevalence estimates. These limitations highlight areas for future research to address these methodological challenges and enhance the validity and reliability of epidemiological studies on diabetes mellitus prevalence in Kazakhstan. In conclusion, our study provides comprehensive insights into the prevalence dynamics of diabetes mellitus in Kazakhstan, highlighting its increasing burden over time. By elucidating the epidemiological trends associated with diabetes, our findings serve as

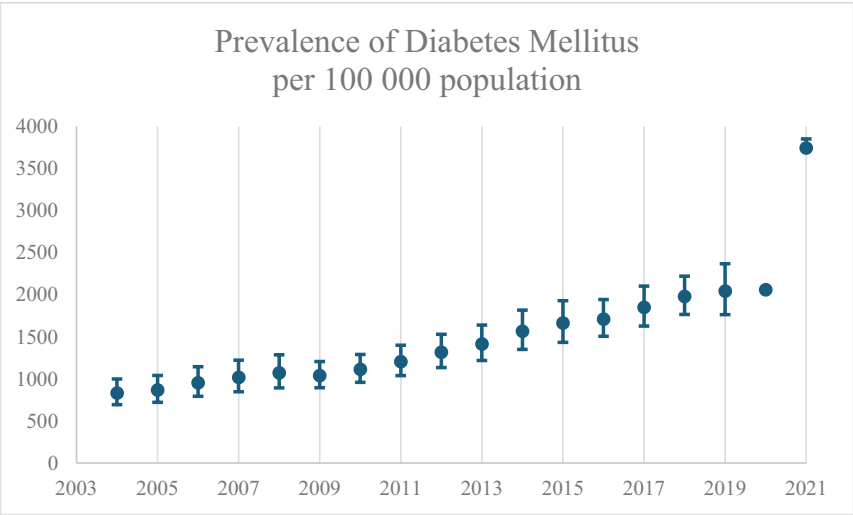

Figure 3. Diabetes mellitus annual prevalence trend.

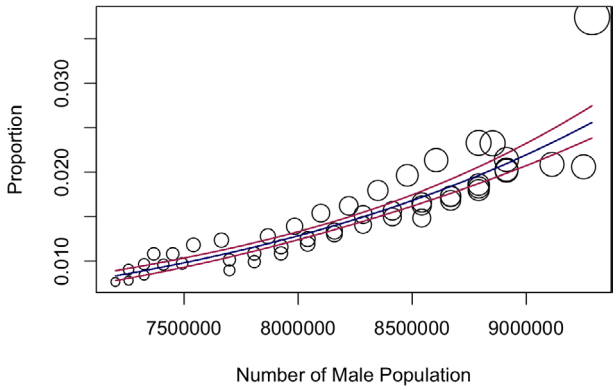

Figure 4. Meta-Regression Analysis of Prevalence Estimates Based on Number of Male Populations.

a foundation for evidence-based public health strategies and healthcare policies aimed at mitigating the growing impact of diabetes on population health and well-being.

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Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Author Contribution: AK: Conceptualization, Methodology, Investigation, Formal Analysis, Writing – Original /draft preparation. ZA: Resources, Software, Investigation, Data curation, Supervision. DA: Investigation; Validation, Writing - Review and Editing. ZB: Writing – Original /draft preparation, Supervision, Project Administration: ZR: Investigation, Resources, Software. KS: Methodology, Writing – Original / draft preparation. MB: Writing – Original /draft preparation, Writing - Review and Editing.

Availability of Data: Data used for the analysis in this study is available from the corresponding author upon reasonable request.

Study Registration: The study protocol has been registered with PROSPERO database (ID: CRD42024488443).

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ANNEX

Table S1. Search Strategy.

1. diabetes [Title/Abstract]
2. diabetes mellitus [Title/Abstract]
3. diabetes [Mesh]
4. diabetes mellitus [Mesh]
5. OR/1-4
6. Kazakhstan [Title/Abstract]
7. Kazakhstan [Mesh]
8. OR/6-7
9. "Prevalence"[Mesh]
10. "Epidemiologic Studies"[Mesh]
11. "Epidemiology"[Mesh:NoExp]
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13. epidemiolog*[Title/Abstract]
14. OR/9-13
15. 5 AND 8 AND 14

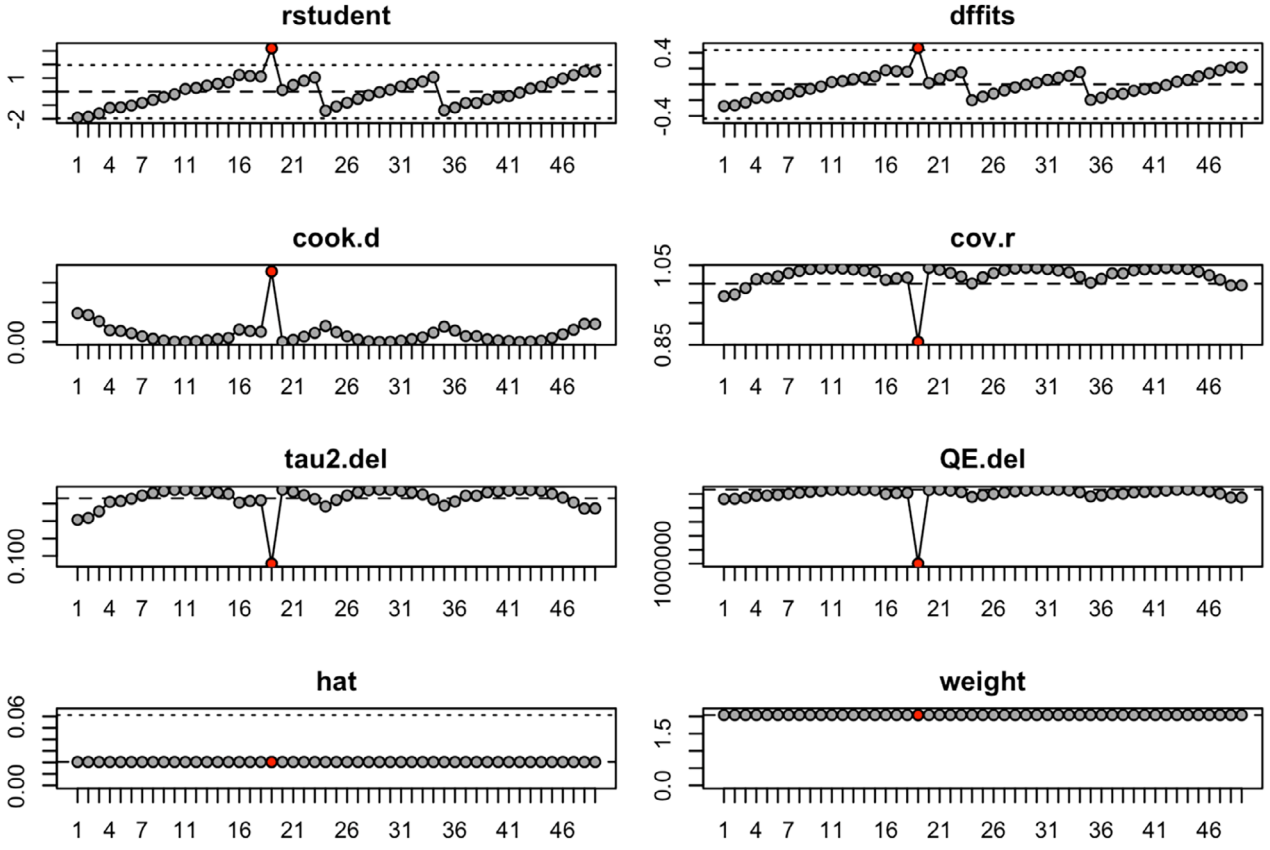

Figure S1. Influential study analysis.

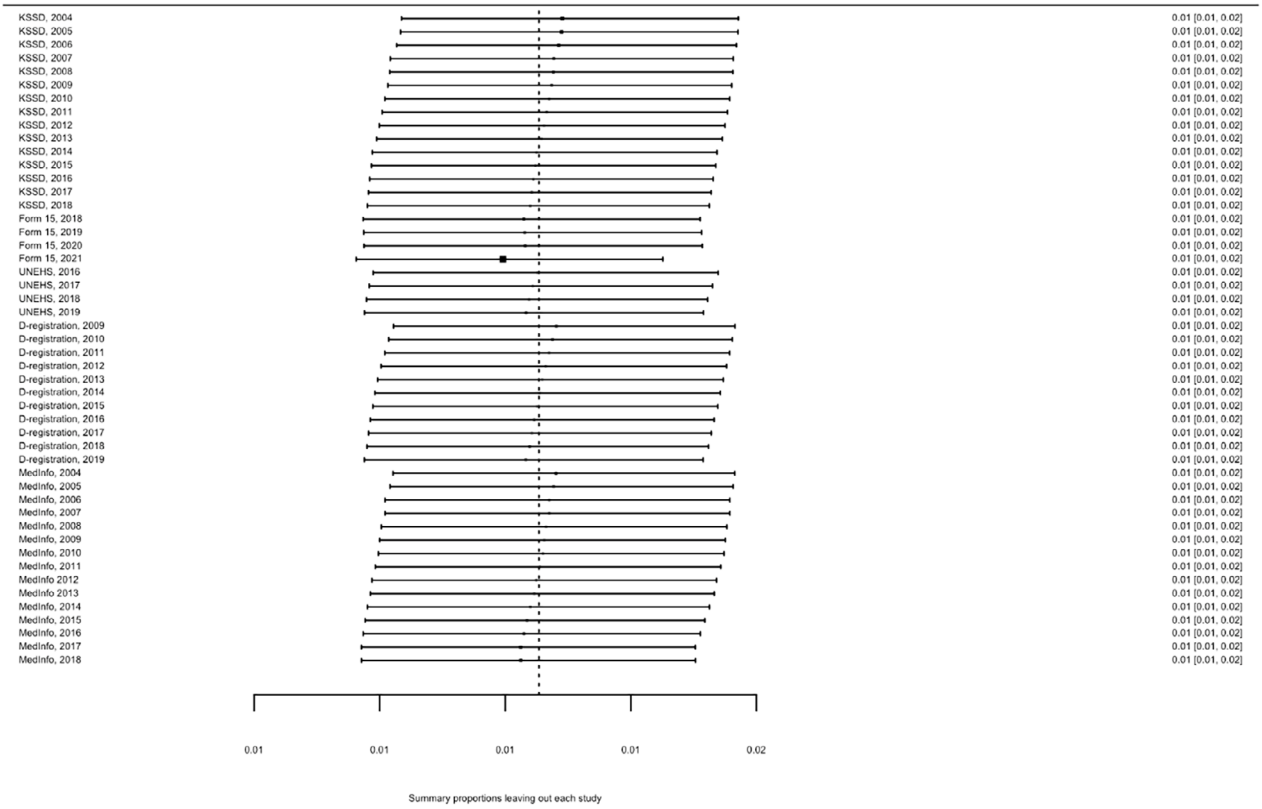

Figure S2. Leave one out analysis results.

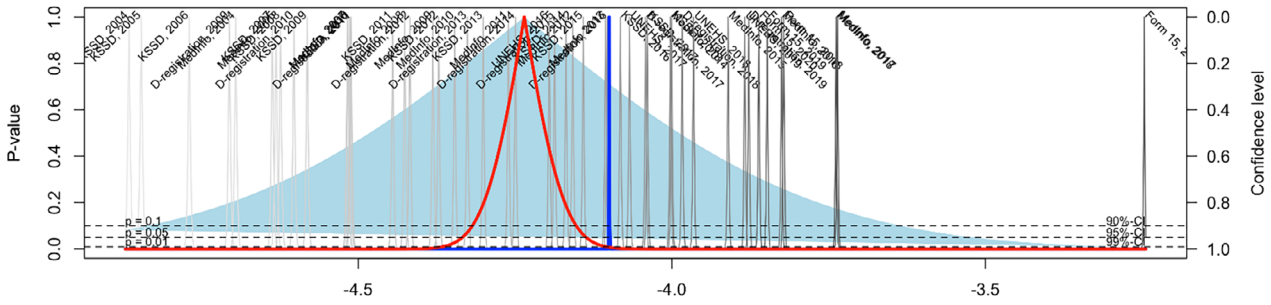

Figure S3. Drapery Plot for the Publication Bias Assessment.