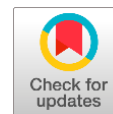


# Symptomatology of hypoglycemia in diabetes: A bibliometric analysis (2000-2022) of bayesian approaches



Afsana Al Sharmin<sup>ab</sup>   | Hani Syahida Zulkafli<sup>a</sup>  | Nazihah Mohamed Ali<sup>a</sup>  |  
Md. Abdullah Al Mamun<sup>c</sup>  | Rubaiya Shafrin<sup>d</sup> 

<sup>a</sup>Department of Mathematics and Statistics, Faculty of Science, Universiti Putra Malaysia, Serdang, Malaysia.

<sup>b</sup>Department of Mathematical and Physical Sciences, Faculty of Sciences and Engineering, East West University, Dhaka, Bangladesh.

<sup>c</sup>Department of Corporate Leadership and Marketing, Szechenyi Istvan University, Győr, Hungary.

<sup>d</sup>Health and Education for All (HAEFA), Dhaka, Bangladesh.

**Abstract** Hypoglycemia poses a critical challenge in managing diabetes. Existing literature, while extensive, lacks a holistic perspective. This study aims to bridge this gap by combining bibliometric analysis and a comprehensive review of Bayesian analysis-related hypoglycemic issues. This study employed data from the SCI-EXPANDED database for bibliometric analysis. The keywords "symptom" or "symptoms," "hypoglycemic" or "hypoglycemia," or "hypoglycaemia" or "hypoglycaemic," and "Diabetes" or "Diabetic" or "Diabetics" were used to locate 1,596 documents from 2000 to 2022. Document types, authorship patterns, and citation metrics were examined. Bayesian methodologies were systematically reviewed across various diabetes types and evaluated using specific assessment tools. Most of the articles published in "Endocrinology & Metabolism" contributed 37.2% of total articles, with a notable *CPP*<sub>2022</sub> (Citations Per Publication (CPP)) of 35, and the main publication type were articles with an average of about six authors and over 32,000 citations in 2022. The United States (US) consistently leads in the number of published articles, followed by China, Japan, and India. Novo Nordisk led institutions with 36 publications and a substantial *CPP*<sub>2022</sub> of 60.9. The comprehensive review emphasized that Bayesian statistical modeling is widely used for adult Type 1 and Type 2 diabetes but is limited in child Type 1 and absent in Gestational Diabetes (GAD) research. In contrast, Bayesian Networks (BNs) are mainly applied to adult Type 2 diabetes, with gaps in other types. Furthermore, Bayesian Neural Networks (BNNs) are prevalent in adult and child Type 1 studies but not applied to Type 2 or GAD. Since 2010, Total Publications (TP) have increased rapidly, indicating increased interest in researching hypoglycemia. Outlining potential research directions and emphasizing the transformative impact of Bayesian methodologies provides valuable insights for clinicians, researchers, and healthcare stakeholders.

**Keywords:** web of science, journal impact factor, document types, authorship patterns, citation impacts

## 1. Introduction

Diabetes mellitus is a long-term metabolic condition characterized by high blood glucose levels, which can result in various complications affecting various body organs and systems (Sharmin & Munima, 2016). Hypoglycemia poses a significant clinical challenge, as it can lead to severe complications, impair quality of life, and even be life-threatening if not managed appropriately (Cryer et al., 2003). Therefore, understanding and identifying the symptoms of hypoglycemia in individuals with diabetes is crucial for their well-being (Sharmin et al., 2024; Zulkafli et al., 2016). In addition, persistent or recurrent hypoglycemic episodes can significantly impact the quality of life of individuals with diabetes (Zammit et al., 2011). By studying the symptoms of hypoglycemia, researchers can identify patterns and factors contributing to low blood sugar events.

Bibliometric analysis is a research methodology that can reveal trends and patterns in the literature related to symptoms of hypoglycemia in diabetes. This information can help identify gaps in knowledge and areas where additional research is required. Moreover, this kind of research can identify key researchers, institutions, or countries actively contributing to hypoglycemia symptoms. Moreover, this information is valuable for collaboration opportunities, recognizing expertise, and understanding the global distribution of research efforts. Thus, by examining citation patterns, bibliometric analysis can assess the impact of specific studies or publications on the field. The Science Citation Index Expanded (SCI-EXPANDED) from Clarivate Analytics is the most practical and commonly utilized data collection for examining scientific achievements across all sectors of research (Ho et al., 2022).

Traditionally, the analysis of hypoglycemia has primarily relied on statistical and clinical methods, often constrained by their inability to capture the intricate web of variables and factors contributing to hypoglycemic events. However, in recent years, Bayesian methods have brought a novel and sophisticated perspective to understanding hypoglycemia in diabetes



(Zulkafli et al., 2020). Accordingly, this study also conducts a comprehensive review of Bayesian analysis applied in research on hypoglycemia in diabetes.

The novelty of this review lies in its holistic approach, integrating bibliometric analysis and Bayesian insights, which represents a unique aspect of the review, contributing to a comprehensive understanding of hypoglycemia in diabetes. This review is special since it offers a data-driven perspective of the research environment, revealing insights about document types, authorship patterns, and citation impacts. It also examines the Bayesian method in understanding hypoglycemia, which has not been explored much previously in reviews, making the review different from what is already available.

Therefore, this research aims to enhance the understanding of hypoglycemia in diabetes, paving the way for precise strategies in prevention and management. Through a blend of bibliometric analysis and Bayesian insights, the study seeks to illuminate new pathways in healthcare research for more effective patient-centered approaches.

## 2. Materials and Methods

The information for this study was sourced from Clarivate Analytics' SCI-EXPANDED database, which was last updated on August 14, 2023. Journal impact factors for 2022 were derived from the Journal Citation Reports (JCR) published on June 30, 2023. To align with the journal impact factor definition, documents published in 2022 were specifically collected from SCI-EXPANDED after June 30, 2023. The search employed the keywords ("symptom" or "symptoms") AND ("hypoglycemic" or "hypoglycemia" or "hypoglycaemia" or "hypoglycaemic") AND ("Diabetes" or "Diabetic" or "Diabetics") as Topic terms within SCI-EXPANDED, resulting in 1,596 documents from 2000 to 2022. Additional coding was performed manually in Microsoft Excel 2016. Affiliations from England, Scotland, Northern Ireland, and Wales were combined under the umbrella category of the United Kingdom (UK) (Islam et al., 2022). Only the most recent corresponding author was identified in circumstances with numerous corresponding authors. Meanwhile, for single-author articles with unspecified corresponding authorship, the single author was considered both the first and corresponding author (Mamun et al., 2023). We employed four citation metrics to assess the citations received by the publications (Ho et al., 2022):

$C_0$ : The total amount of Web of Science Core Collection citations in the publishing year.

$C_{year}$ : The total number of citations from the Web of Science Core Collection received in a given year, with " $C_{2022}$ " denoting citations in the year 2022.

$TC_{year}$ : The total number of citations from the Web of Science Core Collection, beginning with the year of publication and continuing until the end of the most recent year. In this study, the most recent year considered is 2022 ( $TC_{2022}$ ).

$CPP_{year}$ : Citations per publication, calculated as  $CPP_{2022} = TC_{2022}/TP$ , where TP represents the total number of articles.

## 3. Results

Table 1 categorizes research document types, presenting that articles are the most prevalent (1,301), with an average of about six authors and over 32,000 citations in 2022. In contrast, corrections are rare (1) and receive no citations. Furthermore, editorial materials (7) averaged about three authors and received around 82 citations. Similarly, letters (2) averaged about 4.5 authors and received approximately ten citations. On the other hand, meeting abstracts (31) averaged about 5.6 authors but received only seven citations. Meanwhile, proceedings papers (44) averaged about 4.5 authors and garnered a substantial 1,487 citations. Additionally, reviews (205) averaged about 4.3 authors and accumulated a significant 9,128 citations. Finally, book chapters (5) averaged about 2.4 authors and received around 26 citations. Thus, this data provides insights into the diversity of research documents, their typical authorship, and their influence based on 2022 citations.

**Table 1** Organizing citations and authors based on document type.

| Document type      | TP <sup>a</sup> | TP* <sup>b</sup> | %    | AU <sup>c</sup> | APP <sup>d</sup> | $TC_{2022}$ | $CPP_{2022}$ |
|--------------------|-----------------|------------------|------|-----------------|------------------|-------------|--------------|
| Article            | 1301            | 1300             | 81.5 | 7639            | 5.9              | 32644       | 25.1         |
| Correction         | 1               | 1                | 0.1  | 1               | 1.0              | 0           | 0.0          |
| Editorial material | 7               | 7                | 0.4  | 23              | 3.3              | 82          | 11.7         |
| Letter             | 2               | 2                | 0.1  | 9               | 4.5              | 10          | 5.0          |
| Meeting abstract   | 31              | 31               | 1.9  | 174             | 5.6              | 7           | 0.2          |
| Proceedings paper  | 44              | 44               | 2.8  | 196             | 4.5              | 1487        | 33.8         |
| Review             | 205             | 205              | 12.8 | 883             | 4.3              | 9128        | 44.5         |
| Book chapter       | 5               | 5                | 0.3  | 12              | 2.4              | 26          | 5.2          |

<sup>a</sup>Total Publications, <sup>b</sup>Author Information Publications, <sup>c</sup>Total Authors, <sup>d</sup>Authors per Publication.

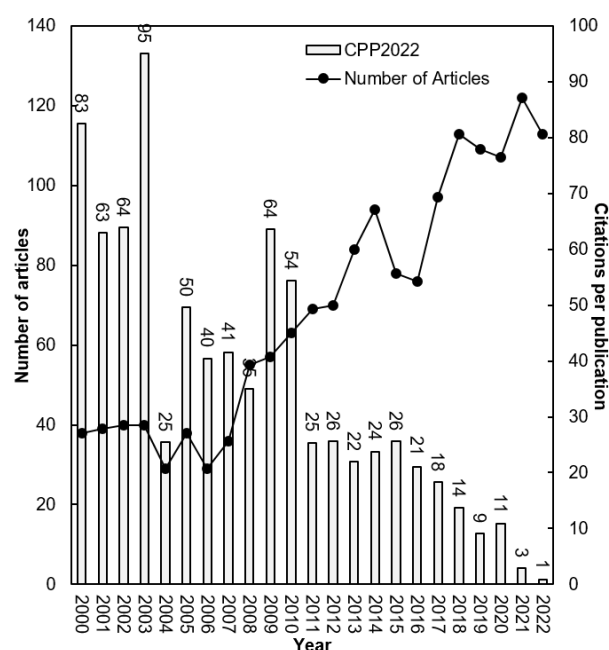
In addition, Table 2 provides an overview of the top 10 productive Web of Science categories, with "Endocrinology & Metabolism" being the most prolific, contributing 37.2% of the total articles. Key metrics include Total Citations ( $TC_{2022}$ ) for "Medicine, General & Internal," reaching 6,775, Citations Per Publication ( $CPP_{2022}$ ) for "Endocrinology & Metabolism," averaging 35, and the total number of authors (AU) in this category totaling 3,471. Moreover, the average number of Authors

Per Publication (APP) was 7.0 in "Multidisciplinary Sciences," which emphasizes collaboration trends and authorship structures in these fields.

**Table 2** The top 10 most productive Web of Science categories.

| Web of Science category                | TP (%)    | TC <sub>2022</sub> | CPP <sub>2022</sub> | AU   | APP |
|--|-----------|--------------------|---------------------|------|-----|
| Endocrinology & Metabolism             | 593(37.2) | 20733              | 35.0                | 3471 | 5.9 |
| Medicine, General & Internal           | 186(11.7) | 6775               | 36.4                | 972  | 5.2 |
| Pharmacology & Pharmacy                | 78(4.9)   | 931                | 11.9                | 401  | 5.1 |
| Endocrinology & Metabolism; Pediatrics | 30(1.9)   | 676                | 22.5                | 161  | 5.4 |
| Pediatrics                             | 25(1.6)   | 263                | 10.5                | 147  | 5.9 |
| Surgery                                | 25(1.6)   | 535                | 21.4                | 141  | 5.6 |
| Medicine, General & Internal;          | 23(1.4)   | 779                | 33.9                | 136  | 5.9 |
| Medicine, Research & Experimental      |           |                    |                     |      |     |
| Multidisciplinary Sciences             | 21(1.3)   | 292                | 13.9                | 146  | 7.0 |
| Medicine, Research & Experimental      | 21(1.3)   | 219                | 10.4                | 129  | 6.1 |
| Nursing                                | 20(1.3)   | 160                | 8.0                 | 71   | 3.6 |

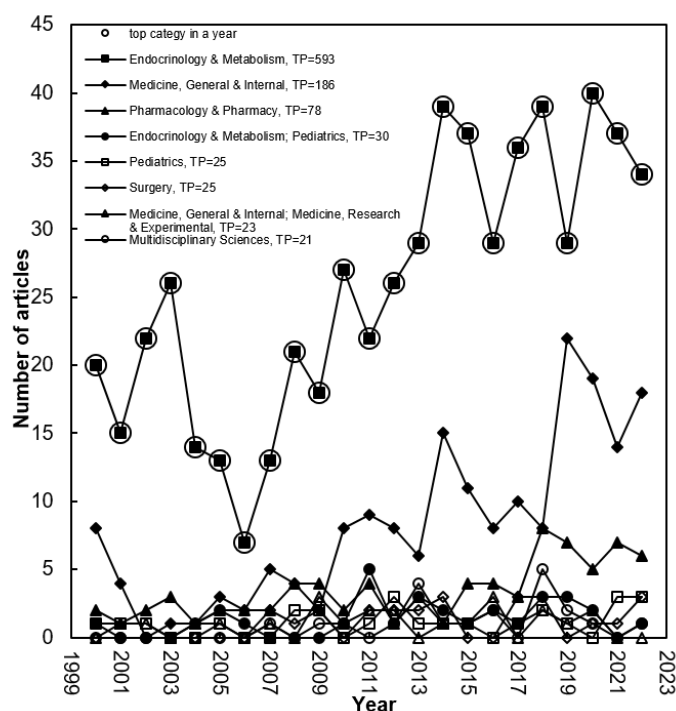
Moving on, the year-by-year distribution of Total Publications (TP) and Citations Per Publication ( $CPP_{2022}$ ), represented as  $TC_{2022}/TP$ , is depicted in Figure 1. For instance, in 2003, 40 publications were released, with the highest  $CPP_{2022}$  of 95. Among these, eight publications (20%) were highly cited, with one classic article by Vinik et al. (2003) receiving over 1,000 citations. Although  $CPP_{2022}$  has been declining since 2010, the TP has steadily increased, reaching 113 in 2022. This demonstrates a growing research interest in hypoglycemia. As a result, it is anticipated that  $CPP_{2022}$  may rise as more articles are published in the coming years.



**Figure 1** Annual Article and Citation Distribution by Publication.

Figure 2 further highlights the historical evolution of the top ten research categories, illustrating the consistent dominance of "Endocrinology & Metabolism," along with "Medicine, General & Internal," and "Pharmacology & Pharmacy," maintaining stable top-five positions since 2000. Notably, key journals in this domain include Diabetes Care, Diabetic Medicine, Diabetes Obesity Metabolism, Diabetology, and Diabetes. Similarly, Figure 3 compares publication trends in the top six high-productivity countries—the United States (US), China, Japan, England, Germany, and India. It highlights that the US consistently leads in the number of published articles, followed by China and Japan, while India has steadily increased over the years.

Furthermore, Table 3 highlights the top 10 institutions in hypoglycemia research. Novo Nordisk leads with 36 publications and a  $CPP_{2022}$  of 60.9, followed by Harvard University with 35 publications and a higher  $CPP_{2022}$  of 91.7. Additionally, the University of London, University of Copenhagen, and University of California System also contributed significantly, demonstrating notable research output and impact.



**Figure 2** Trends in the top Web of Science categories.

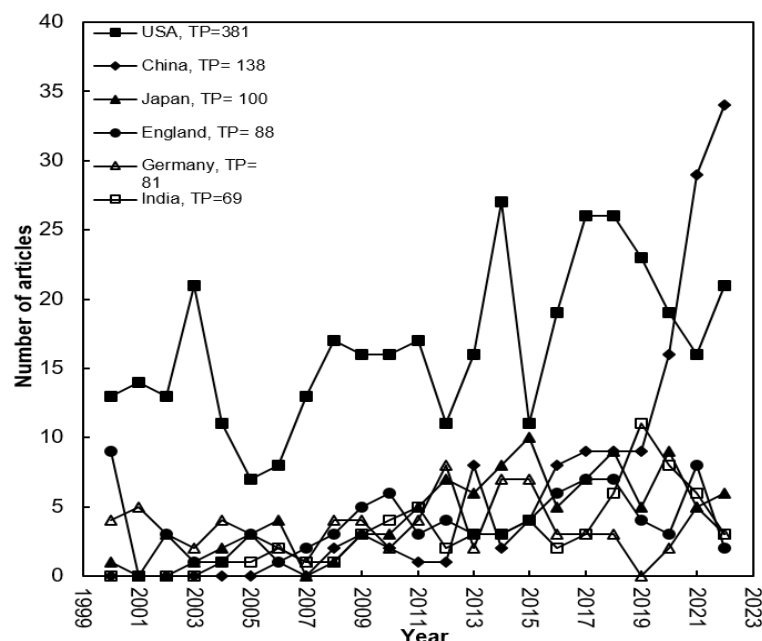
**Table 3** Institutions with the Highest Research Productivity.

| Institute                          | TP | TPR(%) <sup>a</sup> | IPR(%) <sup>b</sup> | CPR(%) <sup>c</sup> | FPR(%) <sup>d</sup> | RPR(%) <sup>e</sup> | SPR(%) <sup>f</sup> | CPP <sub>2022</sub> |
|------------------------------------|----|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| Novo Nordisk                       | 36 | 1(2.3)              | 4(0.9)              | 3(3.5)              | 19(0.6)             | 10(0.5)             | N/A <sup>g</sup>    | 60.9                |
| Harvard University                 | 35 | 2(2.2)              | N/A                 | 1(3.9)              | 5(1.0)              | 18(0.4)             | 4(1.4)              | 91.7                |
| University of London               | 33 | 3 (2.1)             | N/A                 | 2(3.7)              | 3(1.1)              | 83(0.1)             | 5(1.4)              | 34.0                |
| University of Copenhagen           | 31 | 4 (1.9)             | 79(0.2)             | 4(3.3)              | 7(0.8)              | 27(0.3)             | 6(1.4)              | 30.4                |
| University of California System    | 29 | 5 (1.8)             | N/A                 | 5(3.2)              | 4(1.1)              | 19(0.4)             | 2(2.9)              | 36.6                |
| Harvard Medical School             | 27 | 6(1.7)              | N/A                 | 6(3.0)              | N/A                 | N/A                 | N/A                 | 110.1               |
| Udice French Research Universities | 25 | 7(1.6)              | N/A                 | 7(2.8)              | N/A                 | N/A                 | 7(1.4)              | 36.7                |
| US Department of Veterans Affairs  | 24 | 8(1.5)              | N/A                 | 8(2.7)              | 18(0.6)             | N/A                 | N/A                 | 54.1                |
| Veterans Health Administration VHA | 24 | 9(1.5)              | N/A                 | 9 (2.7)             | N/A                 | 28(0.3)             | N/A                 | 54.1                |
| Kings College London               | 22 | 10(1.4)             | N/A                 | 10 (2.4)            | N/A                 | 5(0.6)              | 8(1.4)              | 17.1                |

<sup>a</sup> Institutional rank and proportion of total articles, <sup>b</sup> Rank and percentage of articles written only by single institute among all articles written by a particular institute, <sup>c</sup> Rank and proportion of inter-institutional collaboration papers among all collaborative articles, <sup>d</sup> The number and percentage of papers in which the first author is linked with the institution out of all first-author articles, <sup>e</sup> Rank and percentage of corresponding-author publications with the corresponding author linked with the institution among all corresponding-author articles, <sup>f</sup> Rank and percentage of articles from the institution written by a single author among all single-author papers, <sup>g</sup>No data available.

In contrast, Table 4 ranks hypoglycemia research articles based on total citations up to 2022 and citations within 2022. It highlights the most influential articles and their contributions. Interestingly, sorting by Total Citations ( $TC_{2022}$ ) produced a different ranking than sorting by citations in 2022 ( $C_{2022}$ ). Of 1,596 publications, 727 (45.6%) did not receive any citations in 2022 ( $C_{2022}=0$ ), and 262 (16.4%) had never been cited up until the end of 2022 ( $TC_{2022}=0$ ). Notably, half of the top 100  $C_{2022}$  articles also ranked in the top 100  $TC_{2022}$  papers.

Figure 4 also illustrates the citation trends of the top five most frequently cited articles ( $TC_{2022}>500$ ), indicating changes in citation counts over time. The study by Vinik et al. (2003) ranked first in total citations ( $TC_{2022}=1,180$ ) but third in 2022 citations ( $C_{2022}=61$ ). Therefore, these findings contribute to a broader understanding of the impact and progression of hypoglycemia research.



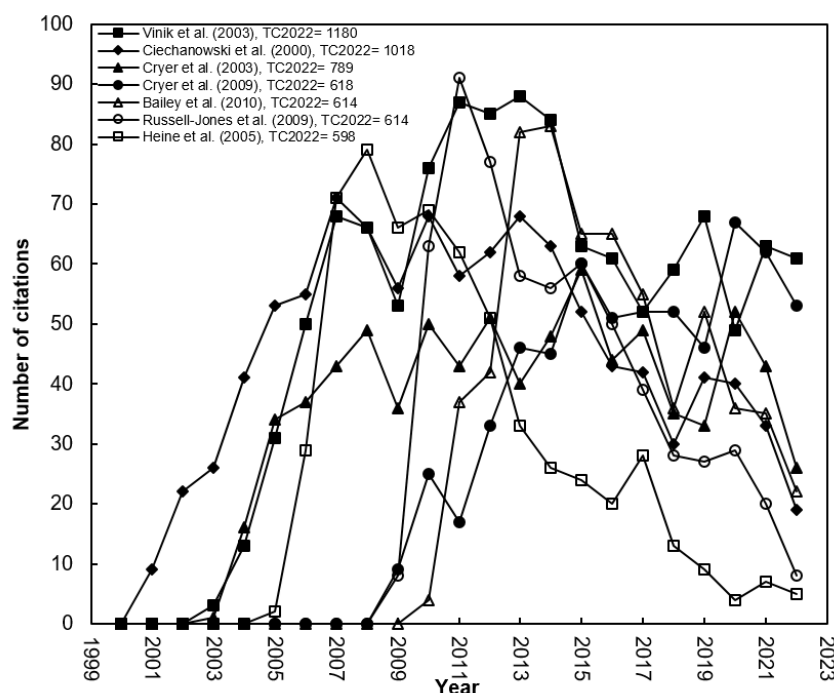
**Figure 3** Comparative Analysis of Progression Trends in the Leading Six High-Productivity Countries.

**Table 4** The top 10 most commonly cited articles containing search keywords or author keywords in their titles.

| R <sup>a</sup><br>(TC <sub>2022</sub> ) | R (C <sub>2022</sub> ) | Title   | Country                                      | Reference                    |
|---|------------------------|---|--|------------------------------|
| 1(1180)                                 | 3(61)                  | Diabetic autonomic neuropathy   | USA  | (Vinik et al., 2003)         |
| 2(1018)                                 | 32(19)                 | Depression and diabetes Impact of depression symptoms on adherence, function, costs   | USA  | (Ciechanowski et al., 2000)  |
| 3(789)                                  | 12(26)                 | Hypoglycemia in diabetes  | USA  | (Cryer et al., 2003)         |
| 4(618)                                  | 4(53)                  | Evaluation and Management of Adult Hypoglycemic Disorders: An Endocrine Society Clinical Practice Guideline   | USA, England                                 | (Cryer et al., 2009)         |
| 5(614)                                  | 119(8)                 | Liraglutide vs insulin glargine and placebo in combination with metformin and sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+SU): a randomised controlled trial                               | England, Denmark, India, Serbia, Spain       | (Russell-Jones et al., 2009) |
| 6(614)                                  | 20(22)                 | Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial   | England, Brazil, Belgium, USA                | (Bailey et al., 2010)        |
| 7(598)                                  | 239(5)                 | Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes - A randomized trial   | USA, Switzerland                             | (Heine et al., 2005)         |
| 8(545)                                  | 88(10)                 | Hypoglycaemia: The limiting factor in the glycaemic management of Type I and Type II Diabetes   | USA  | (Cryer, 2002)                |
| 9(529)                                  | 16(24)                 | Dapagliflozin Monotherapy in Type 2 Diabetic Patients With Inadequate Glycemic Control by Diet and Exercise A randomized, double-blind, placebo-controlled, phase 3 trial                                   | Italy, Mexico, USA, Spain                    | (Ferrannini et al., 2010)    |
| 10(502)                                 | 1(87)                  | Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial   | Sweden, Spain, Netherlands, Germany, Austria | (Bolinder et al., 2016)      |
| 11(431)                                 | 40(17)                 | Effects of glucagon-like peptide 1 on counterregulatory hormone responses, cognitive functions, and insulin secretion during hyperinsulinemic, stepped hypoglycemic clamp experiments in healthy volunteers | Germany                                      | (Nauck et al., 2002)         |

|         |        |  |   |                        |
|---------|--------|--|---|------------------------|
| 12(417) | 25(20) | The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study | USA   | (Bonds et al., 2010)   |
| 13(374) | 2(68)  | COVID-19 and diabetes: Knowledge in progress   | Norway, Brazil, Belgium, India, Netherlands | (Hussain et al., 2020) |
| 14(356) | 24(21) | A critical review of the literature on fear of hypoglycemia in diabetes: Implications for diabetes management and patient education                    | USA   | (Wild et al., 2007)    |
| 15(354) | 10(34) | Increased Mortality of Patients with Diabetes Reporting Severe Hypoglycemia  | USA   | (McCoy et al., 2012)   |

\*R: ranking in 1,596 articles.



**Figure 4** Top five highly cited articles with keywords in their titles or author keywords ( $TC_{2022} > 500$ ) and their citation lifespans.

In addition, a comprehensive search on August 14, 2023, using PubMed, Web of Science, and Scopus, was conducted to evaluate the efficacy of Bayesian methods in managing hypoglycemia. Keywords included ("hypoglycemia" OR "hypoglycaemia" OR "hypoglycemic" OR "hypoglycaemic") AND ("diabetes" OR "diabetics" OR "diabetic") AND ("Bayesian"), while deliberately excluding the keyword "symptom" to avoid narrowing the search results. Regarding eligibility criteria, research that used Bayesian analysis for hypoglycemia in individuals with Types 1, 2, or Gestational Diabetes (GAD) was included in this study. However, studies without full-text availability, editor notes, non-English content, grey literature, and non-peer-reviewed articles were excluded. Moreover, review papers, randomized control trials, and meta-analyses were not considered. Duplicate studies were removed, and the eligibility screening involved title, abstract, and full-text assessments by the authors, as displayed in Figure 5's Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Table 5 outlines various Bayesian modeling approaches used in diabetes research, with assessments based on specific tools like credible intervals, deviance, Root Mean Squared Error (RMSE), and Receiver-operating characteristic curve (ROC) curves. Models such as logistic-type latent variable models, Bayesian hierarchical logistic regression, and Bayesian Neural Networks (BNNs) have been applied in diabetes management, with techniques like Markov Chain Monte-Carlo (MCMC), Area under the curve (AUC), and Bayesian Information Criterion (BIC) used to evaluate their performance. For example, the Glucose-Insulin Mixture (GIM) model was evaluated through RMSE, precision, recall, and MCMC. Bayesian smoothing with closed-loop control algorithms and Bayesian Generalized Linear mixed models were assessed using Bayesian regularization approaches. Latent glucose variability models and dual-hormone closed-loop dosing algorithms were evaluated through RMSE and DIC. Bayesian latent profiling approaches used BIC and Log-Pseudo Marginal Likelihood (LPML). Bayesian Networks (BNs), including naïve networks and Reverse Engineering Forward Simulation (REFS), were assessed using AUC, sensitivity, specificity, and odds ratios. BNN, both optimal and adaptive, were evaluated through ROC, confusion matrix, mean squared error, and stochastic



variation inference methods. These tools collectively contribute to the comprehensive assessment of diverse Bayesian models in the context of diabetes management research.

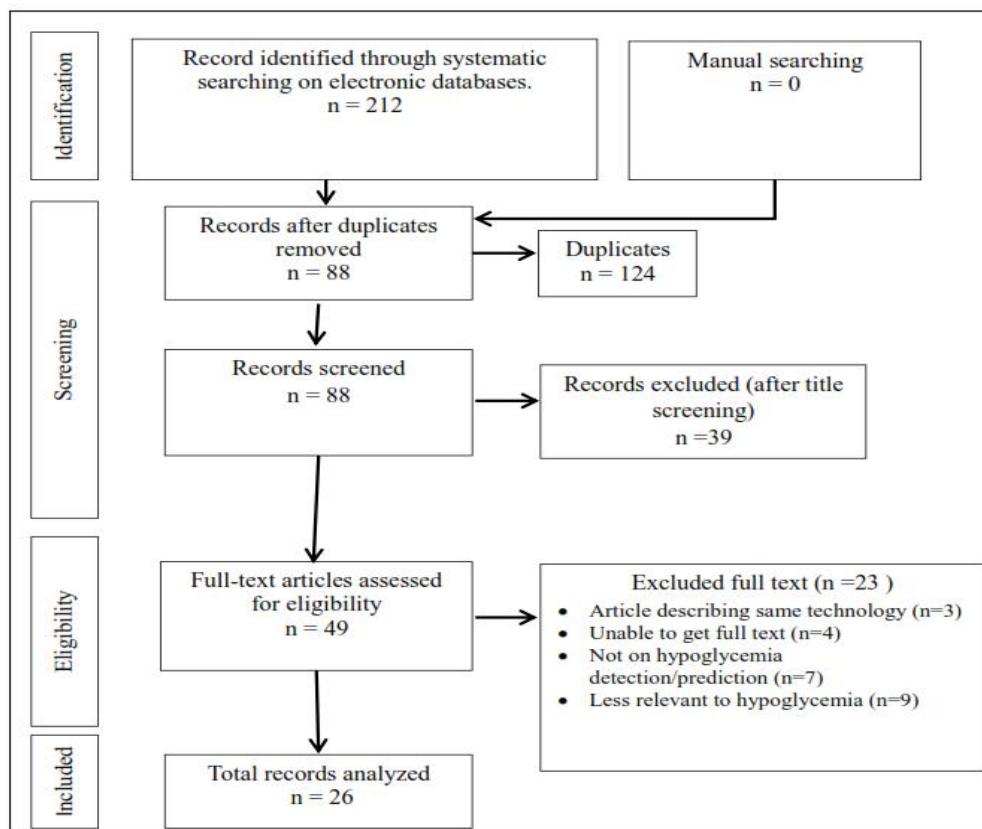


Figure 5 PRISMA flow diagram.

Table 5 Classification of the papers by Types of various Bayesian techniques.

| Techniques         | Models  | Assessment tools  | References                 |
|--------------------|---|---|----------------------------|
| Bayesian modelling | Logistic-type latent variable model   | Credible Interval, Deviance, DIC  | (Zammit et al., 2011)      |
|                    | Logistic-type latent variable model   | Credible Interval, DIC  | (Zulkafli et al., 2016)    |
|                    | Logistic-type latent variable model   | Credible Interval, Stochastic latent residual, posterior predictive checking,               | (Zulkafli et al., 2020)    |
|                    | Bayesian hierarchical logistic regression model   | Posterior predictive distribution   | (Yuan et al., 2023)        |
|                    | A data-driven meal bolus decision method  | Gaussian process regression and Bayesian optimization                                       | (Cai et al., 2021)         |
|                    | Copula-based modeling, conditional distribution modeling, and hierarchical correlation modeling | posterior predictive checking and DIC   | (Zhao et al., 2013)        |
|                    | A model-based iterative algorithm   | MCMC, Weighted residual, Root Mean Square Error (RMSE)                                      | (Fathi et al., 2021)       |
|                    | Glucose-Insulin Mixture (GIM) model   | Root Mean Square Error (RMSE), Gelman-Rubin ratios, MCMC, accuracy, precision, recall       | (Wang et al., 2021)        |
|                    | Bayesian smoothing with closed-loop control algorithms and prediction algorithms                | Bayesian regularization approach  | (Zecchin et al., 2013)     |
|                    | Bayesian smoothing with Kalman filter   | Monte Carlo simulation and Glucoday system  | (Facchinetti et al., 2011) |
|                    | Bayesian Generalized Linear mixed model   | Credible Interval, MCMC, trace plot, Multivariate Potential Scale Reduction Factor (MPSRF). | (LaLonde & Qu, 2020)       |

|                         |  |   |  |
|-------------------------|--|---|--|
|                         | Bayesian Generalized Linear mixed model  | Back-transformed posterior mean, credible intervals, posterior probability (pp) of coefficient  | (Jeyam et al., 2021)                                   |
|                         | Latent glucose variability with genetic programming algorithm  | RMSE, Parkes error grid, Kernel Density Estimation (KDE), the Nemenyi test, and Plackett–Luce distribution over ranking   | (Contador et al., 2021)                                |
|                         | Bayesian estimation with dual-hormone closed-loop dosing algorithms and artificial pancreas technology   | MCMC, DIC, mean weighted residuals  | (Emami et al., 2017)                                   |
|                         | Bayesian latent profiling approach Under the framework of Multiple Imputation (MI)                       | Bayesian Information Criterion (BIC) and the Log-Pseudo Marginal Likelihood (LPML), leave-one-out cross-validation, posterior predictive check, credible Interval | (Si et al., 2020)                                      |
| Bayesian Network        | Naïve network  | Area under the receiver operating characteristic curve (AUC), sensitivity, and specificity  | (Wang et al., 2022)                                    |
|                         | Reverse Engineering Forward Simulation (REFS)  | AUC, Odds ratio   | (Mueller et al., 2020)                                 |
| Bayesian Neural Network | Optimal BNN with feed-forward neural network   | ROC, sensitivity, and specificity   | (Nguyen, Ghevondian, Nguyen, & Jones, 2007)            |
|                         | Optimal BNN with feed-forward neural network   | Sensitivity and specificity   | (Nguyen, Jones, & leee, 2010)                          |
|                         | Adaptive Optimal BNN   | Conjugate gradient, quasi-Newton, and scaled conjugate gradient algorithms, confusion matrix, sensitivity, and specificity  | (Nguyen, 2008)   |
|                         | Optimal BNN with Electroencephalogram (EEG) spectral features and Clarke's error grid analysis           | Sensitivity and specificity   | (Ngo et al., 2019; Ngo et al., 2020; Ngo et al., 2021) |
|                         | Bayesian regularized neural network with Electroencephalogram (EEG) spectral features and Welch's method | Area under Curve (AUC), sensitivity, and specificity  | (Ngo et al., 2018)                                     |
|                         | Deterministic Feed-Forward Neural Networks (FFNN) and Bayesian Feed-Forward Neural Networks (BFNN)       | Mean squared error, Kullback–Leibler divergence, stochastic gradient descend method, stochastic variational inference method                                      | (Ngo et al., 2020; Shi et al., 2019)                   |

Finally, Table 6 classifies reviewed studies by diabetes type and the Bayesian methods used. It reveals that Bayesian modeling is prevalent in adult Type 1 and Type 2 diabetes research while also highlighting a lack of studies on child-related Type 2 Diabetes (T2DM) and GAD. Moreover, most BNN applications focus on Type 1 Diabetes (T1DM), indicating a need for more research on GAD and Type 2 diabetes in children.

**Table 6** Classification of the reviewed papers by Types of diabetes and Bayesian techniques.

| Types of diabetes              | Type 1   |                      | Type 2                                    |       | GAD   |
|--------------------------------|--|----------------------|---|-------|---|
|                                | Adult  | Child                | Adult                                     | Child |   |
| Bayesian statistical modelling | (Zecchin et al., 2013; Cai et al., 2021; Contador et al., 2021; Emami et al., 2017; Facchinetti et al., 2011; Jeyam et al., 2021; Wang et al., 2021; Zammitt et al., 2011) | (Fathi et al., 2021) | (Yuan et al., 2023; Zhao et al., 2013)    | NA    | NA  |
| Bayesian network               | NA   | NA                   | (Mueller et al., 2020; Wang et al., 2022) | NA    | NA  |
|                                |  |                      |   |       | Adult with both Type 1 and Type 2 (LaLonde & Qu, 2020; Si et al., 2020; Zulkafli et al., 2016; Zulkafli et al., 2020) |



|                               |  |   |    |    |    |    |
|-------------------------------|--|---|----|----|----|----|
| Bayesian<br>neural<br>network | (Ngo et al., 2020; Ngo et al., 2019;<br>Ngo et al., 2018; Ngo et al., 2020;<br>Shi et al., 2019) | (Ngo et al., 2021;<br>Nguyen, 2008;<br>Nguyen et al., 2007;<br>Nguyen et al., 2010) | NA | NA | NA | NA |
|-------------------------------|--|---|----|----|----|----|

4. Discussion

The analysis of hypoglycemia research published up to 2022 reveals significant trends in authorship, citation impact, and methodological approaches, particularly focusing on Bayesian statistical modeling. The data indicates that articles remain the predominant document type in this field, with an impressive total of 1,301 publications and an average citation count exceeding 32,000 in 2022. This underscores the growing interest and relevance of hypoglycemia research among scholars and practitioners alike.

Notably, the category of "Endocrinology & Metabolism" emerged as the most prolific, contributing 37.2% of total articles. This suggests a concentrated effort within this specialty to address critical issues related to diabetes management and hypoglycemia. The findings align with previous studies that have identified similar trends in research output within endocrinology, indicating a sustained focus on metabolic disorders.

Moreover, the year-by-year distribution of publications illustrates a decline in CPP since 2010 despite an increase in TP. This trend may suggest that while more research is being conducted, the impact or novelty of individual studies may be diminishing. The peak CPP observed in 2003 (95) coincides with the publication of seminal works such as that by Vinik et al., which has continued to influence subsequent research.

The citation trajectory analysis revealed that a significant portion of published articles (45.6%) received no citations in 2022. This could indicate a potential disconnect between newly published research and its integration into ongoing scholarly discourse or clinical practice. Conversely, the top-cited articles demonstrate that foundational studies continue to shape current understanding and methodologies in hypoglycemia research.

A key finding from this study is the prevalent use of Bayesian modeling techniques across various diabetes types, particularly Types 1 and 2 diabetes. The diversity of Bayesian approaches employed—from logistic regression models to neural networks—highlights their adaptability and effectiveness in addressing complex clinical questions related to hypoglycemia management. However, there remains a notable gap in research focused on GAD and pediatric populations with Type 2 diabetes, suggesting areas ripe for future investigation.

The comprehensive evaluation of Bayesian methods also indicates that while these techniques enhance predictive accuracy and decision-making processes in diabetes management, further investigation is warranted to standardize methodologies and validate findings across diverse populations.

The insights gained from this analysis underscore the need for continued exploration into innovative statistical methods and their application in clinical settings. Thus, future studies should aim to bridge the existing gaps in the literature concerning under-researched demographics, such as children with Type 2 diabetes and individuals with GAD. Additionally, fostering collaborations among institutions noted for high publication output could enhance knowledge exchange and drive forward impactful research initiatives.

5. Final Considerations

The study employs a two-fold approach, combining bibliometric analysis and a comprehensive review of Bayesian approaches. Using the SCI-EXPANDED database, the bibliometric analysis provides a data-driven understanding of the research landscape on hypoglycemia in diabetes. Key document types, authorship patterns, and citation impact are explored, offering insights into the diversity and influence of research documents.

The findings extend to the examination of Web of Science categories, the evolution of leading countries in publication, and the top institutions contributing to hypoglycemia research. Notable institutions such as Novo Nordisk and Harvard University stand out in terms of productivity and impact. Articles are the most common publication type, and the US consistently leads in the number of published articles, followed by China, Japan, and India. Moreover, TP has significantly increased since 2010, demonstrating growing scientific interest in hypoglycemia.

In addition, the review introduces a new perspective on hypoglycemia research in diabetes, focusing on Bayesian approaches. Various Bayesian modeling methods are comprehensively assessed, utilizing evaluation tools such as Credible Interval, Deviance, Gelman-Rubin ratios, RMSE, precision, AUC, sensitivity, specificity, and odds ratios. The study highlights the significance of BNNs in hypoglycemia prediction.

An innovative algorithm, "Hypo Mon," demonstrates the optimal use of BNNs for real-time hypoglycemia detection in children with T1DM. Comparatively, BNs offer a comprehensive view of complex factor interactions, while BNNs provide personalized, uncertainty-aware predictions, acknowledging challenges in interpretability.

Despite limitations in assessment tools, Bayesian models contribute significantly to improving diabetes management. Alternative approaches, such as latent residuals, are also explored to validate a grouped symptom consistency model, which



excels in predicting symptoms during hypoglycemia and offers a valuable tool for assessing patients' symptom-reporting abilities.

Moreover, Bayesian statistical modeling is commonly used in studies of adult Type 1 and Type 2 diabetes, though its application in child T1DM is limited, and it is absent in GAD research. BNs have primarily been applied to adult Type 2 diabetes. However, there are noticeable gaps in their use across other types of diabetes, including Type 1, children, and GAD. Meanwhile, BNNs are heavily employed in both adult and child T1DM studies. However, there is no evidence of their application to Type 2 diabetes or GAD.

In conclusion, the study highlights the potential of Bayesian methodologies to enhance diabetes care. It emphasizes the need for further targeted research in specific areas, particularly in the context of GAD and children.

## Acknowledgment

We thank Universiti Putra Malaysia for their valuable support in providing access to the computer lab. No funding was received for this research.

## Ethical Considerations

Not applicable.

## Conflict of Interest

The authors declare no conflicts of interest.

## Funding

This research did not receive any financial support.

## References

- Bailey, C. J., Gross, J. L., Pieters, A., Bastien, A., & List, J. F. (2010). Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial. *Lancet*, 375(9733), 2223-2233. [https://doi.org/10.1016/S0140-6736\(10\)60407-2](https://doi.org/10.1016/S0140-6736(10)60407-2)
- Bolinder, J., Antuna, R., Geelhoed-Duijvestijn, P., Kröger, J., & Weitgasser, R. (2016). Novel glucose-sensing technology and hypoglycaemia in type 1 diabetes: a multicentre, non-masked, randomised controlled trial. *Lancet*, 388(10057), 2254-2263. [https://doi.org/10.1016/S0140-6736\(16\)31535-5](https://doi.org/10.1016/S0140-6736(16)31535-5)
- Bonds, D. E., Miller, M. E., Bergenstal, R. M., Buse, J. B., Byington, R. P., Cutler, J. A., Hoogwerf, B. J. B. (2010). The association between symptomatic, severe hypoglycaemia and mortality in type 2 diabetes: retrospective epidemiological analysis of the ACCORD study. *BMJ (Online)*, 340(7738), 137. <https://doi.org/10.1136/bmj.b4909>
- Cai, D. H., Liu, W., Ji, L. N., & Shi, D. W. (2021). Bayesian optimization assisted meal bolus decision based on Gaussian processes learning and risk-sensitive control. *Control Engineering Practice*, 114, 11. <https://doi.org/10.1016/j.conengprac.2021.104881>
- Ciechanowski, P. S., Katon, W. J., & Russo, J. E. J. A. o. i. m. (2000). Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Archives of internal medicine*, 160(21), 3278-3285. <https://doi.org/10.1001/archinte.160.21.3278>
- Contador, S., Velasco, J. M., Garnica, O., & Hidalgo, J. I. (2021). Glucose forecasting using genetic programming and latent glucose variability features. *Applied Soft Computing*, 110, 12. <https://doi.org/10.1016/j.asoc.2021.107609>
- Cryer, P. E., Axelrod, L., Grossman, A. B., Heller, S. R., Montori, V. M., Seaquist, E. R., . . . Metabolism. (2009). Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, 94(3), 709-728. <https://doi.org/10.1210/jc.2008-1410>
- Cryer, P. E., Davis, S. N., & Shamon, H. J. D. c. (2003). Hypoglycemia in diabetes. *Diabetes care*, 26(6), 1902-1912. <https://doi.org/10.2337/diacare.26.6.1902>
- Cryer, P. J. D. (2002). Hypoglycaemia: the limiting factor in the glycaemic management of type I and type II diabetes. *Diabetologia*, 45, 937-948. <https://doi.org/10.1007/s00125-002-0822-9>
- Emami, A., El Youssef, J., Rabasa-Lhoret, R., Pineau, J., Castle, J. R., & Haidar, A. (2017). Modeling Glucagon Action in Patients With Type 1 Diabetes. *IEEE Journal of Biomedical and Health Informatics*, 21(4), 1163-1171. <https://doi.org/10.1109/jbhi.2016.2593630>
- Facchinetti, A., Sparacino, G., & Cobelli, C. J. I. T. o. B. E. (2011). Online denoising method to handle intraindividual variability of signal-to-noise ratio in continuous glucose monitoring. *IEEE Transactions on Biomedical Engineering*, 58(9), 2664-2671. <https://doi.org/10.1109/TBME.2011.2161083>
- Fathi, A. E., Kearney, R. E., Palisaitis, E., Boulet, B., & Haidar, A. (2021). A Model-Based Insulin Dose Optimization Algorithm for People with Type 1 Diabetes on Multiple Daily Injections Therapy. *IEEE Transactions on Biomedical Engineering*, 68(4), 1208-1219. <https://doi.org/10.1109/TBME.2020.3023555>
- Ferrannini, E., Ramos, S. J., Salsali, A., & Tang, W. (2010). Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. *Diabetes care*, 33(10), 2217-2224. <https://doi.org/10.2337/dc10-0612>
- Heine, R. J., Van Gaal, L. F., Johns, D., Mihm, M. J., Widell, M. H., Brodows, R. G., & medicine, G. S. G. J. A. o. i. (2005). Exenatide versus insulin glargine in patients with suboptimally controlled type 2 diabetes: a randomized trial. *Annals of internal medicine*, 143(8), 559-569.
- Ho, Y.-S., Fahad Halim, A., Islam, M. T. J. F. i. B., & Biotechnology. (2022). The trend of bacterial nanocellulose research published in the science citation index expanded from 2005 to 2020: a bibliometric analysis. *Frontiers in Bioengineering and Biotechnology*, 9, 795341. <https://doi.org/10.3389/fbioe.2021.795341>
- Ho, Y.-S., Sharmin, A. A., Islam, M. T., & Halim, A. F. (2022). Future direction of wound dressing research: Evidence From the bibliometric analysis. *Journal of Industrial Textiles*, 52, 15280837221130518. <https://doi.org/10.1177/15280837221130518>



- Hussain, A., Bhowmik, B., do Vale Moreira, N. C. J. D. r., & practice, c. (2020). COVID-19 and diabetes: Knowledge in progress. 162, 108142.
- Islam, M. T., Farhan, M. S., Faiza, F., Halim, A. F., & Sharmin, A. A. (2022). Pigment coloration research published in the science citation index expanded from 1990 to 2020: a systematic review and bibliometric analysis. *Colorants*, 1(1), 38-57. <https://doi.org/10.3390/colorants1010005>
- Jeyam, A., Gibb, F. W., McKnight, J. A., Kennon, B., O'Reilly, J. E., Caparrotta, T. M., & Scottish Diabet Res Network, S. E. (2021). Marked improvements in glycaemic outcomes following insulin pump therapy initiation in people with type 1 diabetes: a nationwide observational study in Scotland. *Diabetologia*, 64(6), 1320-1331. <https://doi.org/10.1007/s00125-021-05413-7>
- LaLonde, A., & Qu, Y. (2020). Estimation of group means using Bayesian generalized linear mixed models. *Pharmaceutical Statistics*, 19(4), 482-491. <https://doi.org/10.1002/pst.2006>
- Mamun, M. A. A., Haji, A., Mahmud, M. H., Repon, M. R., & Islam, M. T. J. C. (2023). Bibliometric Evidence on the Trend and Future Direction of the Research on Textile Coloration with Natural Sources. *Coatings*, 13(2), 413. <https://doi.org/10.3390/coatings13020413>
- McCoy, R. G., Van Houten, H. K., Ziegenfuss, J. Y., Shah, N. D., Wermers, R. A., & Smith, S. A. J. D. c. (2012). Increased mortality of patients with diabetes reporting severe hypoglycemia. *Diabetes care*, 35(9), 1897-1901. <https://doi.org/10.2337/dc11-2054>
- Mueller, L., Berhanu, P., Bouchard, J., Alas, V., Elder, K., Thai, N., & Miller-Wilson, L. A. (2020). Application of Machine Learning Models to Evaluate Hypoglycemia Risk in Type 2 Diabetes. *Diabetes Therapy*, 11(3), 681-699. <https://doi.org/10.1007/s13300-020-00759-4>
- Nauck, M. A., Heimesaat, M. M., Behle, K., Holst, J. J., Nauck, M. S., Ritzel, R., . . . Metabolism. (2002). Effects of glucagon-like peptide 1 on counterregulatory hormone responses, cognitive functions, and insulin secretion during hyperinsulinemic, stepped hypoglycemic clamp experiments in healthy volunteers. *The Journal of Clinical Endocrinology & Metabolism*, 87(3), 1239-1246. <https://doi.org/10.1210/jcem.87.3.8355>
- Ngo, C. Q., Chai, R. F., Jones, T. W., & Nguyen, H. T. (2021). The Effect of Hypoglycemia on Spectral Moments in EEG Epochs of Different Durations in Type 1 Diabetes Patients. *IEEE Journal of Biomedical and Health Informatics*, 25(8), 2857-2865. <https://doi.org/10.1109/jbhi.2021.3054876>
- Ngo, C. Q., Chai, R. F., Nguyen, T. V., Jones, T. W., Nguyen, H. T., & Ieee. (2019, Jul 23-27). *Nocturnal Hypoglycemia Detection using Optimal Bayesian Algorithm in an EEG Spectral Moments Based System*. Paper presented at the 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, GERMANY.
- Ngo, C. Q., Chai, R., Nguyen, T. V., Jones, T. W., & Nguyen, H. T. (2020). Electroencephalogram Spectral Moments for the Detection of Nocturnal Hypoglycemia. *IEEE Journal of Biomedical and Health Informatics*, 24(5), 1237-1245. <https://doi.org/10.1109/JBHI.2019.2931782>
- Ngo, C. Q., Truong, B. C. Q., Jones, T. W., Nguyen, H. T., & Ieee. (2018, Jul 18-21). *Occipital EEG Activity for the Detection of Nocturnal Hypoglycemia*. Paper presented at the 40th Annual International Conference of the IEEE-Engineering-in-Medicine-and-Biology-Society (EMBC), Honolulu, HI.
- Ngo, P., Tejedor, M., Tayefi, M., Chomutare, T., & Godtliebsen, F. (2020). Risk-averse food recommendation using bayesian feedforward neural networks for patients with type 1 diabetes doing physical activities. *Applied Sciences (Switzerland)*, 10(22), 1-13. <https://doi.org/10.3390/app10228037>
- Nguyen, H. T. (2008). Intelligent technologies for real-time biomedical engineering applications. *International Journal of Automation and Control*, 2(2-3), 274-285. <https://doi.org/10.1504/IJAAC.2008.022181>
- Nguyen, H. T., Ghevondian, N., Nguyen, S. T., & Jones, T. W. (2007). Optimal Bayesian neural-network detection of hypoglycemia in children with type 1 diabetes using a non-invasive and continuous monitor (HypoMon). *Diabetes*, 56, A115-A115.
- Nguyen, H. T., Jones, T. W., & Ieee. (2010). *Detection of Nocturnal Hypoglycemic Episodes using EEG Signals*. Paper presented at the 32nd Annual International Conference of the IEEE Engineering-in-Medicine-and-Biology-Society (EMBC 10), Buenos Aires, ARGENTINA.
- Russell-Jones, D., Vaag, A., Schmitz, O., Sethi, B., Lalic, N., & Antic, S. (2009). Liraglutide vs insulin glargine and placebo in combination with metformin and sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+ SU): a randomised controlled trial. *Diabetologia*, 52, 2046-2055. <https://doi.org/10.1007/s00125-009-1472-y>
- Sharmin, A. A., & Munima, H. (2016). Susceptible Factors of Type-2 Diabetes in a Population of Bangladesh. *Universal Journal of Public Health*, 4(1), 40-42. <https://doi.org/10.13189/ujph.2016.040106>
- Sharmin, A. A., Zulkafli, H. S., & Ali, N. M. (2024). Establishing cut-off points for consistency in reporting hypoglycemia symptoms among diabetes patients. *JP Journal of Biostatistics*, 24(1), 31-46. <https://doi.org/10.17654/0973514324004>
- Shi, D., Dassau, E., & Doyle, F. J., 3rd. (2019). Multivariate learning framework for long-term adaptation in the artificial pancreas. *Bioeng Transl Med*, 4(1), 61-74. <https://doi.org/10.1002/btm2.10119>
- Si, Y. J., Palta, M., & Smith, M. (2020). Bayesian profiling multiple imputation for missing hemoglobin values in electronic health records. *Annals of Applied Statistics*, 14(4), 1903-1924. <https://doi.org/10.1214/20-aos1378>
- Vinik, A. I., Maser, R. E., Mitchell, B. D., & Freeman, R. J. D. c. (2003). Diabetic autonomic neuropathy. *Diabetes Care*, 26(5), 1553-1579. <https://doi.org/10.2337/diacare.26.5.1553>
- Wang, W. J., Wang, S. P., Wang, X. J., Liu, D., Geng, Y. X., & Wu, T. (2021). A Glucose-Insulin Mixture Model and Application to Short-Term Hypoglycemia Prediction in the Night Time. *IEEE Transactions on Biomedical Engineering*, 68(3), 834-845. <https://doi.org/10.1109/tbme.2020.3015199>
- Wang, Y., Zhang, W. S., Hao, Y. T., Jiang, C. Q., Jin, Y. L., Cheng, K. K., & Xu, L. (2022). A Bayesian network model of new-onset diabetes in older Chinese: The Guangzhou biobank cohort study. *Frontiers in Endocrinology*, 13. <https://doi.org/10.3389/fendo.2022.916851>
- Wild, D., von Maltzahn, R., Brohan, E., Christensen, T., Clauson, P., Gonder-Frederick, L. J. P. e., & counseling. (2007). A critical review of the literature on fear of hypoglycemia in diabetes: implications for diabetes management and patient education. *Patient education and counseling*, 68(1), 10-15. <https://doi.org/10.1016/j.pec.2007.05.003>
- Yuan, K., Xie, M. D., Hou, H. J., Chen, J. J., Zhu, X. Y., Wang, H. M., & Liu, X. F. (2023). Association of glycemic gap with stroke recurrence in patients with ischemic stroke. *Journal of Diabetes*, 10. <https://doi.org/10.1111/1753-0407.13432>
- Zammit, N. N., Streftaris, G., Gibson, G. J., Deary, I. J., & Frier, B. M. (2011). Modeling the consistency of hypoglycemic symptoms: High variability in diabetes. *Diabetes Technology and Therapeutics*, 13(5), 571-578. <https://doi.org/10.1089/dia.2010.0207>

- Zecchin, C., Facchinetti, A., Sparacino, G., Dalla Man, C., Manohar, C., Levine, J. A., & Cobelli, C. (2013). Physical activity measured by physical activity monitoring system correlates with glucose trends reconstructed from continuous glucose monitoring. *Diabetes Technology and Therapeutics*, 15(10), 836-844. <https://doi.org/10.1089/dia.2013.0105>
- Zhao, Y., Shen, W., & Fu, H. (2013). Joint modeling of clinical efficacy and safety with an application to diabetes studies. *Journal of Biopharmaceutical Statistics*, 23(5), 1155-1171. <https://doi.org/10.1080/10543406.2013.813520>
- Zulkafli, H. S., Streftaris, G., Gibson, G. J. J. M., & Statistics. (2020). Stochastic latent residual approach for consistency model assessment. *Mathematics and Statistics*, 8(5), 583-589. <https://doi.org/10.13189/ms.2020.080513>
- Zulkafli, H. S., Streftaris, G., Gibson, G. J., & Zammitt, N. N. (2016). Bayesian modelling of the consistency of symptoms reported during hypoglycaemia for individual patients. *Malaysian Journal of Mathematical Sciences*, 10(S), 27-39.