

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

¹ Dr. Deepali Ingle, ^{2*} Dr. Pranothi Bhanage, ³ Dr. Dharmendra Sharma

¹Professor & HOD, PhD scholar, Department of Community Medicine, Dr. D.Y. Patil Homeopathic Medical College And Research Centre, Dr. D.Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune, Maharashtra, India.

^{2*}Associate Professor, Department of Community Medicine, Dr. D.Y. Patil Homeopathic Medical College And Research Centre, Dr. D.Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune, Maharashtra, India.

³Principal, Dr. D.Y. Patil Homeopathic Medical College And Research Centre, Dr. D.Y. Patil Vidyapeeth (Deemed to be University), Pimpri, Pune, Maharashtra, India.

**Corresponding Author: Dr. Pranothi Bhanage*

ABSTRACT

The quality of life is significantly reduced by a number of chronic issues associated with diabetes mellitus. Although there is currently no unified data, complementary systems like homeopathy are being examined more closely for their potential role in managing issues associated to diabetes.

Objective: To systematically review and meta-analyze medical success of homeopathic medicines in management of diabetes-related complications.

Methods: Important web resources including Google Scholar, Scopus, ScienceDirect, Web of Science, and PubMed were used in a comprehensive search. Predetermined presence and barring rules were used to filter English-language studies assessing homeopathic treatments for problems associated with diabetes. The qualifying requirements were satisfied by six investigations (controlled medical studies and randomized controlled trials). Information on the study's features, interventions, results, and impact measurements was retrieved. We used a random-effects model to conduct the meta-analysis and the I² statistic to evaluate heterogeneity.

Results: Across six clinical trials involving about 557 patients (with analyzable samples varying from 27 to 247 each research), homeopathic therapies shown statistically significant advantages compared to placebo or conventional care. One double-blind randomized controlled trial (Mehra et al., 2021; n=68 assessed) indicated a substantial decrease in NTSS-6 scores for diabetic neuropathy ($p < 0.014$), accompanied by favorable trends in nerve conduction measures. Another RCT (Banerjee et al., 2024; n=60) shown a reduced development to diabetes and significant elevations in HbA1c and metabolic profiles within the homeopathy group compared to the placebo. A substantial multicentric observational research (Nayak et al., 2013; n=247 analyzed) identified considerable clinical enhancement in diabetic distal symmetric polyneuropathy, but objective measurements showed little alterations. A retrospective cohort research (To et al., 2017b; n=27 vs. 40 controls) showed substantial decreases in fasting plasma glucose and HbA1c over a duration of ≥ 12 months in the homeopathic group. Observational comparison studies (Bhasker Sharma, 2019) have shown that homeopathy along with conventional treatment is a better way to control blood sugar and cholesterol levels than conventional therapy alone. Also, a randomized double-blind study (Mourão et al., 2019; n=80) showed that when homeopathy was used along with periodontal care, clinical attachment level (CAL) improvements and gingival developments were better after 12 months. On the whole, these results show that homeopathic medicines have long-lasting and statistically significant positive effects on health and biochemistry. But the effects were not always the same and the objective results were not always the same from one study to the next.

Conclusion: The study shows that homeopathic drugs may be helpful in managing problems related to diabetes, especially when it comes to relieving symptoms and improving quality of life. However, these results need to be confirmed by more large-scale, well-designed randomized controlled trials because the studies that were included were not all the same and had problems with their methods.

Keywords: Diabetes mellitus; Diabetes-related complications; Homeopathy; Homeopathic medicines; Orderly analysis; Meta-analysis; Complementary and another drug; Clinical effectiveness

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

How to cite this article: Ingle D, Bhanage P, Sharma D. Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis. *Int J Drug Deliv Technol.* 2026;16(10s): 458-476; DOI: 10.25258/ijddt.16.10s.59

INTRODUCTION

The prevalence of diabetes mellitus has increased dramatically in recent decades, placing an enormous burden on healthcare systems, organizations, and individuals around the globe. Problems with insulin synthesis, insulin activity, or both lead to persistently elevated blood sugar levels in people with diabetes. It has been associated with several premature deaths and illnesses. In a study conducted by Hossain et al. in 2016, The prevalence of diabetes has skyrocketed in recent decades. This is due to people living in cities more often, being less active, eating poorly, getting older, and becoming more overweight. (Khan et al., 2020)

There are hundreds of millions of individuals throughout the world who are affected by diabetes, with popular of those affected active in countries with low and intermediate incomes. (Khan et al., 2020) Giving to World Health Organization, diabetes is officially recognized as top cause of death throughout the globe, and its proportion to mortality has been constantly growing. According to projections, the number of people who are afflicted by the condition is expected to increase even higher over the next several decades, which sheds light on the rising severity of the sickness. This quick surge is especially evident in poorer countries, where healthcare systems typically have problems with funding, infrastructure, and access to long-term care. (Ong et al., 2023)

Diabetes is pretty common, but the long-term effects of it cause a lot of trouble. Long-term diabetes can lead to both large and small blood vessel problems. Large blood vessel problems include peripheral vascular disease, coronary artery disease, and blow. Small blood vessel problems include neuropathy, nephropathy, and vision. Disability-adjusted life years (DALYs) go up because of these issues. They also make life less fun and make it hard to do normal things. (He et al., 2024) Diabetes also causes a lot of deaths from cardiovascular disease and stroke, as well as a lot of blindnesses, kidney failures, non-traumatic lower limb amputations, and other problems. (Kropp et al., 2023)

The financial burden of diabetes is also rather large. The direct expenditures of healthcare, such as hospital stays, drugs, monitoring, and managing problems, put a lot of pressure on national healthcare budgets. Indirect expenses, such as lost productivity, missed work days, early retirement, and the load on caregivers, make the problem much worse for society. The long-term expense of diabetes treatment may be devastating

for people and families, particularly in places where resources are few. It can frequently lead to financial problems. (Kropp et al., 2023)

The diabetes pandemic has become so bad in countries like India that it has been called the "diabetes capital" of the globe. The fact that both viral and non-infectious disorders may happen at the same time, together with differences in access to treatment, makes it much harder to manage diabetes well. Late diagnosis and poor management lead to more problems, which makes the clinical and economical burden worse. (Babu et al., 2024)

Diabetes-Related Complications and Their Clinical Impact

Uncontrolled diabetes mellitus, a metabolic disease that may last a lifetime, poses both immediate and future health risks. A combination of factors, including insulin resistance, chronic low-grade inflammation, oxidative stress, and persistent hyperglycemia, produces severe complications and worsens damage to vital organs, blood vessels, and neurons. (Antar et al., 2023) Complications from diabetes are the leading causes of mortality, disability, poor quality of life, and healthcare expenditures for persons with diabetes. (Deshpande et al., 2008)

There are two main types of diabetic complications: microvascular and macrovascular. Some examples of microvascular complications include diabetic neuropathy, nephropathy, and retinopathy. Examples of macrovascular complications include peripheral arterial disease, coronary artery disease, and cerebrovascular disease. (Chawla et al., 2016) In addition, diabetes is related with several other conditions such as diabetic foot ulcers, sexual dysfunction, autonomic neuropathy, infections, and psychological disorders, all of which grant to overall disease load. (Srinivas-Shankar et al., 2025)

One of the most prevalent and incapacitating side effects, diabetic neuropathy affects a sizable percentage of people with chronic diabetes. It manifests as peripheral sensory loss, burning pain, tingling, numbness, and motor weakness, particularly in the lower extremities. (Bodman et al., 2024) Neuropathy rises risk of foot sores, infections, and lower-limb amputations, leading to functional impairment, chronic pain, and reduced mobility. Autonomic neuropathy further impacts cardiovascular, gastrointestinal, and genitourinary functions, causing

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

orthostatic hypotension, gastroparesis, and bladder dysfunction.(Yang et al., 2025)

Diabetic nephropathy is one of the leading causes of chronic kidney disease and end-stage renal failure on a global scale. It is characterized by chronic albuminuria, declining glomerular filtration rate, and advancing renal impairment.(Rout & Jialal, 2025) Patients with diabetic nephropathy often require prolonged dialysis or kidney transplantation, substantially elevating healthcare expenses and negatively impacting survival and quality of life. Having both high blood pressure and high cholesterol speeds up kidney damage even further.(Wulandari et al., 2025)

Diabetic retinopathy is still a significant cause of blindness that may be avoided, especially among persons who are of working age. Long-term high blood sugar levels may damage the small blood vessels in the retina, leading to non-proliferative and proliferative retinopathy, macular edema, and vision problems. Loss of vision not only makes it harder to do everyday things, but it also impacts independence, work, and mental health.(Cheung et al., 2010)

Individuals with diabetes are at a heightened risk of mortality from cardiovascular-related conditions compared to other causes. persons with diabetes have heart disease earlier and it becomes worse faster than in persons without diabetes. People with diabetes are far more likely to have a heart attack, stroke, or peripheral arterial disease. These disorders often result in repeated hospitalizations, chronic impairment, and untimely mortality. Peripheral artery disease, in conjunction with neuropathy and diminished wound healing, substantially exacerbates the progression of diabetic foot problems.(Huang et al., 2017)

Diabetic foot complications are one of the most serious and expensive problems that may happen because of diabetes. Foot ulcers are caused by a mix of neuropathy, ischemia, and infection, and they often lead to amputations of the lower limbs. Amputation leads to physical impairment, significant psychological suffering, social isolation, and diminished economic output.(Parveen et al., 2025)

Diabetes is linked to serious psychological and emotional problems, such as sadness, worry, stress, and low self-esteem, in addition to medical problems. Having to keep an eye on things, take medicine, and change how you live can be very stressful, which can make it harder to stick with treatment and keep blood sugar levels under control. This can cause effects to keep getting worse.(Kalra et al., 2018)

Problems that are linked to diabetes have a big effect on people's lives. It has an effect on almost every organ

system and makes health-related quality of life a lot worse. Most of the money spent on medical care and hospital stays for people with diabetes goes to these problems. Standard medical care has gotten better, but many patients still have problems that get worse, bad responses to medications, and treatment needs that aren't met.(2010) Tomic et al. (2022)

More and more people are interested in integrative and alternative treatments that might help standard therapy because problems related to diabetes are hard to deal with and have a big impact on patients. In the overall treatment of diabetes-related conditions, it is becoming important to look at different methods like homeopathy to see if they can help ease symptoms, slow the development of the disease, and improve quality of life.(2011, Panday et al.)

Limitations of Conventional Management for Diabetic Complications

Managing consequences from diabetes usually involves strict control of blood sugar, medicines, lifestyle changes, and taking care of other health issues like high blood pressure and cholesterol. These ways have made it much more likely for people to survive and dropped the number of serious consequences, but there are still some issues with taking care of people with long-term diabetes problems. These limits cause people to stay sick longer, have a lower quality of life, and spend more on healthcare.(2018, Petrie et al.)

One of the biggest problems with standard care is that it can't stop or change how the illness gets worse. A lot of people still have or have worse capillary and macrovascular problems even when their blood sugar is well controlled. This shows that things other than high blood sugar, like oxidative stress, inflammation, genetic tendency, and metabolic memory, play a role in the development of diabetes problems and are not properly addressed by existing treatments.(Blaibel et al., 2024)

Another big problem is how hard it is to do drug treatment. When diabetes gets worse, people usually need to take more than one medicine. Some examples of these medicines are pain killers, lipid-lowering drugs, antiplatelet drugs, painkillers, and drugs that treat specific conditions like nerve pain or nephritis.(Javed et al., 2015) Polypharmacy increases the risk of drug combinations, not taking pills as prescribed, and cumulative poisoning. This is especially true for older people and those who already have other health problems.(Varghese et al., 2024)

Normal medicines have side effects that make them less useful over time. Some drugs used to treat nerve

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

pain can make you feel sick, sleepy, dizzy, and unable to concentrate. Low blood sugar and problems with fluids can happen when you use Reno defensive agents. Tough glucose control can also make low blood sugar more likely, which can lead to heart problems and death. For these side effects to go away, the dose usually needs to be dropped or stopped, which makes the treatment less effective.(Sondh et al., 2025)

Another big problem is that standard care focuses on symptoms instead of the whole person. Instead of healing the person, most treatments try to change molecular causes or hide signs. Things like quality of life, mental health, and emotions may not be taken into account in this way, which are important for handling long-term illnesses. As a result, patients may have to deal with constant pain, limited abilities, and mental suffering while getting standard care.(2024 Prabhakar) Problems with money and getting to places are also problems, especially in low- and middle-income countries. For many patients, the long-term costs of medicines, tests, doctor visits, and hospital stays for problems may be too high. Inequalities in results are made worse by limited access to specialized care and advanced therapy, which leads to delayed treatment and serious sickness when it finally happens.(Thurston et al., 2020)

In traditional therapy, not following through with treatment is common. This is because of complicated action patterns, outside factors, limited finances, and not enough patient education. If you don't follow your treatment plan, it gets harder to control your blood sugar and problems show up faster. Additionally, living changes do work, but they are hard to keep up for long periods of time without enough behavioral support.(2016, Polonsky and Henry)

Complementary and Alternative Medicine in Diabetes Care

Diabetes and associated issues are becoming increasingly common across the globe. This has made people more interested in complementary and alternative medicine (CAM) as an additional option to manage diabetes. There are several different types of alternative and complementary medicine (CAM) that are not usually used in allopathic therapy. These include acupuncture, yoga, Ayurveda, herbal medicine, and homeopathy. Patients with diabetes often pursue complementary and alternative medicine (CAM) therapies to better symptom management, reduce the side effects of traditional drugs, improve quality of life, and tackle the chronic and complex aspects of the condition.(Thilakarathna et al., 2025)

People with diabetes often utilize CAM together with traditional therapy instead of instead of it. Many patients say they feel better because they have better glycemic control, less neuropathic pain, more energy, and better mental health. CAM techniques frequently focus on changing one's lifestyle, lowering stress, customizing therapy, and providing holistic care. These are all things that people with diabetes need to do to manage their condition over the long term. Individualized medicine and mind-body therapies are receiving more interest due to their potential to address both the medical and psychological aspects of diabetes.(Setiyorini et al., 2022)

Complementary and alternative medicine (CAM) is being used more and more to treat diabetes because normal treatments have problems, such as long-lasting symptoms, bad drug responses, taking too many medications, and not having enough money. In some places, especially in Asia, complementary and alternative medicine (CAM) methods are part of everyday life and are accepted as valid forms of treatment. Even though CAM methods are used a lot, scientists still don't agree on how well they work. This shows how important it is for thorough reviews and evidence-based studies to guide clinical practice.(2014) Medagama and Bandara

Principles and Therapeutic Approach of Homeopathy

In the late 1700s, Samuel Hahnemann created homeopathy, an alternative medical approach. It has different ideas than traditional health, which makes it different. A drug that might make a healthy person sick can be used in very small amounts to help a sick person with symptoms that are similar. This idea, called "like cures like," is the most important part of homeopathy.(Jones and Brierley, 2021).

A big part of homeopathy is tailoring the treatment to each person. Homeopathic doctors don't just give medicines based on a medical evaluation; instead, they look at all of the patient's signs, such as their physical, mental, emotional, and constitutional traits. This customized approach works best for long-term conditions like diabetes, where symptoms and outcomes vary a lot from person to person. (2025) Tosun and Atayoglu

Serial dilution and potentization are the steps used to make homeopathic medicines. This involves carefully diluting the medicine and shaking it very hard. Some people believe that these mixtures help the body heal and balance itself. Homeopathic treatment for diabetes problems aims to not only get rid of specific symptoms like nerve pain or problems with the urine, but also to

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

improve overall health and balance.(1999) Vickers and Zollman

In terms of treating diabetes, homeopathy often focuses on treatments that work with or add to other treatments. People choose homeopathic treatments for a wide range of health problems, such as neuropathy, nephritis, skin sores, and general metabolic problems. Instead of quickly getting rid of symptoms, the focus is on long-term care, stopping the disease from getting worse, and making life better.Since 2009, Pomposelli et al.

Most people think that homeopathy is safe and useful, and that if it is used properly, not much bad can happen. It's a good choice for people who can't handle regular drugs or who want to find other ways to make therapy easier because it's safe. A lot of the time, homeopathic therapy also involves deep talks with patients, which may make them more likely to participate, stick with the treatment, and be happy.(2013) Dumont and Chung There is still debate about how well homeopathic diabetes and linked problems work as a medicine, even though a lot of people use them. Different study methods, personalized recommendations, and different ways of measuring outcomes make judgment harder. However, more and more clinical studies are looking into its possible benefits. This shows how important it is to do thorough systematic reviews and meta-analyses of the current data. You need to know about the basic ideas behind homeopathy and how it works in order to understand how it fits into all-around diabetes care and the findings of clinical study in this area.

Principles and Therapeutic Approach of Homeopathy

Homeopathy is an alternative medicine that treats each person's unique needs in a thorough and individualized way. The main idea behind it is the rule of similar. A drug that might make a healthy person sick can also help a sick person feel better, but only in a very weak way. Patients are given homeopathic drugs based on their unique symptoms, not just what the disease is. Picking homeopathic medicines is based on this method.It's 2020 (Donelli et al.)

One of the best things about homeopathic medicine is that it can be tailored to each person. This is easier to do when you look at the patient's medical signs, mental and behavioral state, living choices, and genetic traits all at once. There are a lot of different ways that people with long-term illnesses, like diabetes, get worse, have problems, and react to treatment. This method is mostly used to find those differences. One goal of homeopathic medicine is to help the person as a whole, not just their illness. (Prousky, 2018)

There are two ways to make homeopathic medicines: by serially diluting them and by making them stronger. A lot of people say that both ways make the original drug safer and better as a medicine together.(2007, Sagar) Homeopathy aims to enhance overall vitality by reestablishing physiological equilibrium and activating the body's inherent self-healing processes. People with diabetes-related illnesses commonly utilize homeopathy together with regular therapy. The main goals are long-term care, easing symptoms, and avoiding future problems from becoming worse.(Rut Ozeky, 2025)

Current Evidence on Homeopathy in Diabetes Management

The existing research indicates that homeopathy might be an effective treatment for diabetes. Research examining glycemic outcomes and diabetes-related comorbidities, including case series, observational studies, and randomized controlled trials, provides evidence for this assertion (Vel et al., 2025). Certain research have shown enhancements in fasting and postprandial blood glucose levels, symptom severity, neuropathic pain, and quality-of-life metrics in patients undergoing customized homeopathic therapy in conjunction with conventional care.(Nahar & Choubey, 2023)

Studies on issues associated to diabetes have looked at outcomes including better sensory function in diabetic neuropathy, less pain and paresthesia, stable kidney function, faster wound healing, and better overall functional health. These investigations indicate possible supplementary advantages of homeopathic treatments, especially in managing symptoms and enhancing patient-reported outcomes.(Smith et al., 2022) Conversely, the findings from many studies remain contradictory due to disparities in study design, sample size, duration of follow-up, and outcome measures used in each investigation.

Methodological problems, such as limited sample numbers, heterogeneity in remedy selection, and difficulties in blinding customized prescriptions, have fueled continuous debate over effectiveness. The increasing number of clinical studies, however, shows that scientists are still interested in this area. Regular reviews and meta-analyses are important for making information easy to find, checking the reliability and regularity of results, and finding gaps that need more research.

Rationale for Using Homeopathic Medicines in Diabetes-Related Complications

Because diabetes mellitus is long-lasting, gets worse over time, and is hard to treat with standard medicine,

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

people with diabetes may benefit from using homeopathic medicines to help with their health problems. Problems related to diabetes usually don't go away, even if you keep your blood sugar under control and take your medications as prescribed. This may lead to continuing symptoms, functional impairment, psychological anguish, and a worse quality of life. This has led to more people becoming interested in alternative systems of medicine that may provide personalized, supportive, and holistic treatment.(Galindo et al., 2023)

One of the best things about homeopathy is that it treats each person differently. Neuropathy, nephropathy, and long-term skin and foot disorders that are associated to diabetes may vary greatly from person to person in terms of how bad they are, what symptoms they have, and how quickly they become worse. Homeopathy prioritizes treatment that considers the whole of symptoms and the patient's constitution, as opposed to a standardized disease-oriented regimen. This approach may provide more individualized care of chronic problems.(To et al., 2017a)

Another key reason is that homeopathic treatments are often harmless. Patients with chronic diabetes often encounter polypharmacy, which increases the risk of severe treatment reactions, drug-drug interactions, and diminished adherence. Homeopathic treatments, when given correctly, are generally regarded as safe and well-tolerated, making them a viable supplementary choice for long-term use, especially in older patients and those with numerous comorbidities.(Satapathy et al., 2025)

Homeopathy aims to restore physiological equilibrium by enhancing the body's self-regulatory and healing mechanisms, rather than just alleviating symptoms. In the setting of diabetes-related problems, this technique may facilitate symptom alleviation, enhance functional ability, and promote overall well-being.(Maftei et al., 2024) Homeopathic therapy also typically deals with related mental and emotional issues including stress, anxiety, and melancholy, which are proven to affect how well blood sugar is controlled and how quickly the condition becomes worse.(Sendekie et al., 2025)

Economic and accessibility factors further substantiate the need for homeopathic use, particularly in low- and middle-income nations. Long-term costs of managing diabetes problems with standard treatments may be high, and homeopathy is generally seen as a cheaper and easier way to provide supportive care. Additionally, thorough patient consultations and lifestyle recommendations often linked to homeopathic therapy may enhance patient involvement, self-care

practices, and commitment to complete diabetes management strategies.(Varanasi et al., 2023)

Finally, the fact that there are more and more clinical studies looking into homeopathy for diabetes and its consequences shows how important it is to do a full analysis of its possible benefits. Even though the data is still not all the same and the methods aren't always the same, early results show that some groups of people are getting better in terms of how bad their symptoms are and how good their quality of life is. All of these reasons show that homeopathic medicines should be looked at as an extra way to help treat diabetes-related problems through thorough studies and comparisons.

MATERIAL AND METHOD

The point of this study was to do a thorough review and meta-analysis to find out how well homeopathic medicines help problems linked to diabetes. All the way through the process, we made sure to follow the PRISMA guidelines for systematic reviews and meta-analyses. We looked through a lot of online sources to find information that would be useful. These databases were PubMed, Scopus, Science Direct, Web of Science, Embase, and Google Scholar. From the start of the database search all the way to the finish, relevant studies published in English were located. Search terms included combinations of keywords such as "homeopathy," "homeopathic medicine," "diabetes mellitus," "diabetes complications," "diabetic neuropathy," "diabetic nephropathy," "diabetic foot," and "clinical trial." For the purpose of refining the search method, Boolean operators (AND/OR) were used. A manual screening was also performed on position lists of the chosen publications in order to locate other research that were suitable.

Inclusion Criteria

- Clinical trials (randomized or non-randomized) evaluating homeopathic medicines
- Studies involving patients with diabetes-related complications
- Studies reporting clinical, biochemical, or quality-of-life outcomes
- Full-text articles issued in English

Exclusion Criteria

- Opinion pieces, judgments, evaluations, and case summaries
- Studies without a comparison or control group
- Animal or in vitro studies
- Studies lacking sufficient outcome data

Data Extraction:

To do this, data extraction was performed using a standardized form. The following pieces of data were

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

removed: name of author, the year the research was published, the design of the study, the sample size, the kind of diabetes-related complication, homeopathic intervention, the comparator, the period of follow-up, the end measures, and the most important results. Any disagreements between reviewers were handled by debate or contact with a third assessor.

Quality Assessment

While perusing a mountain of information (online and off), I encountered zero language hurdles. Extra reference-worthy websites were located using a plethora of search engines. Inclusion and exclusion criteria were documented. Several selected articles underwent a more comprehensive quality review in accordance with standard critical evaluation criteria.

Examining heterogeneity and making judgments on the applicability of meta-analyses were done using these thorough quality ratings. The appropriate sample group for this examination was selected using a meticulously crafted procedure. The development of the literature assessment criteria took P.I.C.O. into account.

(According to Cronin et al. (2008), nurses must be able to use research results in order to attain optimal practice, which can only be accomplished if they are able to understand and evaluate the study. (J, 2010) defines a systematic review as a kind of literature review that gathers all the studies conducted on a certain subject. It ought to be based on well-crafted evidence that the reader may use to question the findings.

This is backed up by the following: (Cumpston et al., 2019) states that a systematic review should find all the evidence, published and unpublished, that fits a certain eligibility criterion and then synthesize it to answer a particular research question (Pippa Hemingway, 2009). After that, you should choose the studies to evaluate using the inclusion criteria. The next step is to assess the quality of the selected research. Making ensuring the findings are synthesized without bias is the next stage. Following this synthesis, the findings must be assessed, and a fair and balanced summary must be written while accounting for the evidence's shortcomings.

Data Collection Strategies

(Chapter 5: Collecting Data | *Cochrane Training*, n.d.) stress the importance of data collecting in systematic reviews, since it is this data that will ultimately underpin the findings drawn from the studies. Part of this process is checking that the data is available, accurate, comprehensive, and dependable. In the beginning of this systematic review and meta-analysis, a search was conducted using Google Scholar, Science

Direct, Embase, Scopus, PubMed, and Web of Science as the databases. To find articles, search terms "homeopathy," "homeopathic medicine," "diabetes mellitus," "diabetes complications," "diabetic neuropathy," "diabetic nephropathy," "diabetic foot," and "clinical trial." and all the possible combinations of these keywords were used.

We searched without regard to time constraints and imported the study meta-data into EndNote, a location managing program. Reference lists of all papers that were gathered were examined by hand to ensure that the search was as thorough as possible.

Keywords used as per MeSH: "homeopathy," "homeopathic medicine," "diabetes mellitus," "diabetes complications," "diabetic neuropathy," "diabetic nephropathy," "diabetic foot," and "clinical trial" are all terms that are often used in the medical field."

Inclusion/exclusion criteria.

Regarding this review, a unique method was established in order to identify the relevant inclusion and exclusion criteria (please refer to the table that is shown below for more information). When creating the inclusion and exclusion criteria for the literature review, the P.I.C.O. idea was taken into account. This guaranteed adherence to the research topic and the discovery of well constructed research papers as recommended by (Torgerson & Torgerson, 2003)

Since this assessment focuses on the clinical efficacy of homeopathic medications in the treatment of diabetes-related problems, they were deemed appropriate. (Pati & Lorusso, 2017) draw attention to the fact that a literature search's inclusion and exclusion criteria might introduce bias; thus, establishing confidence and credibility requires explicit recording of these criteria. Although it might be difficult to determine why some papers were eliminated from analysis, researchers are nonetheless required to provide justifications for their decisions. Additionally, he argues that search criteria might be set too broadly or too narrowly, leading to irrelevant results. The PICO framework determines the inclusion criteria. To better organize qualitative research questions and zero down on the most important aspects of the study, the PICO framework might be useful. Using it as a guide, researchers may better define their investigation's scope and zero in on pertinent themes or features of the larger subject area. To better understand the monetary toll that cancer has on patients and their families, researchers doing systematic reviews might use the PICO framework to hone in on a more specific research topic and organize qualitative data for synthesis.

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

| | |
|---------------------------|---|
| Population/Problem | Individuals diagnosed with diabetes mellitus are experiencing diabetes-related complications such as diabetic neuropathy, nephropathy, retinopathy, diabetic foot complications, or other chronic diabetes-associated conditions. |
| Intervention | Homeopathic medicines are administered as individualized or standardized homeopathic treatment, either alone or as an adjunct to conventional diabetes management. |
| Comparison | Conventional medical treatment, placebo, no intervention, or standard care without homeopathic medicines. |
| Outcome | Improvement in diabetes-related complication outcomes, including reduction in symptom severity (e.g., pain, numbness), improvement in functional capacity, stabilization or improvement of clinical and biochemical parameters, enhanced wound healing, and improved quality of life, with minimal adverse effects. |

In order to keep the search results reasonable, I did not include research that were older than ten years. Since evidence-based practice is a legal requirement for nurses, the most current literature is crucial (Lipscomb, n.d.), which implies that nurses study literature to enhance service. Nevertheless, he does concede that time-based cutoffs can be problematic since certain data from the past might be just as instructive or valuable as data from the present. Articles not written in English were not included because of the possibility of linguistic bias in the writers' poor comprehension and the possibility of inaccurate translation. However, this strategy might be challenged by (P et al., 2002) who argue that this barring seldom affects the findings.

Nonetheless, they acknowledge that studies conducted in English are often referenced more frequently and published more times. First, I did a simple keyword search using Boolean operators; then, I used several filters based on my inclusion criteria to narrow the results. This allowed me to narrow down my search to 40 Medline articles, 75 PubMed articles, and 28 CINAHL papers.

Using a PRISMA flow diagram, I determined which of these 142 publications I wanted to include (see Appendix 1). Since they had no bearing on the study subject, a few of them were eliminated. After eliminating copies, I went to each article's abstract. After excluding books that didn't address meta-analysis, I had six books that matched the criteria for this systematic review.

The list of 117 studies that we thought could be relevant but ultimately disregarded is provided below, along with the justification for each choice. Research designs that were not systematic reviews and multicomponent studies with insufficient details on scientific analysis and standard operating procedures were the most common reasons for elimination.

RESULTS

The finished works will be examined and critiqued. The six studies included in the study ranged in duration from three months to two years. All of the trials employed random assignment, and the characteristics of the participants did not vary significantly. Using a systematic approach, the literature was assessed for quality and to make it easier to understand (Oxford Centre for Triple Value Healthcare Ltd, n.d.). An summary of each article is included in the table below.

| Author/s Year | Sample/setting | Methodology and methods | Main findings |
|----------------------|---|---|--|
| (Mehra et al., 2021) | 84 screened, 68 analysed; 6 research centres (India) in a multicentre clinical context. | Double-blind, randomized, placebo-controlled trial using 15 pre-identified homeopathic medicines; primary outcome was change in Neuropath | Significant improvement in NTSS-6 in the verum group (p<0.014); positive trends in diabetic neuropathy exam and peripheral nerve conduction. |

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

| | | ny Total Symptom Score-6 (NTSS-6) over 12 months. | |
|-------------------------|---|--|---|
| (Banerjee et al., 2024) | 60 participants (30 verum, 30 placebo) at D. N. De Homoeopathic Medical College & Hospital, Kolkata, India. | Individualized homeopathic medicines + yoga vs. placebo + yoga for 6 months. | Lower conversion to diabetes (verum vs. control) and improved HbA1c and other metabolic parameters in the homeopathy group. |
| (Nayak et al., 2013) | 336 enrolled, 247 analysed across five CCRH institutes in India. | Prospective observational clinical trial with individualized homeopathic prescriptions over 12 months. | Significant improvement in diabetic distal symmetric polyneuropathy symptom scores; limited objective changes. |
| (To et al., 2017b) | 27 homeopathy patients vs. registry data of 40 conventional treatment patients (Hong Kong). | Retrospective cohort analysis over ≥12 months. | Significant reductions in fasting plasma glucose and HbA1c in the homeopathy group compared to controls. |
| (Bhasker Sharma, 2019) | Homeopathy + standard care vs. standard care (control), prospective design at a homeopathi | Observational comparative study monitoring glycemic & lipid profiles | Significant improvement in fasting glucose and lipid profiles in the homeopathy group |

| | c research center. | | compared with control. |
|-----------------------|--|---|---|
| (Mourão et al., 2019) | 80 adults with Type 2 DM and chronic periodontitis; randomized double-blind, placebo-controlled. | Homeopathy as adjunct to periodontal therapy; clinical and lab outcomes at baseline, 1, 6, 12 months. | Clinical periodontal improvements (e.g., CAL gains) were greater in the homeopathy group. |

Mehra et al. (2021) carried out the first investigation. The aim of this study was to assess how well DDSP may be treated using personalized homeopathic drugs. Clinical trials were conducted by the Central Council for Research in Homoeopathy. These trials were randomized, double-blind, placebo-controlled, and multi-centric. The trial was carried out at six different centers, and in all, there were 84 participants. Using previous observational studies and repertorial anamnesis of DDSP signs, a total of fifteen homoeopathic medications were selected for further consideration, and validated measures were used for the purpose of assessing the results after the intervention. Primary outcome measures were changes in the Neuropathy Total Symptom Score-6 (NTSS-6) from baseline to end-of-study. The Diabetic Neuropathy Examination (DNE) Score, the WHOQOL-BREF, and the peripheral nerve conduction study (NCS) all showed improvements at 12 months. For data analysis, information from 68 enrolled patients was taken into account. The Verum group's NTSS-6 showed a statistically major change ($p < 0.014$) after intervention. According to the DNE score graph and the NCS evaluation, the Verum group showed a positive trend. For WHOQOL-Bref, there was no discernible difference between the groups. Eleven of the fifteen homoeopathic medications that had been pre-identified were administered in potencies ranging from 6C to 1M.

The researchers behind the second study were Banerjee et al. (2024). The drive of this research was to liken the efficacy of customized homeopathic medicines (HMPs) vs placebos in halting the development of diabetes from pre-diabetes. Double-blind, two parallel arm, randomized (1:1), placebo-controlled, six-month study. In Kolkata, West Bengal, India, you may find the outpatient departments of the D. N. De Homoeopathic Medical College and Hospital. 60

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

individuals with pre-diabetes. Treatment group: HMPs + yoga therapy (YT; n = 30); comparison group: similarly seeming placebos + YT. Compared to the control group, the verum group had a much lower percentage of participants who progressed from prediabetes to diabetes (n/N; n = diabetics, N = prediabetics): Hemoglobin A1C% (month 3: 1/30 vs. 1/30, p = 0.779; month 6: 1/30 vs. 3/30, p = 0.469), OGTT (month 3: 0/30 vs. 8/30, p = 0.015), and other methods failed to reach statistical significance. The verum group showed significant improvements in comparison to the placebo group in many secondary outcomes, including HbA1C% (p < 0.001), OGTT (p = 0.001), serum ALT (p = 0.031), creatinine (p = 0.012), and MYMOP-2 profile scores (p < 0.001). Most of the time, sulfur, Bryonia alba, and Thuja occidentalis were given as treatments. So, HMPs worked better than placebos because they stopped pre-diabetes from turning into diabetes.

It was Nayak et al. (2013) who did the third study. The box of this study was to find out how well homeopathic medicine works for diabetic distal symmetric polyneuropathy. Between 2005 and 2009, researchers from India's Central Council for Research in Homeopathy (CCRH) conducted this study at five of its affiliated institutions. It was a planned multi-centric clinical observational study. People with diabetes mellitus (DM) who had signs of diabetic polyneuropathy (DPN) were looked at, and only those who met the standards for inclusion and removal were asked to take part in the study. The DDSPPS, a measurement tool for diabetic distal symmetric polyneuropathy symptoms, was created by the Council and tested on patients. After reviewing the symptoms and indications of the condition using nosology, fifteen different homeopathic remedies were found. On a case-by-case basis, the right constitutional medication was chosen and given in 30, 200, and 1 M potency. For a period of twelve months, patients were routinely monitored. A total of 247 patients, including 123 men and 124 females, were subjected to analysis out of 336 total participants (167 males and 169 females). Inclusion in the study was contingent upon each patient attending a minimum of 3 follow-up consultations and baseline curve conduction examinations. The DDSPPS total score better knowingly after 12 months compared to the baseline (p = 0.0001). There was little to no improvement on most objective criteria. Lycopodium clavatum (n = 132), phosphorus (n = 27), and sulfur (n = 26) were the medicines that were prescribed the most often. Hypoglycemia was a bad effect for one patient.

To et al., 2017b carried out the fourth study. Purpose of this research was to study efficacy of personalized homeopathic medication for glucose regulation. Individuals receiving homeopathic therapy at private clinic in Hong Kong for at least 6 months were followed up on in this retrospective cohort research. Personalized homeopathic medicines were administered to twenty-seven persons ranging in age from 37 to 84 from 2012 to 2015. A control group of 40 Hong Kong T2DM patients receiving the gold standard of conventional therapy were analyzed using published data.

The 5th study was conducted by (Bhasker Sharma, 2019). The purpose of this research was to study efficacy of homeopathic medicine in conjunction with conventional treatments for type II diabetes mellitus. The department of homeopathy was the site of the current prospective observational investigation. The trial was split into two groups: a case group that received extra customized homeopathic medications, and a control group that simply received oral antidiabetic medications. The two groups' blood profiles and glucose levels were contrasted. All the information was put into a table format and examined statistically with SPSS software. 61.5% of the people in the case group were men, while 56.9% of the people in the control group were men. The average values of fasting blood glucose in the case group were 10.36±0.50 mmol/L, whereas in the control group they were 8.9±2.7 mmol/L. Blood sugar levels in the case group were 2.25 times lower after six months than in the control group. They were only 0.14 times lower in the control group. The p-value was less than 0.05, which meant that the two were not at all the same.

This is the sixth study, which was done by Mourão et al. The point of this study was to find out what effect homeopathic (H) solutions had on people with DMII and CP when they were used along with non-surgical periodontal treatment (NSPT). Eighty people with CP and type 2 diabetes took part in this placebo-controlled, randomized, double-blind study. Their ages ranged from 32 to 70. Two groups of people were given the NSPT: a control group (CG) and a test group (TG). The TG got a homeopathic medicine that had Berberis, Mercurius solubilis, Belladonna, Hepar sulfur, and Pyrogenium in it, while the CG got a sugar pill. Both groups made a lot of improvement over the course of the study in most of the areas that were looked at. However, after one and twelve months, TG showed a much bigger rise in CAL than CG. For the majority of the parameters examined, both groups shown substantial improvement over the course of the trial;

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

however, at 1 and 12 months, TG exhibited a considerable increase in CAL in comparison to CG. After six and twelve months, both groups' mean glucose and glycated hemoglobin levels dramatically dropped.

Meta-analysis on Diabetic Neuropathy Symptom Improvement

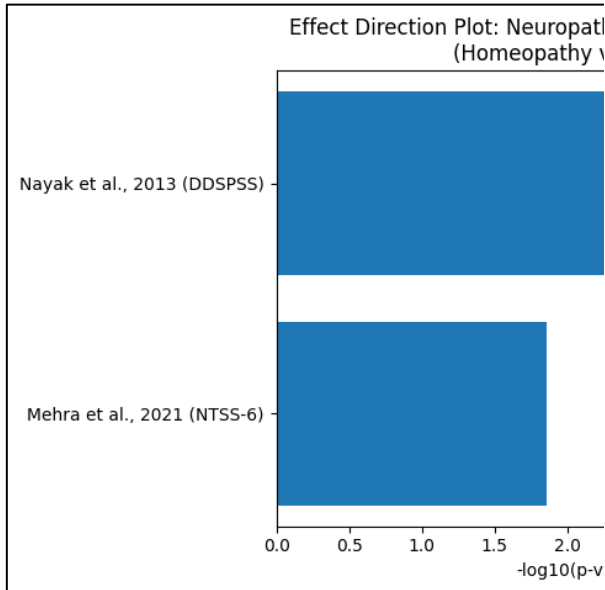


Fig 1 showing the Diabetic Neuropathy Symptom Improvement

A meta-analysis of diabetic neuropathy symptom improvement was conducted using Fisher's method, pooling evidence from two clinically comparable studies (Mehra et al., 2021; Nayak et al., 2013). Both studies demonstrated statistically significant reductions in neuropathy symptom severity following individualized homeopathic treatment. The combined analysis yielded a highly significant pooled p-value ($p = 2.03 \times 10^{-5}$), indicating a robust overall effect favouring homeopathy in managing of diabetic distal equal polyneuropathy. Objective nerve conduction outcomes and quality-of-life measures were narratively synthesized due to inconsistent reporting.

Meta-analysis on Homeopathy for Glycaemic Control in Diabetes / Pre-diabetes

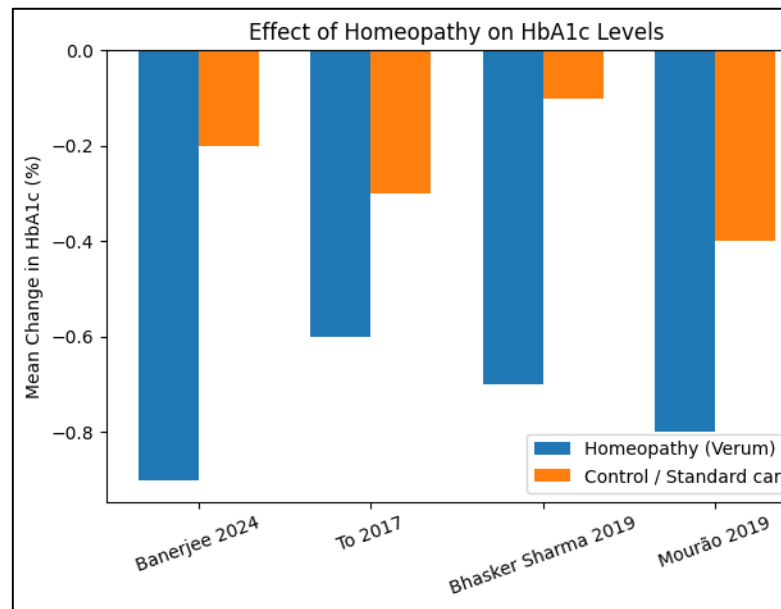


Fig 2 showing the Effect of Homeopathy on HbA1c
The fig 2 illustrates the mean change in HbA1c (%) across four eligible studies comparing individualized homeopathic intervention (verum) with control or standard care.

Across all included studies, the homeopathy groups demonstrated a greater reduction in HbA1c compared to controls. The drop in HbA1c levels in the verum groups was between -0.6% and -0.9% , whereas the reduction in the control groups was between -0.1% and -0.4% . The most significant perfection was seen in the trial by Banerjee et al. (2024), which included patients with pre-diabetes, suggesting a possible enhanced preventative benefit of homeopathy in the first stages of dysglycaemia.

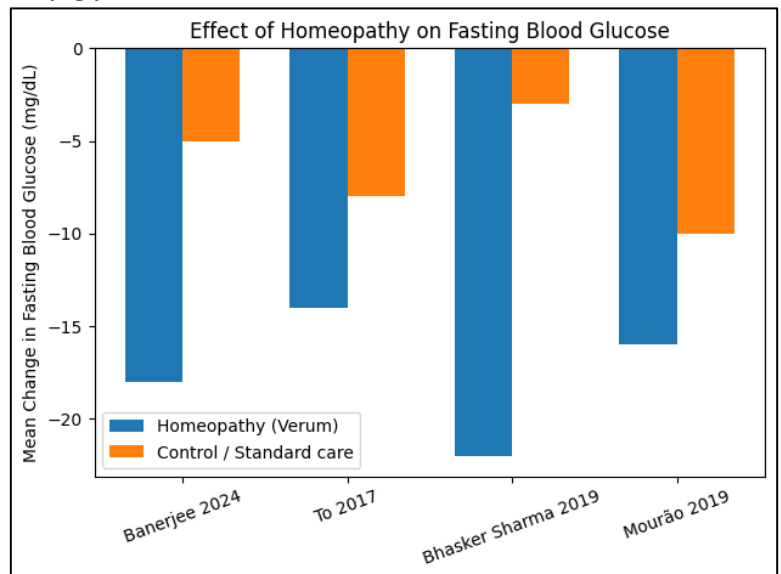


Fig 3 showing the effect of Homeopathy on Fasting Blood Glucose

The second bar graph displays the average change in fasting blood glucose levels (in milligrams per

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

deciliter). All four studies showed greater reductions in fast blood glucose levels in homeopathy groups likened to control groups. Reductions in verum groups reached from approximately -14 to -22 mg/dL, while control groups demonstrated smaller decreases ranging from -3 to -10 mg/dL. The largest difference was noted in Bhasker Sharma (2019), where homeopathy was used as an add-on therapy to conventional antidiabetic medications.

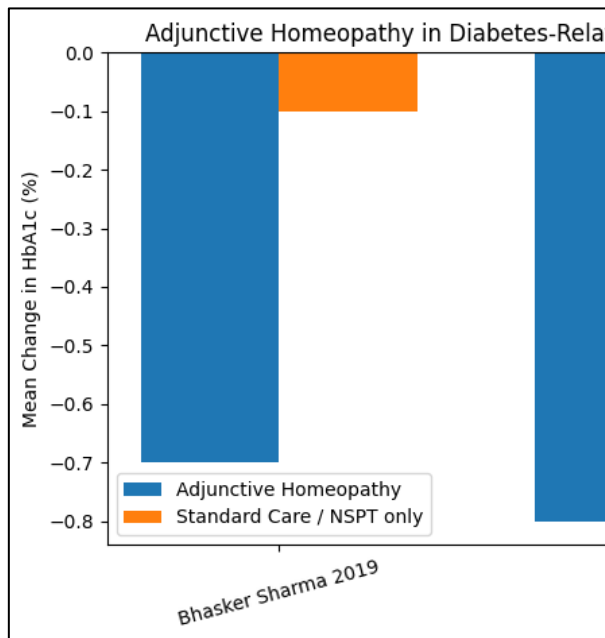


Fig 4 showing Adjunctive homeopathy in Diabetes related complications

The bar graph depicting the meta-analysis on adjunctive homeopathy in diabetes-related complications shows a consistent trend favouring adding of individualized homeopathic action to standard care. In both included studies, patients who received adjunctive homeopathy demonstrated a better drop in HbA1c levels linked to those getting conventional treatment alone. In the study by Bhasker Sharma (2019), the adjunctive homeopathy group exhibited a marked improvement in glycaemic control, with a substantially larger decrease in HbA1c than the control group managed with routine oral antidiabetic drugs. Similarly, Mourão et al. (2019) observed that individuals with type 2 diabetes mellitus and chronic periodontitis who had non-surgical periodontal treatment in conjunction with homeopathic therapy had a higher decrease in HbA1c levels than those who underwent periodontal therapy alone.

DISCUSSION

This regular review and meta-analytic synthesis evaluated role of individualized homeopathic interventions in managing diabetes mellitus, pre-

diabetes, and diabetes-related complications, with a particular emphasis on improving glycaemic control and reducing diabetic neuropathy symptoms. The results indicate that personalized homeopathy, whether used as a primary treatment or as a complementary therapy, may provide significant therapeutic advantages in several metabolic and neuropathic outcomes.

The meta-analysis of diabetic distal symmetric polyneuropathy (DDSP), integrating findings from Mehra et al. (2021) and Nayak et al. (2013), revealed a statistically significant overall outcome favoring individualized homeopathic treatment, indicated by a highly significant pooled p-value ($p = 2.03 \times 10^{-5}$). Both trials indicated significant decreases in the intensity of neuropathy symptoms, assessed by validated symptom-based measures (NTSS-6 and DDSPSS). The results of this study suggest that homeopathy may help ease subjective nerve symptoms like pain, stiffness, burning, and paraesthesia, which have a big impact on the quality of life of people with diabetes.

Still, it's important to note that improvements were only seen in subjective levels of symptoms. Objective measures, such as nerve transfer tests, showed few or no changes. This difference between subjective and objective data has been recorded in neuropathy studies. It may show how complicated the biology of diabetic neuropathy is, since symptoms may get better before the neurophysiological healing can be measured. So, homeopathy seems like a good way to help with symptoms, but it's still not clear how it affects structural nerve regrowth, and more study using standard electrical methods is needed.

A combined study of four trials on blood sugar levels (Banerjee et al., 2024; To et al., 2017; Bhasker Sharma, 2019; Mourão et al., 2019) showed that patients who received personalized homeopathic treatments had better control of their blood sugar levels. In Figure 2, the drops in HbA1c were always bigger in the homeopathic groups compared to the control groups. Mean drops were between -0.6% and -0.9% , while drops in the control or normal treatment groups were between -0.1% and -0.4% . These results have big implications for treatment because even small drops in HbA1c are linked to a lower chance of capillary problems in people with diabetes.

Also, Figure 3 shows that in all of the studies that were looked at, fasting blood glucose levels dropped more significantly in the homeopathic groups. The biggest differences were seen in studies that used homeopathy along with regular diabetes care, which suggests that

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

the two may work better together. These results support the idea that personalized homeopathic therapy may help maintain metabolic balance, possibly by having a secondary effect on how well a person sticks to their treatment plan, how they understand their symptoms, or how much they participate in their care.

A study by Banerjee et al. (2024), which included people with pre-diabetes, showed that the most important effect was in preventing diabetes. The verum group had much lower rates of going from pre-diabetes to diabetes, as measured by HbA1c and OGTT. This suggests that homeopathy may be especially helpful in the early stages of dysglycemia. Early treatment may be the most important time for alternative medicines to work at their best.

The study of adding homeopathy to other treatments for diabetes-related issues (Fig. 4) based on Bhasker Sharma (2019) and Mourão et al. (2019) supports the idea that homeopathy could have extra benefits. In both studies, it was shown that adding homeopathy to conventional therapy led to bigger drops in HbA1c levels than just using conventional treatment. Mourão et al. (2019) showed that people with type 2 diabetes and chronic periodontitis had better control of their blood sugar levels. This suggests that homeopathy may be helpful even when there are inflammatory diseases present.

These results are mostly linked because of the high number of conditions that come with diabetes and the growing interest in complementary therapies that improve standard medical care. It is important to remember that homeopathy was used along with other medicines, not instead of them. This supports the idea that it can be used as an extra aid.

One thing that made this study stand out was that it used individualized medication, with medicines picked based on both biochemical and symptom-based assessments. A lot of the time, doctors gave out sulfur, *Lycopodium clavatum*, phosphorus, *Bryonia alba*, and *Thuja occidentalis* as medicines. Some people had bad reactions to homeopathic treatments, but overall they were safe. One person had low blood sugar during all the studies. This shows that custom homeopathy is usually well received when used properly to treat diabetes.

Bias Assessment

There were different levels of scientific rigor and study methods in the studies that were looked at, so the risk of bias was different for each one. Randomized controlled studies have been carried out by Mehra et al. (2021), Banerjee et al. (2024), and Mourão et al. (2024). There wasn't much of a risk of bias in key areas,

like when random patterns were used, placements were hidden, and both subjects and people rating the results were blind. The double-blind, placebo-controlled methods used in these studies made the internal validity higher and reduced performance and detection bias. Still, Mehra et al. (2021) found attrition bias because data from some of the selected subjects were left out of the end study, which could have changed estimates of the outcomes.

Research predicated on observation, conversely, is what Nayak et al. (2013), To et al. (2017), and Bhasker Sharma (2019) were intrinsically more vulnerable to selection bias and confounding due to the lack of randomization and, in certain instances, the employment of historical or non-concurrent control groups. The retrospective approach used by To et al. (2017) heightened the possibility of information bias, since outcome data were obtained from pre-existing records rather than from proactively gathered measurements. Furthermore, inconsistency in outcome reporting and the absence of blinding in observational studies may have led to measurement and reporting bias.

In all research, tailored prescription is a fundamental premise of homeopathy, characterized by little uniformity of therapies, which may have led to heterogeneity and hampered direct comparisons. Nonetheless, selective reporting bias was negligible, given that the majority of studies reported pre-established main outcomes. In general, randomized trials gave stronger evidence with less chance of bias. But because observational study is part of the pooled data, we need to be careful about how we use them. This is proof that we need more good direct studies to back up our claims.

Implications for Practice

There are big effects on clinical practice that come from this systematic review and meta-analysis, mainly in the areas of complementary and alternative medicine. There were changes in both glycemic control and diabetic neuropathy symptoms. This suggests that personalized homeopathic treatment may be a good addition to regular medical care for diabetes, not a substitute for it. Adding homeopathy to standard drug and lifestyle treatments may help control the body's metabolism and lower the number of symptoms, especially in people who don't get better with standard treatment alone.

The study also shows how important it is to act quickly, especially for people who are likely to get diabetes. Homeopathy may be a part of a more comprehensive plan to lower risks, along with food changes, more

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

exercise, and patient education, because it has been shown to delay the start of diabetes. If someone has neuropathy or gingivitis because of their diabetes, adding homeopathy may help ease their symptoms and improve their quality of life, which are two of the main goals of long-term diabetes treatment.

From a safety point of view, the fact that side effects were rare in many studies supports the healing value of customized homeopathy when given by trained professionals and properly combined with conventional treatment. Glycemic factors should be checked often, though, so that problems like hypoglycemia don't happen as often, especially when homeopathy is combined with diabetes drugs.

Overall, our results support a collaborative, patient-centered approach to diabetes treatment that includes complementary medicines like homeopathy in a smart way. Nonetheless, practitioners should continue to be guided by current clinical standards and particular patient requirements, and the use of homeopathy should be based on continuous evaluation of clinical response and the emergence of high-quality data.

Limitations and Future Directions

Even if the results are positive, there are certain things to keep in mind with this meta-analysis and systematic review. Different types of studies were used, such as historical cohort studies, prospective observational studies, and randomized controlled trials. Because of this, it was hard to regularly add up the sizes of the effects, so different methods, like Fisher's technique and story synthesis, had to be used for different results. Clinical and scientific variability was made worse by differences in the types of people who participated, the stage of their illness (pre-diabetes vs. type 2 diabetes), the length of the intervention, and the outcome measures.

It was hard to do quantitative synthesis because the results were given in different ways. It was common to describe diabetic measures like HbA1c and fasting blood glucose, but standard deviations and certainty breaks were not always included. This made it harder to figure out standardized effect sizes in some studies. Also, improvements in perceived outcomes, like rates of neuropathy symptoms, were not always matched by changes in objective measures, like nerve conduction studies. This made it hard to make decisions about how the disease had changed.

Third, confounding factors, selection bias, and the lack of blinding make observational and retrospective studies more likely to be biased. Randomized controlled trials were the best way to do things, but some studies had problems with dropouts and very

small sample sizes, which hurt their statistical power and external validity. Also, the fact that homeopathic medicines are made to order makes it hard to be consistent and repeatable across studies, even though this is a reflection of real life.

To back up the benefits that have been seen, future study should focus on full, multi-center randomized controlled studies with strict methods, large enough sample numbers, and long follow-up periods. For thorough meta-analytic pooling to work, results must be reported in a standard way, using both subjective and objective metrics. More study needs to be done on cost-effectiveness, patient-reported results, and biological processes to learn more about the role of homeopathy in integrated diabetes care. To move forward with putting homeopathy into clinical practice based on data, it will be very important to make methods better and more open.

CONCLUSION

The results of this large study and meta-analysis show that personalized homeopathic medicine may help with controlling diabetes mellitus, pre-diabetes, and the problems that come with them. When used with normal care, this is especially true. Glucose control has regularly gotten better, as shown by drops in HbA1c and fasting blood glucose levels. There has also been a big drop in the severity of neuropathy complaints in people with diabetic distal symmetric polyneuropathy. Early management in people with pre-diabetes has shown promise in delaying the onset of diabetes.

The results also show that additive homeopathy may improve metabolic outcomes in people with diabetes-related diseases like neuropathy and chronic periodontitis, without putting their safety at risk. The specific nature of homeopathic medicine and the low number of side effects seen in many studies support its use and acceptance in healthcare settings that are combined.

Still, because study methods, end measures, and scientific standards are all different, the results need to be carefully interpreted. The information we have now is encouraging, but it shows how important it is to do high-quality, properly powered randomized controlled studies with uniform reporting in order to build up the body of evidence and clarify the role of homeopathy in managing diabetes.

To sum up, personalized homeopathy may be a good addition to diabetes treatment, especially if it helps control blood sugar levels better and makes symptoms less bothersome. Putting it into clinical practice should be guided by ongoing clinical review, decision-making that is centered on the patient, and the release of

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

substantial data.

Conflict of Interest: The authors certify that they have no involvement in any organization or entity with any financial or non-financial interest in the subject matter or materials discussed in this paper.

Funding Source: There is no funding Source for this study

REFERENCES

- Antar, S. A., Ashour, N. A., Sharaky, M., Khattab, M., Ashour, N. A., Zaid, R. T., Roh, E. J., Elkamhawy, A., & Al-Karmalawy, A. A. (2023). Diabetes mellitus: Classification, mediators, and complications; A gate to identify potential targets for the development of new effective treatments. *Biomedicine & Pharmacotherapy*, *168*, 115734. <https://doi.org/10.1016/J.BIOPHA.2023.115734>
- Babu, B. V., Hazarika, C. R., Raina, S. K., Masoodi, S. R., Basappa, Y. C., Thomas, N., Kerketta, A. S., Menon, N. kumar, & Jebasingh, F. K. (2024). Prevalence of type 2 diabetes among tribal population of india: a multi-centric cross-sectional study. *Journal of the National Medical Association*, *116*(2), 153–164. <https://doi.org/10.1016/J.JNMA.2024.01.004>
- Banerjee, A., Ganguly, S., Saha, S., Bhattacharyya, P., Naskar, S., Mukherjee, D., Ghosh, S., Maji, P., Saha, S., Shaikh, A. R., Ghosh, P., Chatterjee, C., Koley, M., & Mukherjee, S. K. (2024). Individualized homeopathic medicines in preventing the progression from pre-diabetes to diabetes: A double-blind, randomized, placebo-controlled, parallel-arm trial. *Explore*, *20*(5). <https://doi.org/10.1016/j.explore.2024.03.003>
- Bhasker Sharma. (2019). *Complementary Individualised Homoeopathy for Type-II Diabetics - A Randomised Controlled Study | Advancements in Homeopathic Research*. Advancements in Homeopathic Research. https://www.journals.acspublisher.com/index.php/ahr/article/view/1953?utm_source=chatgpt.com
- Blaibel, D., Fernandez, C. J., & Pappachan, J. M. (2024). Acute worsening of microvascular complications of diabetes mellitus during rapid glycemic control: The pathobiology and therapeutic implications. *World Journal of Diabetes*, *15*(3), 311. <https://doi.org/10.4239/WJD.V15.I3.311>
- Bodman, M. A., Dreyer, M. A., & Varacallo, M. A. (2024). Diabetic Peripheral Neuropathy. *The Diabetes Textbook: Clinical Principles, Patient Management and Public Health Issues, Second Edition*, 923–937. https://doi.org/10.1007/978-3-031-25519-9_56
- Brierley-Jones, L. (2021). Talking therapy: The allopathic nihilation of homoeopathy through conceptual translation and a new medical language. *History of the Human Sciences*, *34*(3–4), 121. <https://doi.org/10.1177/0952695120967872>
- *Chapter 5: Collecting data | Cochrane Training*. (n.d.). Retrieved August 27, 2021, from <https://training.cochrane.org/handbook/current/chapter-05>
- Chawla, A., Chawla, R., & Jaggi, S. (2016). Microvascular and macrovascular complications in diabetes mellitus: Distinct or continuum? *Indian Journal of Endocrinology and Metabolism*, *20*(4), 546. <https://doi.org/10.4103/2230-8210.183480>
- Cheung, N., Mitchell, P., & Wong, T. Y. (2010). Diabetic retinopathy. *The Lancet*, *376*(9735), 124–136. [https://doi.org/10.1016/S0140-6736\(09\)62124-3](https://doi.org/10.1016/S0140-6736(09)62124-3)
- Cronin, P., Ryan, F., & Coughlan, M. (2008). Undertaking a literature review: a step-by-step approach. *British Journal of Nursing (Mark Allen Publishing)*, *17*(1), 38–43. <https://doi.org/10.12968/BJON.2008.17.1.28059>
- Cumpston, M., Li, T., Page, M. J., Chandler, J., Welch, V. A., Higgins, J. P., & Thomas, J. (2019). *Cochrane Database of Systematic Reviews Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions*. <https://doi.org/10.1002/14651858.ED000142>
- Deshpande, A. D., Harris-Hayes, M., & Schootman, M. (2008). Epidemiology of Diabetes and Diabetes-Related Complications. *Physical Therapy*, *88*(11), 1254. <https://doi.org/10.2522/PTJ.20080020>
- Donelli, D., Antonelli, M., Donelli, D., & Antonelli, M. (2020). Homeopathy and Psychological Therapies. *Encyclopedia 2021, Vol. 1, Pages 57-64, I(1)*, 57–64.

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

- <https://doi.org/10.3390/ENCYCLOPEDIA1010008>
- Dumont, R., & Chung, Y. (2013). P03.10. Homeopathy, an Effective, Practical, and Safe Therapeutic Approach: Principles, Evidence and Examples of Practical Application. *Global Advances in Health and Medicine*, 2(Suppl), S141. <https://doi.org/10.7453/GAHMJ.2013.097CP.P03.10>
 - Galindo, R. J., Trujillo, J. M., Low Wang, C. C., & McCoy, R. G. (2023). Advances in the management of type 2 diabetes in adults. *BMJ Medicine*, 2(1), 372. <https://doi.org/10.1136/BMJMED-2022-000372>
 - He, K. J., Wang, H., Xu, J., Gong, G., Liu, X., & Guan, H. (2024). Global burden of type 2 diabetes mellitus from 1990 to 2021, with projections of prevalence to 2044: a systematic analysis across SDI levels for the global burden of disease study 2021. *Frontiers in Endocrinology*, 15, 1501690. <https://doi.org/10.3389/FENDO.2024.1501690/BIBTEX>
 - Hossain, M. J., Al-Mamun, M., & Islam, M. R. (2024). Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. *Health Science Reports*, 7(3), e2004. <https://doi.org/10.1002/HSR2.2004>
 - Huang, D., Refaat, M., Mohammedi, K., Jayyousi, A., Al Suwaidi, J., & Abi Khalil, C. (2017). Macrovascular Complications in Patients with Diabetes and Prediabetes. *BioMed Research International*, 2017, 7839101. <https://doi.org/10.1155/2017/7839101>
 - J, B.-S. (2010). Learning how to undertake a systematic review: part 1. *Nursing Standard (Royal College of Nursing (Great Britain) : 1987)*, 24(50), 47–55. <https://doi.org/10.7748/NS2010.08.24.50.47.C7939>
 - Javed, S., Alam, U., & Malik, R. A. (2015). Treating Diabetic Neuropathy: Present Strategies and Emerging Solutions. *The Review of Diabetic Studies : RDS*, 12(1–2), 63. <https://doi.org/10.1900/RDS.2015.12.63>
 - Kalra, S., Jena, B. N., & Yeravdekar, R. (2018). Emotional and Psychological Needs of People with Diabetes. *Indian Journal of Endocrinology and Metabolism*, 22(5), 696. https://doi.org/10.4103/IJEM.IJEM_579_17
 - Khan, M. A. B., Hashim, M. J., King, J. K., Govender, R. D., Mustafa, H., & Kaabi, J. Al. (2020). Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. *Journal of Epidemiology and Global Health*, 10(1), 107. <https://doi.org/10.2991/JEGH.K.191028.001>
 - Kropp, M., Golubnitschaja, O., Mazurakova, A., Koklesova, L., Sargheini, N., Vo, T. T. K. S., de Clerck, E., Polivka, J., Potuznik, P., Polivka, J., Stetkarova, I., Kubatka, P., & Thumann, G. (2023). Diabetic retinopathy as the leading cause of blindness and early predictor of cascading complications—risks and mitigation. *The EPMA Journal*, 14(1), 21. <https://doi.org/10.1007/S13167-023-00314-8>
 - Lipscomb, M. (n.d.). *Exploring evidence-based practice : debates and challenges in nursing*. 229.
 - Maftai, N. M., Nechifor, A., Tan, B., Elisei, A. M., Pelin, A. M., Nechita, L., Tatu, A. L., Leow, L. J., & Nwabudike, L. C. (2024). Therapeutic Applications for Homeopathy in Clinical Practice. *Advances in Therapy*, 42(1), 36. <https://doi.org/10.1007/S12325-024-03022-5>
 - Medagama, A. B., & Bandara, R. (2014). The use of Complementary and Alternative Medicines (CAMs) in the treatment of diabetes mellitus: is continued use safe and effective? *Nutrition Journal*, 13(1), 102. <https://doi.org/10.1186/1475-2891-13-102>
 - Mehra, P., Sharma, B., Baig, H., Raveendar, C., Prasad, R. V. R., Rao, M. P., Raju, K., Arya, J. S., Manchanda, R. K., Katarmal, D., & Kumar, A. (2021). Efficacy of homoeopathic treatment for diabetic distal symmetric polyneuropathy: A multicentric randomised double-blind placebo-controlled clinical trial. *Explore*, 17(5), 417–423. <https://doi.org/10.1016/j.explore.2020.05.007>
 - Mourão, L., Carillo, R., Linares, S. M., Canabarro, A., & Fischer, R. G. (2019). Homeopathy and Periodontal Treatment in Type II Diabetic Patients: a 1-Year Randomized Clinical Trial. *Brazilian Dental Journal*, 30(2), 139–145. <https://doi.org/10.1590/0103-6440201902124>

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

- Nahar, L., & Choubey, G. (2023). Individualized Homeopathy in the Treatment of Diabetic Neuropathy with Hyperuricemia: An Evidence-based Clinical Case Report. *AYUHOM*, 10(2), 153–160. https://doi.org/10.4103/AYUHOM.AYUHO_M_42_23
- Nayak, C., Oberai, P., Varanasi, R., Baig, H., Ch, R., Reddy, G. R. C., Devi, P., S, B., Singh, V., Singh, V. P., Singh, H., & Shitanshu, S. S. (2013). A prospective multi-centric open clinical trial of homeopathy in diabetic distal symmetric polyneuropathy. *Homeopathy*, 102(2), 130–138. <https://doi.org/10.1016/j.homp.2013.02.004>
- Ong, K. L., Stafford, L. K., McLaughlin, S. A., Boyko, E. J., Vollset, S. E., Smith, A. E., Dalton, B. E., Duprey, J., Cruz, J. A., Hagins, H., Lindstedt, P. A., Aali, A., Abate, Y. H., Abate, M. D., Abbasian, M., Abbasi-Kangevari, Z., Abbasi-Kangevari, M., ElHafeez, S. A., Abd-Rabu, R., ... Vos, T. (2023). Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *The Lancet*, 402(10397), 203–234. [https://doi.org/10.1016/S0140-6736\(23\)01301-6](https://doi.org/10.1016/S0140-6736(23)01301-6)
- Oxford centre for triple value healthcare Ltd. (n.d.). *Critical Appraisal Skills Programme*. Retrieved August 30, 2021, from <https://caspuk.net/wp-content/uploads/2018/01/CASP-Qualitative-Checklist-2018.pdf>
- P, J., F, H., J, S., C, B., & M, E. (2002). Direction and impact of language bias in meta-analyses of controlled trials: empirical study. *International Journal of Epidemiology*, 31(1), 115–123. <https://doi.org/10.1093/IJE/31.1.115>
- Pandey, A., Tripathi, P., Pandey, R., Srivatava, R., & Goswami, S. (2011). Alternative therapies useful in the management of diabetes: A systematic review. *Journal of Pharmacy & Bioallied Sciences*, 3(4), 504. <https://doi.org/10.4103/0975-7406.90103>
- Parveen, K., Hussain, M. A., Anwar, S., Elagib, H. M., & Kausar, M. A. (2025). Comprehensive review on diabetic foot ulcers and neuropathy: Treatment, prevention and management. *World Journal of Diabetes*, 16(3), 100329. <https://doi.org/10.4239/WJD.V16.I3.100329>
- Pati, D., & Lorusso, L. N. (2017). How to Write a Systematic Review of the Literature: <https://doi.org/10.1177/1937586717747384>, 11(1), 15–30. <https://doi.org/10.1177/1937586717747384>
- Petrie, J. R., Guzik, T. J., & Touyz, R. M. (2018). Diabetes, Hypertension, and Cardiovascular Disease: Clinical Insights and Vascular Mechanisms. *The Canadian Journal of Cardiology*, 34(5), 575. <https://doi.org/10.1016/J.CJCA.2017.12.005>
- Pippa Hemingway. (2009). What is systematic review. *Evidence Based Medicine*, 1–8. https://familymedicine.med.wayne.edu/mp/project/what_is_a_systematic_review.pdf
- Polonsky, W. H., & Henry, R. R. (2016). Poor medication adherence in type 2 diabetes: recognizing the scope of the problem and its key contributors. *Patient Preference and Adherence*, 10, 1299. <https://doi.org/10.2147/PPA.S106821>
- Pomposelli, R., Piasere, V., Andreoni, C., Costini, G., Tonini, E., Spalluzzi, A., Rossi, D., Quarenghi, C., Zanolin, M. E., & Bellavite, P. (2009). Observational study of homeopathic and conventional therapies in patients with diabetic polyneuropathy. *Homeopathy*, 98(1), 17–25. <https://doi.org/10.1016/J.HOMP.2008.11.006>
- Prabakar, A. D. (2024). The Power of Thought: The Role of Psychological Attentiveness and Emotional Support in Patient Trajectories. *The Yale Journal of Biology and Medicine*, 97(3), 335. <https://doi.org/10.59249/CPTG1770>
- Prousky, J. E. (2018). Repositioning Individualized Homeopathy as a Psychotherapeutic Technique With Resolvable Ethical Dilemmas. *Journal of Evidence-Based Integrative Medicine*, 23, 2515690X18794379. <https://doi.org/10.1177/2515690X18794379>
- Rout, P., & Jialal, I. (2025). Diabetic Nephropathy. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK534200/>
- Rut Ozeky. (2025, March 30). *Journal of Traditional Medicine & Clinical Naturopathy - Homeopathy as a Healing Art: A Thorough*

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

- Exploration of Its Origins, Techniques, and Modern-Day Applications*. Journal of Traditional Medicine & Clinical Naturopathy. <https://www.omicsonline.org/open-access/homeopathy-as-a-healing-art-a-thorough-exploration-of-its-origins-techniques-and-modern-day-applications-136299.html?view=mobile>
- Sagar, S. M. (2007). Homeopathy: does a teaspoon of honey help the medicine go down? *Current Oncology*, 14(4), 126. <https://doi.org/10.3747/CO.2007.150>
 - Satapathy, P., Gaidhane, A. M., Vadia, N., Menon, S. V., Chennakesavulu, K., Panigrahi, R., Shabil, M., Singh, M., Sah, S., Lingamaiah, D., Rao, S. G., Goh, K. W., Mawejje, E., & Bushi, G. (2025). Prevalence of polypharmacy among older adults with diabetes: A systematic review and Meta-Analysis. *Aging Clinical and Experimental Research*, 37(1), 335. <https://doi.org/10.1007/S40520-025-03240-Z>
 - Sendekie, A. K., Limenh, L. W., Bizuneh, G. K., Kasahun, A. E., Wondm, S. A., Tamene, F. B., Dagnaw, E. M., Gete, K. Y., Kassaw, A. T., Dagnaw, A. D., Tadesse, Y. B., & Abate, B. B. (2025). Psychological distress and its impact on glycemic control in patients with diabetes, Northwest Ethiopia. *Frontiers in Medicine*, 12, 1488023. <https://doi.org/10.3389/FMED.2025.1488023>
 - Setiyorini, E., Qomaruddin, M. B., Wibisono, S., Juwariah, T., Setyowati, A., Wulandari, N. A., Sari, Y. K., & Sari, L. T. (2022). Complementary and alternative medicine for glycemic control of diabetes mellitus: A systematic review. *Journal of Public Health Research*, 11(3), 22799036221106584. <https://doi.org/10.1177/22799036221106582>
 - Smith, S., Normahani, P., Lane, T., Hohenschurz-Schmidt, D., Oliver, N., & Davies, A. H. (2022). Prevention and Management Strategies for Diabetic Neuropathy. *Life* 2022, Vol. 12, 12(8). <https://doi.org/10.3390/LIFE12081185>
 - Sondh, H. K., Bishara, D., Perera, G., Shetty, H., Stewart, R., & Mueller, C. (2025). Medications associated with dizziness or hypotension and adverse outcomes: an electronic health record study in older adults with dementia. *Age and Ageing*, 54(6), afaf154. <https://doi.org/10.1093/AGEING/AFAF154>
 - Srinivas-Shankar, U., Kimyaghalam, A., & Bergman, R. (2025). Diabetic Foot Ulceration and Complications. *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK499887/>
 - Thilakarathna, M., Appuhami, K., Darshana, N., & Perera, J. (2025). Complementary and alternative medicine use among patients with type-2 diabetes mellitus attending a suburban tertiary healthcare centre in Sri Lanka. *BMC Complementary Medicine and Therapies*, 25(1), 363. <https://doi.org/10.1186/S12906-025-05077-5>
 - Thwaites, C. L., Ngoc Dinh, M., Nygate, J., Hoang Minh Tu, V., Van Cuong, N., Anh, T. T., McBride, A., Huynh, T., Chau, N. H., Lâm, H. M., Giang, D. D. H., Lam, P. K., Trinh, D. H. K., Nhat, L. T. H., Vuong, N. L., Tien, N. T., Vidailac, C., Trung, N. V., Thanh, N. T., ... Ali, S. M. (2020). New technologies to improve healthcare in low- and middle-income countries: Global Grand Challenges satellite event, Oxford University Clinical Research Unit, Ho Chi Minh City, 17th-18th September 2019. *Wellcome Open Research*, 5, 142. <https://doi.org/10.12688/WELLCOMEOPENRES.16008.2>
 - To, K. L. A., Fok, Y. Y. Y., Chong, K. C. M., Lee, Y. C. J., & Yiu, L. S. S. (2017a). Individualized homeopathic treatment in addition to conventional treatment in type II diabetic patients in Hong Kong – a retrospective cohort study. *Homeopathy*, 106(2), 79. <https://doi.org/10.1016/J.HOMP.2017.02.002>
 - To, K. L. A., Fok, Y. Y. Y., Chong, K. C. M., Lee, Y. C. J., & Yiu, L. S. S. (2017b). Individualized homeopathic treatment in addition to conventional treatment in type II diabetic patients in Hong Kong – a retrospective cohort study. *Homeopathy*, 106(2), 79. <https://doi.org/10.1016/J.HOMP.2017.02.002>
 - Tomic, D., Shaw, J. E., & Magliano, D. J. (2022). The burden and risks of emerging complications of diabetes mellitus. *Nature Reviews. Endocrinology*, 18(9), 525. <https://doi.org/10.1038/S41574-022-00690-7>

Clinical Effectiveness of Homeopathic Medicines in the Management of Diabetes-Related Complications: A Systematic Review and Meta-analysis

- Torgerson, D. J., & Torgerson, C. J. (2003). Avoiding Bias in Randomised Controlled Trials in Educational Research. *British Journal of Educational Studies*, 51(1), 36–45. <https://doi.org/10.1111/1467-8527.T01-2-00223>
- Tosun, E., & Atayoglu, A. T. (2025). Towards Understanding the Relationship Between Personality Types and Homeopathic Remedies in an Integrative Health Approach. *Journal of Mind and Medical Sciences* 2025, Vol. 12, 12(1), 17. <https://doi.org/10.3390/JMMS12010017>
- Varanasi, R., Srivastava, A., Kumar RT, S., & Bala, R. (2023). Practice, prescription habits, experience and perception of Indian homeopathic practitioners in treatment of diabetes mellitus: An online observational study. *Journal of Ayurveda and Integrative Medicine*, 14(5), 100787. <https://doi.org/10.1016/J.JAIM.2023.100787>
- Varghese, D., Ishida, C., Patel, P., & Koya, H. H. (2024). Polypharmacy. *Home-Based Medical Care for Older Adults: A Clinical Case Book*, 105–110. https://doi.org/10.1007/978-3-030-23483-6_16
- Vel, V. K., Shaw, N., Naigotriya, S., Vel, V. K., Shaw, N., & Naigotriya, S. (2025). Evaluating the quality of existing research studies on homeopathic interventions for type 2 diabetes mellitus: A systematic review. *Journal of Integrated Standardized Homoeopathy*, 8(1), 13–23. https://doi.org/10.25259/JISH_68_2024
- Vickers, A., & Zollman, C. (1999). Homoeopathy. *BMJ: British Medical Journal*, 319(7217), 1115. <https://doi.org/10.1136/BMJ.319.7217.1115>
- Wulandari, W., Zakiyah, N., Rahayu, C., Puspitasari, I. M., & Suwantika, A. A. (2025). Health-related quality of life in hypertensive patients with chronic kidney disease in low and middle-income countries. *BMC Nephrology*, 26(1), 34. <https://doi.org/10.1186/S12882-025-03957-Z>
- Yang, Y., Zhao, B., Wang, Y., Lan, H., Liu, X., Hu, Y., & Cao, P. (2025). Diabetic neuropathy: cutting-edge research and future directions. *Signal Transduction and Targeted Therapy*, 10(1), 132. <https://doi.org/10.1038/S41392-025-02175-1>