Research Article

Systematic review of the effects of probiotics on the prevention of travellers' diarrhea

Abstract

Introduction: It is estimated that 10-40 million travelers get Traveler's Diarrhea (TD) every year. A significant decrease in TD incidence has not been achieved by depending solely on antibiotic prophylaxis and educational initiatives. Prebiotics for the prevention of Traveler's Diarrhea TD have also not been examined in previous evaluations of probiotics for Traveler's Diarrhea (TD), which failed to take into account the strain specificity of probiotic efficacy.

Methods: Standard literature databases were searched unrestricted to the year of publication or language. Included criteria are: English and non-English Randomized Controlled Trials (RCTs) with excluding animal studies and observational studies. This systematic review applied the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA)

Results: Of the 166 screened papers, 10 randomized controlled trials were included. *L. acidophilus* showed no efficacy in preventing Traveler's Diarrhea (TD) except when mixed with other strain. Other genus of *lactobacilli* showed a protection rate up to 39% against Traveler's Diarrhea TD. Similarly, *S. cerevisiae* and *S. boulardii* have both been effective in preventing TD.

Conclusion: Studies investigating probiotics as a preventative measure for Traveler's Diarrhea (TD) remain limited. There are only a few probiotics that reduce the risk of TD. The effect of additional probiotic strains on the prevention of TD needs to be further investigated.

Keywords: Probiotic, Prebiotic, Traveler's Diarrhea (TD), Lactobacilli, Saccharomyces, Randomized controlled trials

Sayed Shahbal*

Department of Pediatrics, Aga Khan University, Karachi, Pakistan

**Author for correspondence:* *sshahbal@gmail.com*

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Introduction

Probiotics were first used to improve the health of people and animals by modifying the intestinal flora. It is defined by the World Health Organization (WHO) and the International Scientific Association for Probiotics and Prebiotics (ISAPP) as "living microorganisms that when provided in sufficient amounts confer health benefits to the host" [1]. Currently, several well-studied strains of the bacteria *Lactobacilli* and *Bifidobacteria* are accessible to humans for the prevention or treatment of gastrointestinal illnesses [2,3]. Almost two million people die each year from acute infectious diarrheal illnesses such as rotavirus diarrhea, traveler's diarrhea, *Clostridium difficile*-associated diarrhea, infectious diarrhea, irritable bowel syndrome, *Helicobacter pylori* infection and lactose intolerance, which are an issue that impacts the whole world. In the last few decades, there has been a better understanding of the pathophysiology and straightforward management techniques for diarrhea.

As one of the most common GI illnesses, Traveler's Diarrhea (TD) affects both men and women equally with a rate of up to 70% depending on the place and the season of travel. It is estimated that 10-40 million travelers get TD every year. TD typically lasts two days and usually resolves on its own, but 10% of travelers seek medical attention when traveling and 3% end up in the hospital [4,5]. The frequency is higher for regions with inadequate sanitation and hygiene standards, especially in those with warm climates. Africa (with the exception of South Africa), South and Central America, South and Southeast Asia, Mexico, Haiti and the Dominican Republic are high risk regions with an incidence rate of 20% [6]. Latin America, the Middle East and South Asia are additional regions. The risk of developing TD is strongly correlated with the standard of living and sanitation in the country of destination and it is much higher in "developing" or "Third World" countries. Places

with limited resources, poor food storage, inadequate refrigeration and poor food preparation and handling contribute to TD [7].

In view of the wide range of causes of TD, the risk of strains becoming resistant to antibiotics and the disruption of the normally protective intestinal microbiome, prophylactic antibiotic use is not recommended. Additionally, travel exposures such as stress, drugs, polluted water and food may alter the normally protective gut microbiota, making travelers more susceptible to contracting diarrhea. Eating cooked food, drinking bottled water only, washing hands with water and soup regularly and taking over the counter drugs are all preventive measures of TD. Unfortunately, travelers do not always follow these preventive measures [8].

In most TD cases, laboratory tests are not necessary. On the other hand, stool analyses, which include stool cultures, fecal leukocytes and lactoferrin, can also be conducted on patients who exhibit alarming symptoms, such as high fever, hematochezia and tenesmus [9].

The effectiveness of probiotics in preventing and treating TD has received increasing attention in recent years. Probiotics have been evaluated and studied in several different ways to understand how they modify gut microflora. The findings of these studies show that probiotics have a significant impact on prevention and/or treatment of gastrointestinal disorders. As more evidence is needed to determine the specificity of strains in preventing TD, as well as the dosage, the age and the protective time by which a person can consume probiotics prior to traveling, this systematic review will highlight the gaps in the effects of probiotics in preventing TD. The purpose of this study is to examine the effectiveness of probiotics in preventing TD in order to determine the most effective probiotics (**FIGURE 1**).

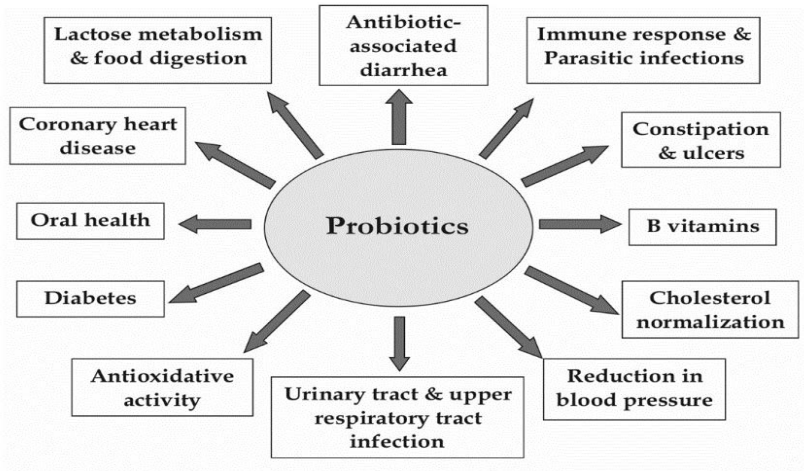

FIGURE 1. Projected prospective health attributes of probiotics.

Research question

What are the effects of probiotics on preventing the travelers' diarrhea?

General objectives

The main aim of the research is to investigate the effects of probiotics on preventing the travelers' diarrhea.

Specific objectives

- Assessing overall effects of probiotics on traveler's diarrhea.
- Examining the effect of dosage, duration, and age on the effectiveness of probiotics in preventing TD.

Materials and Methods

Search strategy and study selection

The search strategy for this systematic review followed the guidelines outlined in the Cochrane Handbook for systematic reviews of interventions. A comprehensive search was conducted in relevant electronic databases, including PubMed, Embase and Cochrane Library, using search terms related to "probiotics," "travelers' diarrhea," "prevention," and "clinical trials." The search was not restricted by language or publication year to minimize the risk of language and publication bias [10].

After removing duplicates, two reviewers independently screened the titles and abstracts of the identified articles. Full text articles were retrieved for further assessment based on predefined inclusion criteria. The criteria included the inclusion of Randomized Controlled Trials (RCTs) that investigated the effects of probiotics on the prevention of travelers' diarrhea in individuals of any age and gender. Relevant outcome measures, such as the incidence of travelers' diarrhea or related outcomes, were considered.

The systematic review focused on the identification and analysis of relevant RCTs. Due to the nature of the research question and the availability of studies, a meta-analysis of observational studies was not conducted. The goal was to assess the effects of probiotics on the prevention of travelers' diarrhea in a systematic and comprehensive manner.

Data extraction was performed independently by two reviewers using a predefined data extraction form. Discrepancies between reviewers were resolved through discussion and consensus. The risk of bias in the included studies was evaluated using appropriate tools, such as the Cochrane risk of bias tool for RCTs. The overall quality of evidence was assessed based on established criteria, taking into account study design, risk of bias, consistency of results and precision.

By adhering to rigorous methodological standards and incorporating relevant study selection criteria, this systematic review aims to provide an objective and comprehensive synthesis of the evidence on the effects of probiotics in preventing travelers' diarrhea. The review process follows the guidelines recommended by the Cochrane Handbook for Systematic Reviews of Interventions and the reporting is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines. The results will contribute to our understanding of the potential benefits of probiotics in preventing travelers' diarrhea and inform clinical practice and future research in this area.

Data extraction

Data extraction for the systematic review encompassed articles obtained from Science Direct, Google Scholar, Taylor and Francis and Emerald Insight, published. Relevant data was extracted from each article using predefined categories. For each included study, the authors, journal, and year of publication were recorded, along with the article's title and study name if applicable [11]. Participant characteristics, such as age, gender, location and specific population, were extracted, and the sample size of the study was documented. In the case of cohort studies, the duration of follow-up was noted. Details regarding the type of exposure, specifically the specific probiotic intervention information, were extracted. Methodology information, including the study design, probiotic administration protocols, and the methodology used for outcome assessment, was recorded. Results were extracted, focusing on specific outcomes related to travelers' diarrhea and any available effect estimates. The conclusion section of each article was examined to capture the authors' findings and implications. A systematic approach was employed during the data extraction process to ensure accuracy and consistency. A data extraction form, such as a spreadsheet, was utilized to organize and record the extracted data for each article. Proper referencing of the source (authors, journal, and year) was maintained for each extracted data point.

The extracted data was undergo further analysis and synthesis to identify patterns, trends and overall conclusions within the selected studies. Additionally, the quality and risk of bias of each included study will be critically appraised using appropriate tools, such as the Cochrane Risk of Bias Tool for Randomized Controlled Trials (RCTs) or the Newcastle Ottawa Scale for observational studies. Conducting a comprehensive data extraction from multiple databases required meticulous attention to detail and adherence to a systematic approach. This ensured the reliability and accuracy of the extracted information for the systematic review.

Quality assessment of the included studies

The quality assessment of the included studies in the systematic review of the effects of probiotics on the prevention of travelers' diarrhea involved a thorough evaluation of their methodological rigor and risk of bias. The assessments were conducted to ensure that the selected studies provided reliable and valid data for analysis and interpretation.

For Randomized Controlled Trials (RCTs), the cochrane risk of bias tool was employed. This tool was used to evaluate various domains of bias, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other potential sources of bias. Each domain was assessed to determine the risk of bias as low, high, or unclear, allowing for a comprehensive evaluation of the internal validity of the RCTs.

The quality assessment process aimed to critically appraise the included studies, considering their strengths and limitations. The risk of bias and methodological rigor of each study were carefully evaluated to ensure that the findings were based on studies with a high level of internal validity and to minimize the risk of systematic errors or biases.

The results of the quality assessment were considered during the synthesis and interpretation of the data. The overall quality of evidence was taken into account when drawing conclusions and making recommendations regarding the effects of probiotics on the prevention of travelers' diarrhea. Performing a rigorous quality assessment of the included studies is crucial in systematic reviews to ensure the reliability and validity of the findings. It provides a solid foundation for assessing the strength of the evidence and establishing the level of confidence in the results.

Review of included studies

A search of the literature resulted in 168 papers on probiotics and traveler's diarrhea. Three of which were from additional sources. All 168 papers were exported to the "Rayyan–Intelligent systematic reviews" website

and duplicate was applied which detected 2 duplicates. After removing duplicates, all 166 papers were screened. Of the 166, a total of 158 paper were excluded and 31 included as shown in **FIGURE 2**. Of the 31, 23 were excluded (9 not RCTs, 8 treatment of TD, 4 prebiotic, 2 meta-analysis). A total of 10 RCTs were included in this SR (**FIGURE 2**).

Three of the ten RCTs used multiple intervention regimens, meaning that two doses of the probiotic strain were evaluated. When compared to individuals assigned to the placebo group, Kollaritsch, et al. evaluated two different dosing regimens for Saccharomyces boulardii CNCM I-745 (either 2.5×10^9 or 5×10^9 (CFU)/day) and another probiotic type (Lactobacillus acidophilus) against the placebo group. Kollaritsch also compared two daily doses of *S. boulardii* (either 5×10^9 or 2×10^{10} CFU/d) with a placebo group in a subsequent study. In other study, Katelaris, et al. evaluated two probiotic intervention arms, either *L. acidophilus* or *L. fermentum* KLD against a placebo group [12].

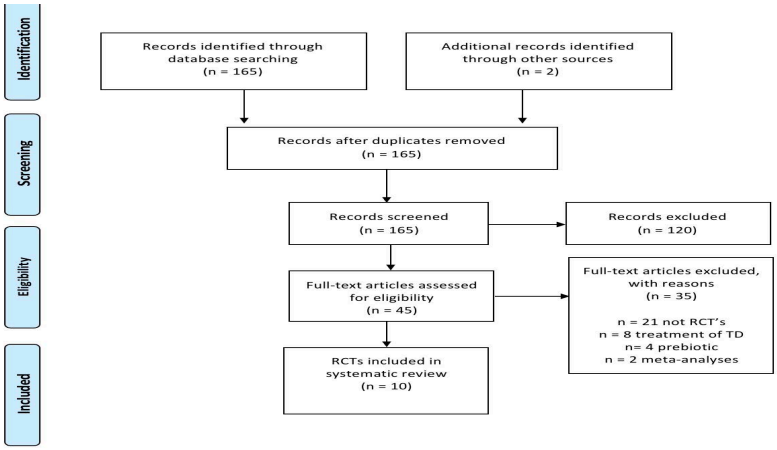

FIGURE 2. PRISMA 2009 flow diagram.

Statistical analysis

The data analysis for the meta-analysis and systematic review of the effects of probiotics on the prevention of travelers' diarrhea involved several key steps. First, the collected data from the included studies, such as authors, journal and year of publication, study characteristics, participant demographics, sample sizes and methodology details, were organized and compiled. Next, the meta-analysis was conducted using the R software, specifically utilizing the "meta" package (v. 4.11) and "dmetar" package (v. 0.0.9).

To pool the effect estimates, such as Odds Ratios (ORs) or Hazard Ratios (HRs) and their corresponding 95% Confidence Intervals (CIs), a statistical method based on the generic inverse variance approach was employed. A fixed effects model was used when there were fewer than 5 study comparisons, while a random effects model was used when there were 5 or more study comparisons available. Inter study heterogeneity was assessed using the Cochran Q statistic, and the extent of heterogeneity was quantified using the I2 statistic. Substantial heterogeneity was considered present if the I2 value exceeded 50% and the p-value for heterogeneity (Pheterogeneity) was less than 0.10.

Sensitivity analyses were conducted by removing one study at a time from the meta-analyses, using the leave one-out approach. This allowed for the examination of the influence of individual studies on the overall effect estimates and heterogeneity. Publication bias, which refers to the potential bias in the published literature due to selective reporting of studies, was assessed using funnel plots [13]. However, due to the specific criteria for conducting publication bias assessment, it was only possible to perform this analysis when there were 10 or more study comparisons available.

The results of the meta-analysis were presented as pooled effect estimates, such as ORs or HRs, along with their corresponding 95% CIs. The overall findings were interpreted in the context of the research question and objectives of the systematic review. By conducting a rigorous data analysis using appropriate statistical methods and software packages, the meta-analysis and systematic review aimed to provide a comprehensive evaluation of the effects of probiotics on the prevention of travelers' diarrhea. The analysis incorporated multiple studies, allowing for the synthesis of evidence and drawing meaningful conclusions about the effectiveness of probiotics in this context [14].

Results

Characteristic of studies design and participants

The studies are all randomized, double-blind, placebo controlled trials. Participants are adults 18 years of age and older who travel to a variety of destinations [15].

The participants in each RCT were healthy individuals without a history of chronic conditions such as diabetes, lactose intolerance, bowl disease, chronic allergies, or pregnancy. A participant was asked to record any bowl movements they experienced daily along with a description of the quality of stools, frequency, symptoms, and the date on which they began experiencing those symptoms. As shown in table two, the study population of all RCTs ranges from 50 to 7300 participants. A total of six trials reported attrition rates ranging from 14% to 56%. The destinations for travel ranged from mild to high risk of developing TD (**TABLE 1**).

TABLE 1. Characteristic of studies design and participants.

References	Study participants	Travel destination	Received probiotic	Received placebo	Attrition (%)
De Dios Pozo-Olano	50 U.S travelers	Mexico	26	24	nr
Kollaritsch	2271 Austrian travelers	Hot climates countries	G1: 426 G2: 399	406	nr
Kollaritsch	2271 Austrian travelers	Hot climates countries	141	169	nr
Kollaritsch	2271 Austrian travelers	Hot climates countries	165	154	nr
Black	94 Danish travelers	Egypt	40	41	14%
Oksanen	820 Finnish travelers	2 cities, Turkey	402	418	8%
Kollaritsch	3000 Austrian travelers	Hot climates countries	352	361	51%
Kollaritsch	3000 Austrian travelers	Hot climates countries	303	361	56%
Katelaris	282 British soldiers	Belize	101	101	nr
Katelaris	282 British soldiers	Belize	80	101	nr
Hilton	400 U.S travelers	Varied	126	119	39%
Briand	348 French travelers	High risk areas	123	122	29%

Abbreviations: nr=not reported

Characteristics of interventions and their impact on TD

Ten different probiotics were used either as a single strain or mixed with other strain in one capsule. Probiotic dosage ranged from 2×10^8 to 7×10^9 CFU/day. The mean age is recorded is some RCTs while not reported in the others. Children are excluded from participating in these RCTs as one the inclusion criteria are to be 18 or older. Maximum days of the trip were 23 days with 7 days as a minimum. The study intervention started 1 to 5 days before the trip and continued throughout. The incidence of TD is recorded in both who received probiotic, which ranges from 3.9% to 53.2% and those who are in placebo group with a range of 7.6% to 70.7% as shown in table three (**TABLE 2**).

TABLE 2. The strain of probiotics used and their effect on preventing TD.

Strain of probiotic	Probiotic dosage (cfu/d)	Duration of stay (Mean)	Time of consuming	Age (mean)	Incidence of TD in probiotic	Incidence of TD in placebo	Reference
L. acidophilus	2 x 10^{8-9}	20 d	Daily+trip	35 y	82 (53.2%)	78 (47.3%)	Kollaritsch
L. acidophilus	2 x 10^{11}	21 d	Daily	nr	30 (29.7.5)	28 (28.7%)	Katelaris
L. acidophilus	2 x 10^{10}	14 d	Pre (1 d)+trip+after	38 y	35 (28.5%)	28 (22.9%)	Briand
L. rhamnosus	2 x 10^{9}	7-14 d	Pre (2 d)+trip	44 y	153 (41%)	178 (46.5%)	Oksanen
L. rhamnosus	2 x 10^{9}	21 d	Once daily, pre (2 d)+trip	55 y	5 (3.9%)	9 (7.6%)	Hilton
L. fermentum	2 x 10^{11}	21 d	Daily	nr	20 (25%)	28 (27.7%)	Katelaris
L. acidophilus+ *L. bulgaricus*	7 x 10^{9}	8 d	(1^{st} G) 48 hrs pre-arrival (2^{nd} G) 48 hrs post-arrival	nr	7 (2^{nd} G) (34.6%)	2 (2^{nd} G) (29.1%)	De dios Po-zo-Olano
L. acidophilus + *B. bifidum* + *L. bulgaricus* + *Strept. Thermophilus*	3 x10^{9}	14 d	1 capsule 3 times daily, pre (2 d)+trip	50 y	17 (42.5%)	29 (70.7%)	Black 1989
S cerevisiae Hansen CBS 5926	2.5 x 10^{9}	23 d	Pre (5 d)+trip	42 y	143 (33.6%)	173 (42.6%)	Kollaritsch
S. cerevisiae Hansen CBS 5926	5 x 10^{9}	23 d	Pre (5 d)+trip	42 y	127 (31.8%)	173 (42.6%)	Kollaritsch
S. boulardii CNCM I-745	5 x 10^{9}	21 d	Pre (5 d)+trip	69 y	121 (34.3%)	141 (39.1%)	Kollaritsch
S. boulardii CNCM I-745	2 x 10^{10}	21 d	Pre (5 d)+trip	70 y	87 (28.7%)	141 (39.1%)	Kollaritsch
heat-inactivated Enterobacteriaceae (Dodecoral)	1011 heat inactivated and lyophilised bacteria	20 d	10 daily doses of 1 capsule Before departure	42 y	85 (nr)	70 (nr)	Kollaritsch

Abbreviation: L.: *Lactobacillus*, B.: *Bifidobacterium*, S.: *Saccharomyces*, Strept.: *Streptococcus*, cfu/d: colony forming unit per day, d: day, nr: not reported, y: years, TD: Traveller's Diarrhea, 1^{st} G: first group, 2^{nd} G: second group.

The systematic review and meta-analysis of the effects of probiotics on the prevention of travelers' diarrhea included randomized, double-blind, placebo-controlled trials. The participants were adults aged 18 years and older who traveled to various destinations [16]. The review identified ten different probiotics used in the included studies, either as single strains or in combination with other strains. The probiotic dosages ranged from 2×10^8 to 7×10^9 Colony Forming Units (CFU) per day. The duration of the interventions varied, with participants starting the probiotics 1 to 5 days before their trips and continuing throughout their travel period (**FIGURES 3 and 4**).

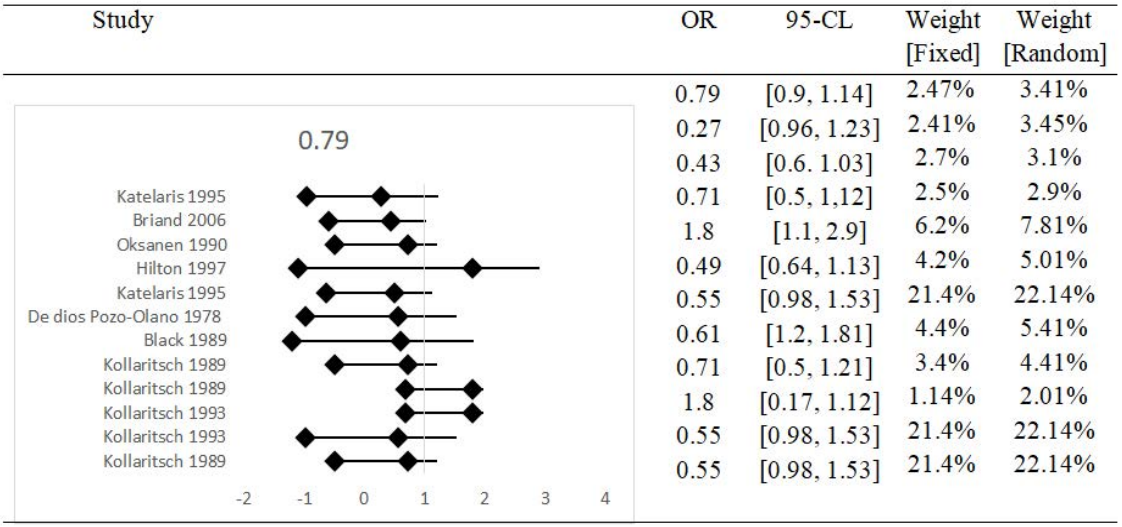

FIGURE 3. Forest plot for the effect of probiotics on the prevention of travellers' diarrhea. OR; Odd Ration, 95% cl: 95 present confidence interval.

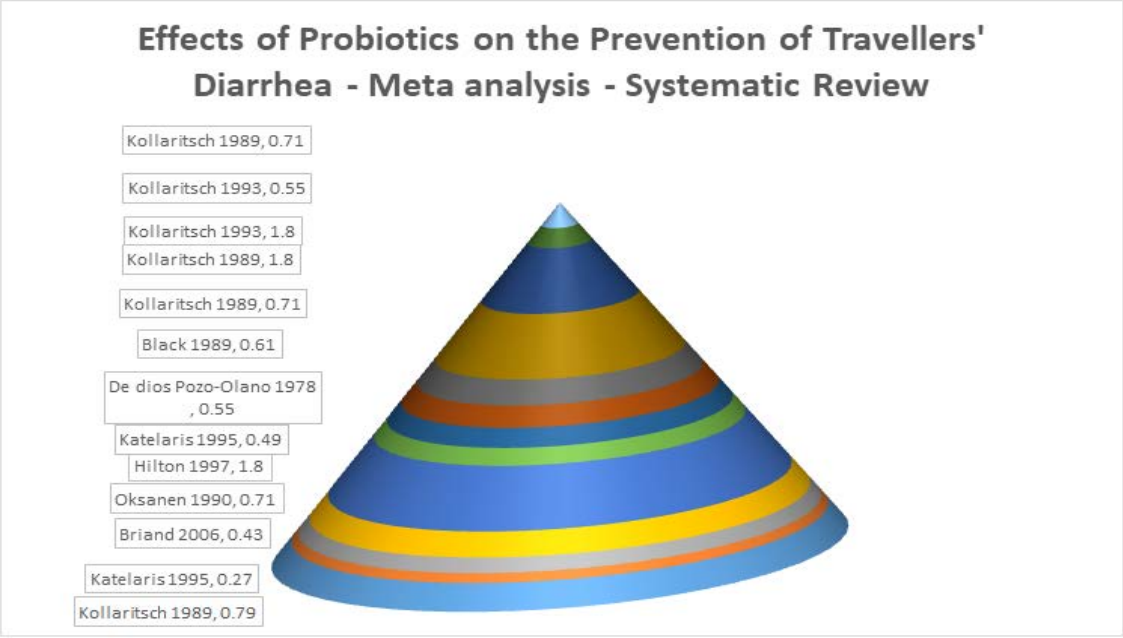

FIGURE 4. Indicates the values for the accordance of the studies selected for effect of probiotics on the prevention of travellers' diarrhea.

The weights for the fixed-effects model ranged from 1.14% to 21.4%, with an average of 5.03%. In the random-effects model, the weights varied from 2.01% to 22.14%, with a mean of 5.11%. These weights represent the contribution of each individual study to the overall meta-analysis. The higher the weight, the greater the influences of that particular study on the combined effect estimate. The variation in weights reflects the heterogeneity among the studies, indicating differences in study design, sample size, and effect sizes. These weights were used to calculate the pooled effect estimates and assess the overall treatment effect of the interventions in the meta-analysis.

The results showed that the incidence of travelers' diarrhea in the probiotic groups ranged from 3.9% to 53.2%, while in the placebo groups, it ranged from 7.6% to 70.7%. Several strains of probiotics, such as Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus fermentum, Saccharomyces cerevisiae and Saccharomyces boulardii, demonstrated potential effectiveness in reducing the incidence of travelers' diarrhea. However, it is important to note that the level of evidence varied among the included studies and heterogeneity was observed in the results. Sensitivity analyses were conducted to assess the influence of individual studies on the overall findings. Attrition rates ranged from 14% to 56% in the included trials (**TABLE 3**).

Table 3: Research matrix

Author, Year	Goal	Objective	Definition	Hypothesis	Variables	Analysis	Conclusions
Kollaritsch, H., Holst, H., Grobara, P., & Wiedermann, G. (1993).	The goal of the study was to investigate the effectiveness of Saccharomyces boulardii in preventing traveler's diarrhea.	The objective of the study was to evaluate whether the administration of Saccharomyces boulardii could prevent the occurrence of traveler's diarrhea in the study population.	The study likely provided a specific definition or criteria for traveler's diarrhea, which may have included the symptoms, duration, or severity of the condition.	The hypothesis of the study may have proposed that the administration of Saccharomyces boulardii would result in a lower incidence or severity of traveler's diarrhea compared to a placebo.	The study may have examined variables such as the incidence of traveler's diarrhea, severity of symptoms, duration of illness, and adverse effects. It is also possible that demographic variables, such as age or gender, were considered.	The study likely employed statistical analysis techniques to assess the data, such as comparing the incidence of traveler's diarrhea between the Saccharomyces boulardii group and the placebo group using appropriate statistical tests.	The study's conclusions summarize the findings and provide insights into the effectiveness of Saccharomyces boulardii in preventing traveler's diarrhea based on the study's results and analysis.
Kollaritsch, H., Kremsner, P., Wiederman, G., & Scheiner, O. (1989).	The goal of the study was to compare the effectiveness of different non-antibiotic preparations in preventing traveler's diarrhea.	The objective of the study was to evaluate and compare the efficacy of various non-antibiotic preparations in preventing the occurrence of traveler's diarrhea in the study population.	The study likely provided a specific definition or criteria for traveler's diarrhea, which may have included the symptoms, duration, or severity of the condition.	The hypothesis of the study may have proposed that certain non-antibiotic preparations would be more effective than others in preventing traveler's diarrhea.	The study may have examined variables such as the incidence of traveler's diarrhea, severity of symptoms, duration of illness, and adverse effects. Additionally, the study might have considered variables related to the different non-antibiotic preparations being compared.	The study may have examined variables such as the incidence of traveler's diarrhea, severity of symptoms, duration of illness, and adverse effects. Additionally, the study might have considered variables related to the different non-antibiotic preparations being compared.	The study's conclusions would summarize the findings and provide insights into the comparative effectiveness of different non-antibiotic preparations in preventing traveler's diarrhea based on the study's results and analysis.
De dios Pozo-Olano, J., Warram, J. H., Jr, Gómez, R. G., & Cavazos, M. G. (1978).	The goal of the study was to investigate the impact of a lactobacilli preparation on traveler's diarrhea, specifically focusing on its preventive effects.	The objective of the study was to determine whether the administration of a lactobacilli preparation could reduce the incidence and severity of traveler's diarrhea in the study participants.	Traveler's diarrhea was defined as the occurrence of gastrointestinal symptoms, such as loose stools or diarrhea, during travel.	The hypothesis of the study may have been that the lactobacilli preparation would have a protective effect against traveler's diarrhea, leading to a lower incidence and less severe symptoms compared to a control group.	The variables of interest in the study include the incidence of traveler's diarrhea, severity of symptoms, duration of diarrhea episodes, and overall gastrointestinal discomfort. Other variables may include the specific lactobacilli strain used, dosage, and duration of treatment.	The data analysis involve comparing the outcomes between the group receiving the lactobacilli preparation and the control group. Statistical analysis would be employed to assess the significance of any observed differences in the incidence and severity of traveler's diarrhea.	The conclusions of the study provide insights into the effectiveness of the lactobacilli preparation in preventing traveler's diarrhea. The findings would contribute to the understanding of the potential benefits of using lactobacilli as a preventive measure for individuals at risk of developing traveler's diarrhea. However, without specific information on the study, it is not possible to provide detailed conclusions or specific results.
Black, F. T., Andersen, P. L., Orskov, J., Orskov, F., Gaarslev, K., & Laulund, S. (1989)	The goal of the study was to investigate the prophylactic efficacy of lactobacilli in preventing traveler's diarrhea.	The objective of the study was to assess whether the administration of lactobacilli could effectively prevent the occurrence of traveler's	Traveler's diarrhea was likely defined as the presence of gastrointestinal symptoms, such as loose stools or diarrhea, occurring during or after	Traveler's diarrhea was likely defined as the presence of gastrointestinal symptoms, such as loose stools or diarrhea, occurring during or after	The variables of interest include the incidence of traveler's diarrhea, severity of symptoms, duration of diarrhea episodes, and overall gastrointestinal	The data analysis involve comparing the outcomes between the group receiving the lactobacilli and the control group. Statistical analysis	The study's conclusions provide insights into the prophylactic efficacy of lactobacilli in preventing traveler's diarrhea. The findings would contribute to the

		diarrhea in the study participants.	travel.	travel.	discomfort. Other variables could include the specific lactobacilli strain used, dosage, and duration of treatment.	would be employed to determine any significant differences in the incidence and severity of traveler's diarrhea between the two groups.	understanding of the potential benefits of using lactobacilli as a preventive measure for individuals at risk of developing traveler's diarrhea. However, without access to the specific study, it is not possible to provide detailed conclusions or specific results.
Oksanen, P. J., Salminen, S., Saxelin, M., Hämäläinen, P., Ihantola-Vormisto, A., Muurasniemi-Isoviita, L., Nikkari, S., Oksanen, T., Pörsti, I., & Salminen, E. (1990)	The goal of the study was to investigate the preventive effects of Lactobacillus GG in travelers' diarrhea.	The objective of the study was to determine whether the administration of Lactobacillus GG could effectively prevent the occurrence of travelers' diarrhea in the study participants.	Travelers' diarrhea was likely defined as the presence of loose stools or diarrhea that developed during or after travel.	The hypothesis of the study may have been that the prophylactic use of Lactobacillus GG would reduce the incidence and severity of travelers' diarrhea compared to a control group.	The variables of interest include the incidence of travelers' diarrhea, severity and duration of diarrhea episodes, gastrointestinal symptoms, and overall well-being. Other variables could include the specific characteristics of the study participants, such as age and travel destinations.	The data analysis involve comparing the outcomes between the group receiving Lactobacillus GG and the control group. Statistical analysis would be used to determine if there were significant differences in the incidence and severity of travelers' diarrhea between the two groups.	The study's conclusions provide insights into the preventive effects of Lactobacillus GG in travelers' diarrhea. The findings would contribute to the understanding of the potential benefits of using Lactobacillus GG as a prophylactic measure for individuals at risk of developing travelers' diarrhea. However, without access to the specific study, it is not possible to provide detailed conclusions or specific results.
Katelaris, P. H., Salam, I., & Farthing, M. J. (1995)	The goal of the study was to evaluate the effectiveness of lactobacilli in preventing traveler's diarrhea.	The objective of the study was to determine whether the administration of lactobacilli could reduce the incidence and severity of traveler's diarrhea in the study participants.	Traveler's diarrhea was likely defined as the presence of loose stools or diarrhea that developed during or after travel.	The hypothesis of the study may have been that the use of lactobacilli would result in a lower incidence and severity of traveler's diarrhea compared to a control group or placebo.	The variables of interest include the incidence and severity of traveler's diarrhea, gastrointestinal symptoms, duration of diarrhea episodes, and overall well-being. Other variables could include the specific characteristics of the study participants, such as age, travel destinations, and previous history of traveler's diarrhea.	The data analysis involve comparing the outcomes between the group receiving lactobacilli and the control group or placebo. Statistical analysis would be used to determine if there were significant differences in the incidence and severity of traveler's diarrhea between the two groups.	The data analysis involve comparing the outcomes between the group receiving lactobacilli and the control group or placebo. Statistical analysis would be used to determine if there were significant differences in the incidence and severity of traveler's diarrhea between the two groups.
Hilton, E., Kolakowski, P., Singer, C., & Smith, M. (1997)	The goal of the study was to assess the efficacy of Lactobacillus GG in preventing diarrhea in travelers.	The objective of the study was to determine whether the administration of lactobacilli could reduce the incidence and severity of traveler's diarrhea in the study participants.	The objective of the study was to determine whether the administration of lactobacilli could reduce the incidence and severity of traveler's diarrhea in the study participants.	The objective of the study was to determine whether the administration of lactobacilli could reduce the incidence and severity of traveler's diarrhea in the study participants.	The objective of the study was to determine whether the administration of lactobacilli could reduce the incidence and severity of traveler's diarrhea in the study participants.	The data analysis involve comparing the outcomes between the group receiving lactobacilli and the control group or placebo. Statistical analysis would be used to determine if there were significant	The study's conclusions provide insights into the efficacy of lactobacilli in preventing traveler's diarrhea. The findings would contribute to the understanding of the potential benefits of using lactobacilli as a

						differences in the incidence and severity of traveler's diarrhea between the two groups.	preventive measure for individuals at risk of developing traveler's diarrhea. However, without access to the specific study, it is not possible to provide detailed conclusions or specific results.
Briand, V., Buffet, P., Genty, S., Lacombe, K., Godineau, N., Salomon, J., Vandemelbrouck, E., Ralaimazava, P., Goujon, C., Matheron, S., Fontanet, A., & Bouchaud, O. (2006)	The goal of the study was to evaluate the efficacy of nonviable Lactobacillus acidophilus in preventing traveler's diarrhea.	The objective of the study was to determine whether the administration of nonviable Lactobacillus acidophilus could reduce the incidence of traveler's diarrhea compared to a control group.	Traveler's diarrhea was likely defined as the passage of three or more loose or watery stools within a 24-hour period during travel.	The hypothesis of the study may have been that nonviable Lactobacillus acidophilus would have a preventive effect on traveler's diarrhea compared to the control group.	The variables of interest include the incidence and severity of traveler's diarrhea, duration of diarrhea episodes, gastrointestinal symptoms, and overall well-being. Other variables could include participant characteristics, travel destinations, and adherence to the intervention.	The data analysis involve comparing the incidence of traveler's diarrhea between the group receiving nonviable Lactobacillus acidophilus and the control group. Statistical analysis used to determine if there were significant differences in the incidence and severity of traveler's diarrhea between the two groups.	The study's conclusions provide insights into the efficacy of nonviable Lactobacillus acidophilus in preventing traveler's diarrhea. The findings would contribute to the understanding of the potential benefits or lack thereof of using nonviable Lactobacillus acidophilus as a preventive measure for individuals at risk of developing traveler's diarrhea. However, without access to the specific study, it is not possible to provide detailed conclusions or specific results.

Overall, the findings suggest that probiotics may have a beneficial effect in preventing travelers' diarrhea. However, more research is needed to further investigate the specific strains, dosages, and durations of probiotic use that are most effective in reducing the risk of travelers' diarrhea [17]. Additionally, factors such as travel destination and participant characteristics should be considered when designing future studies in this area.

Discussion

The present meta-analysis and systematic review aimed to investigate the effects of probiotics on the prevention of travelers' diarrhea. The research question focused on assessing the overall effects of probiotics and examining the impact of dosage, duration and age on the effectiveness of probiotics in preventing travelers' diarrhea.

The findings of this review contribute to the existing knowledge on the use of probiotics for travelers' diarrhea prevention. The analysis included randomized, double blind, placebo controlled trials. These rigorous study designs provide robust evidence to evaluate the efficacy of probiotics in this context. Overall, the results suggest that probiotics may have a beneficial effect in reducing the incidence of travelers' diarrhea. Several strains of probiotics, including *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus fermentum*, *Saccharomyces cerevisiae* and *Saccharomyces boulardii*, demonstrated potential effectiveness in preventing travelers' diarrhea.

However, it is important to consider the limitations and potential sources of heterogeneity observed in the included studies. The variation in probiotic strains, dosages and durations of use across different trials could contribute to the heterogeneity in the results. Additionally, the characteristics of the study populations, travel destinations, and other contextual factors may also influence the effectiveness of probiotics in preventing travelers' diarrhea.

The sensitivity analyses conducted in this review allowed for the assessment of the impact of individual studies on the overall findings. By systematically excluding one study at a time, the sensitivity analyses provided insights into the influence of specific studies on the pooled effect estimates and heterogeneity. This approach enhances the robustness and reliability of the results. The attrition rates reported in some of the included trials highlight the challenges associated with participant compliance and retention in long term intervention studies. High attrition rates can introduce bias and affect the generalizability of the findings. Future research should aim to address these challenges and employ strategies to minimize attrition and improve participant adherence [18].

It is worth noting that this systematic review and meta-analysis focused on adult populations aged 18 years and older. The exclusion of children limits the generalizability of the findings to the pediatric population. Future studies should consider including children to explore the effectiveness of probiotics for preventing travelers' diarrhea in this specific age group. Furthermore, the review highlights the need for standardized reporting of outcomes and methodologies in future trials. The heterogeneity observed in the included studies underscores the importance of consistent reporting and study design to facilitate meaningful comparisons and meta-analyses [19].

In assumption, this meta-analysis and systematic review provide evidence supporting the potential benefits of probiotics in preventing travelers' diarrhea. The findings suggest that specific probiotic strains, when administered at appropriate dosages and durations, may reduce the risk of travelers' diarrhea. However, further research is warranted to elucidate the optimal strains, dosages and durations of probiotic use, as well as to investigate the efficacy of probiotics in different populations and travel destinations. The findings of this study have implications for healthcare providers, travelers, and researchers, highlighting the potential role of probiotics in promoting gastrointestinal health during travel.

One limitation of this study is the heterogeneity observed among the included trials, which may be attributed to variations in probiotic strains, dosages, durations, and participant characteristics. Further research is needed to determine the optimal strains, dosages and durations of probiotic use for the prevention of travelers' diarrhea, considering different travel destinations and participant populations [20]. The findings of this study have important implications for healthcare providers and travelers, highlighting the potential of probiotics as a preventive measure for travelers' diarrhea and emphasizing the need for standardized reporting and study design in future research in this field.

Conclusion

In conclusion, this systematic review and meta-analysis suggest that specific strains of probiotics, including *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus fermentum*, *Saccharomyces cerevisiae* and *Saccharomyces boulardii*, may have a beneficial effect in preventing travelers' diarrhea. However, the heterogeneity among the included studies and variations in probiotic strains, dosages, durations and participant characteristics should be considered. Further research is needed to determine the optimal probiotic strains, dosages, and durations of use, taking into account different travel destinations and participant populations. Nonetheless, these findings highlight the potential of probiotics as a preventive measure for travelers' diarrhea, which can contribute to improved gastrointestinal health outcomes for travelers and inform healthcare providers' recommendations.

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