INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Artificial intelligence in the studies of gastrointestinal microbiome: protocol for a systematic review

Zhou, Z[1]; Zhou, Z[2]; Li, H[3]; Liao, W[4].

Review question / Objective: **What are the applications, performance and prospects of artificial intelligence (AI) in the studies of gastrointestinal microbiome? P: researches about gastrointestinal microbiome I: AI techniques C: conventional methods and expert systems O: quantitative assessment of the applications, performance and prospects of AI in this field S: primary studies.**
Information sources: **We will search the English electronic database including PubMed, Medline(OVID interface, 2000 onwards), Embase(OVID interface, 2000 onwards), Google Scholar, Cochrane library, Web of science, ISI and Scopus; we will also search the Chinese electronic database such as CNIK, WanFang, VIP, CBM and CMCC. Finally we will also consider the OpenGrey to get grey literatures. We will contact the author if we can't find the full-text online.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 April 2021 and was last updated on 01 April 2021 (registration number INPLASY202140004).

INTRODUCTION

Review question / Objective: **What are the applications, performance and prospects of artificial intelligence (AI) in the studies of gastrointestinal microbiome? P: researches about gastrointestinal microbiome I: AI techniques C: conventional methods and expert systems O: quantitative assessment of the applications, performance and prospects of AI in this field S: primary studies.**

Rationale: Gastrointestinal microbiome has become a research hotspot in recent years due to their crucial role in the health or disease of their host. To study these microorganisms, scientists use the high-throughput sequencing techniques to identify their compositions, metabolism and functions, which also brings huge amounts of data representation far beyond human understanding. In such a case, artificial intelligence (AI) is implemented to find the intrinsic structures from those data and solve the problem automatically. More interestingly, the more datasets are given, the more precise and accurate the prediction will be. Therefore, AI algorithms could become a robust tool to solve the data dilemma in the domain of gastrointestinal researches. In this review, we aim to critically appraise the applications, performance and prospects of artificial intelligence (AI) in the studies of gastrointestinal microbiome. Endpoints here refer to: 1) Profile the applications of AI algorithm in diverse domains of the gastrointestinal microbiome research; 2) Assess the overall performance and interpretability of AI in different segments of studies with regard to gastrointestinal microbiome; 3) Identify which AI algorithm is more capable of certain tasks in the gastrointestinal microbiome study; 4) Offer a guideline for scientific workers to select the appropriate AI technique to better deal with some specific problems; 5) Predict the potential utilities of AI in the gastrointestinal microbiome research in the future.

Condition being studied: Gastrointestinal microbiome exerts a remarkable impact on the homeostasis or disease of their host. On one hand, they can benefit the host in diverse ways such as reinforcing gut integrity or shaping the intestinal epithelium, assisting the host to harvest energy, resisting exotic pathogens and regulating host immunity. On the other hand, the susceptibility of the gastrointestinal microbiota being disrupted by multiple factors makes it a crucial factor to trigger local disturbance and even systemic diseases. Moreover, the gastrointestinal microorganisms seem to have interesting interactions with other segments of human body, especially one of the most complex parts—— the brain. To study these microorganisms, scientists use the high-throughput sequencing techniques to identify their compositions, metabolism and functions with high efficiency. However, the interpretability of the high-volume data from metagenomic analysis is far beyond the human ability, and the accuracy of prediction can hardly be guaranteed using traditional linear models. Artificial intelligence (AI) is capable of building a computational model to automatically figure out the intrinsic patterns of the given data and predicting the outcomes based on the patterns it has learned. Due to its data-dependent operating principle, AI is endowed with a fascinating property that the more datasets are given ,the more precise and accurate the prediction will be.

METHODS

Search strategy: Following the guidelines from Preferred reporting items for systematic review and meta-analysis (PRISMA), our team will figure out the keywords for searching by applying the PICOS rule. Then the search strategies will be developed using a combination of medical subject headings (MeSH) and text words related to the keywords above. A draft PubMed search strategy is included in Appendix 1. After the PubMed strategy is finalized, it will be adapted to the syntax and subject headings of the other databases. Both qualitative and quantitative studies will be sought. No study design, date or language limits will be imposed on the search. To ensure literature saturation, we will scan the reference lists of included studies or relevant reviews identified through the search. We will also search the authors' personal files to make sure that all relevant material has been captured. The search will be updated toward the end of the review, after being validated to ensure that the PubMed strategy retrieves a high proportion of eligible studies found through any means but indexed in PubMed. Appendix 1 1#: "Gastrointestinal

Microbiome"[MeSH] 2#: "Gastrointestinal Microbiomes" OR "Microbiome, Gastrointestinal" OR "Microbiome, Gastrointestinal" OR "Gut Microbiome" OR "Gut Microbiomes" OR "Microbiome, Gut" OR "Gut Microflora" OR "Microflora, Gut" OR "Gut Microbiota" OR "Gut Microbiotas" OR "Microbiota, Gut" OR "Gastrointestinal Flora" OR "Flora, Gastrointestinal" OR "Gut Flora" OR "Flora, Gut" OR "Gastrointestinal Microbiota" OR "Gastrointestinal Microbiotas" OR "Microbiota, Gastrointestinal" OR "Gastrointestinal Microbial Community" OR "Gastrointestinal Microbial Communities" OR "Microbial Community, Gastrointestinal" OR "Gastrointestinal Microflora" OR "Microflora, Gastrointestinal" OR "Gastric Microbiome" OR "Gastric Microbiomes" OR "Microbiome, Gastric" OR "Intestinal Microbiome" OR "Intestinal Microbiomes" OR "Microbiome, Intestinal" OR "Intestinal Microbiota" OR "Intestinal Microbiotas" OR "Microbiota, Intestinal" OR "Intestinal Microflora" OR "Microflora, Intestinal" OR "Intestinal Flora" OR "Flora, Intestinal" OR "Enteric Bacteria" OR "Bacteria, Enteric" 3#: 1# OR 2# 4#: ((((((("Artificial Intelligence"[Mesh]) OR "Machine Learning"[Mesh]) OR "Deep Learning"[Mesh]) OR "Supervised Machine Learning"[Mesh]) OR "Support Vector Machine"[Mesh]) OR "Unsupervised Machine Learning"[Mesh]) OR "Neural Networks, Computer"[Mesh] 5#: "Learning, Deep" OR "Hierarchical Learning" OR "Learning, Hierarchical" OR "Learning, Machine" OR "Transfer Learning" OR "Learning, Transfer" OR "Intelligence, Artificial" OR "Computational Intelligence" OR "Intelligence, Computational" OR "Machine Intelligence" OR "Intelligence, Machine" OR "Computer Reasoning" OR "Reasoning, Computer" OR "AI (Artificial Intelligence)" OR "Computer Vision System*" OR "System*, Computer Vision" OR "Knowledge Representation*" OR "Knowledge Acquisition*" 6#: 4# OR 5# 7#: 3# AND 4# 8#: 3# AND 5# 9#: 3# AND 6# 10#: (Gastrointestinal Microbiome) AND artificial intelligence.

Participant or population: Researches about gastrointestinal microbiome.

Intervention: AI techniques.

Comparator: conventional methods and expert systems.

Study designs to be included: Primary studies.

Eligibility criteria: Study designs: we will include primary researches in the field of gastrointestinal microbiome. But non-original studies such as review articles, subject surveys, Annual summary of disciplines, guidelines, meeting reports as well as letters to editors will be excluded. Population: Obviously our population here refers to researches of gastrointestinal microbiome. Literatures focusing on the composition, characteristic, function and impact on health or disease of gastrointestinal microbiome will be included. But we will exclude studies merely considering one or several specific species of gastrointestinal microorganisms instead of the bioecological entity. Papers that do not concentrate on gastrointestinal microbiome, though may mention this item will also be excluded. Intervention: Our intervention here are AI techniques. The AI algorithm should be implemented independently or with other kinds of AI techniques in at least one specific and distinct step in selected literatures for this review. Literatures that are not related to AI or have no clear description of where a specific type of AI are used will be excluded. Comparator: The comparators here are conventional techniques and expert systems in the studies of gastrointestinal microbiome. Papers comparing the performance of AI algorithms with traditional techniques or addressing the difference between AI and other method will definitely be included. Those with comparisons of the applications and performance among different types of AI algorithms will also be included. However, researches with no comparison can only be included if they have qualitative or quantitative assessments of the AI performance. outcome: We are seeking for comparable and at best standardized outcomes of the AI performance evaluation. We will include literatures with

measurable and quantitative outcomes of AI performance such as accuracy, sensitivity, specificity, receiver operating characteristic (ROC) curve, areas under the curve (AUC), interclass correlation coefficient (ICC) and positive/negative prediction value (PPV/NPV). Those without quantitative evaluation but with clear and valid qualitative assessment will also be included. But if the validation can't be testified clearly, then the paper will be excluded. other criteria: We will include relative articles formally published in English or Chinese from 2000 till now. The related grey literatures will also be included. But literatures without available or accessible full-text will be excluded.

Information sources: We will search the English electronic database including PubMed, Medline(OVID interface, 2000 onwards), Embase(OVID interface, 2000 onwards), Google Scholar, Cochrane library, Web of science, ISI and Scopus; we will also search the Chinese electronic database such as CNIK, WanFang, VIP, CBM and CMCC. Finally we will also consider the OpenGrey to get grey literatures. We will contact the author if we can't find the full-text online.

Main outcome(s): Study characteristics: Different research aspects using AI in gastrointestinal microbiome, different types of AI algorithm used in gastrointestinal microbiome studies, different data types that AI will process, specific segments that AI algorithm involves in and the overall performance of AI in these studies. And we will also respectively discuss the specific applications and performance of some AI algorithms in different crucial part of such researches.

Data management: Endnote software will be used to manage data and select the literatures.

Quality assessment / Risk of bias analysis: To assess the risk of bias within included studies, the methodological quality of potential studies will be assessed by using the Newcastle-Ottawa scale (NOS), Using the NOS, studies will be awarded a maximum of nine points on items related to the selection of the study groups, the comparability of the groups, and the ascertainment of outcome of interest. Using this modified score, papers will be eligible for a maximum of six points. This will be undertaken by two separate reviewers. Where there is disagreement, a third reviewer will be used as an arbitrator.

Strategy of data synthesis: After removing the duplications across different electronic databases, our team will then conduct the screening in two stages based on the inclusion and exclusion criteria. In the first stage, two reviewers will independently screen the titles and abstracts yielded by the search against the inclusion criteria. We will obtain full reports for all titles that appear to meet the inclusion criteria or where there is any uncertainty. In the second stage, Review author pairs will then screen the full text reports and decide whether these meet the inclusion criteria. We will seek additional information from study authors when necessary to resolve questions about eligibility. We will resolve disagreement through discussion. We will record the reasons for excluding trials. Neither of the reviewers will be blind to the journal titles or to the study authors or institutions If studies are sufficiently homogeneous in terms of design and comparator, we will conduct meta-analyses using a random-effects model by the RevMan software.

Subgroup analysis: Subgroup analyses will be used to explore possible sources of heterogeneity, based on the following: research domains of gastrointestinal microbiome; types of AI algorithm specific applications and functions of AI.

Sensitivity analysis: Sensitivity analysis will be performed in order to explore the source of heterogeneity as follows: Quality components, including full-text publications versus abstracts, preliminary results versus mature results, published versus unpublished data; Risk of bias (by omitting studies that are judged to be at high risk of bias).

Language: Literatures in English or Chinese will be included, but those in other languages will be excluded.

Country(ies) involved: China.

Keywords: gastrointestinal microbiome; artificial intelligence; application; performance; prospect.

Contributions of each author:

Author 1 - Zhou Zirui initialized the idea, contributed to the development of the selection criteria, the risk of bias assessment strategy and data extraction criteria, developed the search strategies and drafted the manuscript.
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Author 2 - Zhou Zilin participated in developing the selection criteria, the risk of bias assessment strategy and data extraction criteria and provided feedback on the final manuscript.
Author 3 - Li Haolin helped develop the selection criteria, the risk of bias assessment strategy and data extraction criteria and provided the statistical expertise.
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