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Preferred Reporting Items for Microbiotherapy (PRIM) Guidelines Across Medical Disciplines: An International Delphi Consensus

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ABSTRACT

Microbiotherapy has opened new avenues for managing dysbiosis-related diseases. However, many studies did not cover all the necessary reporting items for microbiotherapy making the interpretation of results, safety assessment, technology extension, and even the transparency of legitimacy difficult. This project consisted of 2 phases. First, we proposed an initial preferred reporting items for microbiotherapy (PRIM) checklist and applied it to oncology studies from 2011 to 2023 according to Meta-Analyses guideline. Only 39.3% ($n = 64$) of these studies ($n = 163$) met all PRIM checklist items. The culture-based microbiotherapy (CMT) studies had higher score than non-culture-based (NMT) ones ($p = 0.018$). In the second phase, the expert panel consisting of 22 specialists from eight countries across Asia, Australia, Europe, and North America refined and finalized the PRIM guidelines (named as PRIM 2024) through Delphi consensus. The PRIM 2024 guidelines conclude 10 statements and 18 points on diagnosis, delivery route, source, classification, preparation, dosage, state, concomitant treatment, efficacy, and safety. The panel defined

less than 80% of all PRIM points (14 points) as low-quality reports. These guidelines are recommended for reporting on microbiotherapy in clinical studies and reports on compassionate use, including but not limited to fecal microbiota transplantation, phage therapy, probiotics, and synbiotics. These consistent and transparent reporting items can help researchers and practitioners better evaluate, compare, implement research findings in microbiotherapy.

1 | Introduction

The human microbiome is a complex community composed of bacteria, fungi, viruses, bacteriophages, archaea, and protists. It has profound effects on human health and disease, including regulation of immune function, metabolism, and nutrition [1]. Different microbiomes reside in various parts of the body e.g., gut, lung, skin, genitourinary and other regions. Therefore, microbiotherapy targeting microbiota, which mainly includes fecal microbiota transplantation (FMT), probiotics, synbiotics, phage, etc., has opened new windows for the management of dysbiosis-related diseases. FMT has been reported to be studied in 85 diseases from 2011 to 2022 globally [2]. Guidelines have recommended FMT for the treatment and prevention of *Clostridioides difficile* infection (CDI) since 2013 [3, 4]. Additionally, VOWST (SER-109), an oral microbiome therapeutic composed of live purified Firmicutes bacterial spores, reduces CDI recurrence without safety signals [5, 6]. Recently, phage therapy has been demonstrated to attenuate *Mycobacterium abscessus* lung infection [7].

The treatments targeting gut microbiota have also extended to cancer management [8, 9]. Accumulating evidence has linked the critical role of gut microbiota and relevant metabolites in modulating the efficacy and toxicity of radiotherapy, chemotherapy, and immunotherapy outside the gut [10–12], making microbiotherapy an emerging avenue in the management of cancers. There is intense interest in adding FMT as an adjunct therapy, either to enhance response or to address adverse effects as a result of anti-cancer therapeutics. A recent review showed that cancer is the third most common indication for FMT trials [13]. In a recent multicenter phase I trial, FMT in combination with the programmed death protein 1 (PD-1) inhibitors achieved a clinical response rate of 65% in 20 treatment naïve patients with advanced melanoma [14]. Patients with immune checkpoint inhibitor (ICI)-induced colitis achieved a high rate of remission after FMT [9, 15]. Furthermore, probiotics reduced the occurrence of chemotherapy-related cognitive impairment in patients with cancer via modulating gut microbiota and plasma metabolites [16, 17]. Synbiotics, a combination of probiotics and prebiotics, ameliorated radiation-induced acute proctitis symptoms and improved quality of life in patients with prostate cancer [18]. Putting together, microbiotherapy in oncology has tremendous potential in improving cancer care.

Despite increasing number of clinical studies being published, many lack sufficient information and transparency on important aspects concerning microtherapy, partially due to the absence of a unified reporting guideline. For example, according to the analysis from a systematic review [19], 89% of the studies did not give details on the methods used to prepare feces for transplantation, and 89% did not give eligibility criteria for donors, nor did they describe characteristics of the donors used. To bridge this gap, our study consists of 2 phases. In the first phase, we proposed an initial preferred reporting items for microbiotherapy (PRIM) framework, and applied it to oncological studies. In the second phase, we invited clinical experts in microbiotherapy from various institutions worldwide to collaborate and refine this framework through Delphi consensus voting. Our goal is to introduce the PRIM guidelines to the field of microbiota medicine across multiple disciplines to improve the quality of reporting in research, making the results interpretable and reproducible.

2 | Methods

2.1 | Systematic Review for the Initial PRIM Framework

Based on different aspects of microbiotherapy that may be of interest to researchers, we proposed the initial PRIM checklist with 10 items, including diagnosis, delivery route, source, classification, preparation, dosage, state, concomitant treatment, efficacy, and safety. The detailed description and explanation of all items were shown in Table 1. Each item in the PRIM checklist was assigned 1 score. Total scores ranged from 0 to 10. Higher scores indicated the higher quality and integrity of the studies. We then performed a systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline [20], including oncology studies as an example.

2.2 | Study Selection and Data Extraction

The search was conducted using PubMed, Embase, and Cochrane databases from January 1, 2011 to December 31, 2023. The detailed search strategy and protocol were shown in the Supplementary file 1. After removing duplicates, two reviewers (X. Wu and Z. Zhang) screened the title and abstract independently. The inclusion criteria were as follows: (1) studies based on humans; (2) patients diagnosed with cancer or cancer treatment-related side effects; (3) patients undergoing microbiotherapy including probiotics, synbiotics, phage, FMT, and spore, etc. (4) the language was restricted to English. Exclusion criteria included: (1) non-original reports including reviews, systematic reviews, meta-analyses, comments, conference papers, and consensus; (2) the full text could not be obtained; (3) duplicate reports. If both reviewers agreed that an abstract met the inclusion criteria, the full-text review was performed. In the case of ambiguities regarding study inclusion, a discussion took place between the researchers until a consensus could be reached. The full-text review and data extraction was conducted independently and in duplicate by the same two reviewers. The following data were extracted from the included studies: study characteristics (research type, year of publication, country, sample size) and clinical parameters (the PRIM checklist involved).

2.3 | Definition of Culture-Based and Non-Culture-Based Microbiotherapy

The studies were divided into two types based on whether the functional ingredients in microbiotherapy involved microbial cell culture process: studies of culture-based microbiotherapy (CMT) (i.e., probiotics, synbiotics, and phages) and studies of non-culture-based microbiotherapy (NMT) (i.e., microbiota transplantation and spores therapy).

2.4 | International Panel and Delphi Process

The panel group was formed by the invited experts in the field of microbiotherapy in the world. The Delphi process was conducted to refine the PRIM framework in reference to the analysis of the initial PRIM, including the addition or omission of some items, and the revision of item descriptions. The experts were required to rate their level of agreement with the relevance and sufficiency of the PRIM framework for reporting on

TABLE 1 | The initial preferred reporting items for microbiotherapy (PRIM).

Items	Description	Score
Diagnosis	Disease, disorder, disease condition.	1
Delivery route	Capsule, gastroscopy, mid-gut tube, colonic transendoscopic enteral tube, colonoscopy, enema, etc.	1
Source	Autologous, allogenic, human-origin, food, environment, etc.	1
Preparation	Fecal microbiota transplantation (manual preparation of fecal microbiota, washed microbiota, spores), bacteria, fungus, phages, virome, engineered bacteria, etc.	1
Classification	Medication, investigational new drug, biologic, ethical-approved medical therapy, food.	1
Dosage	Dose (bacteria count, colony forming unit, plaque forming unit, unit, volume, weight, etc.) and frequency (time, course, timeline of courses).	1
State	Fresh, frozen, lyophilized, live, dead, etc.	1
Concomitant treatment	Details on medication, nutrition, prebiotics, postbiotics, fiber, etc.	1
Efficacy	Cure, remission, improvement, survival, non-response, etc.	1
Safety	Severity and relevance of adverse events, short-term, long-term, etc.	1

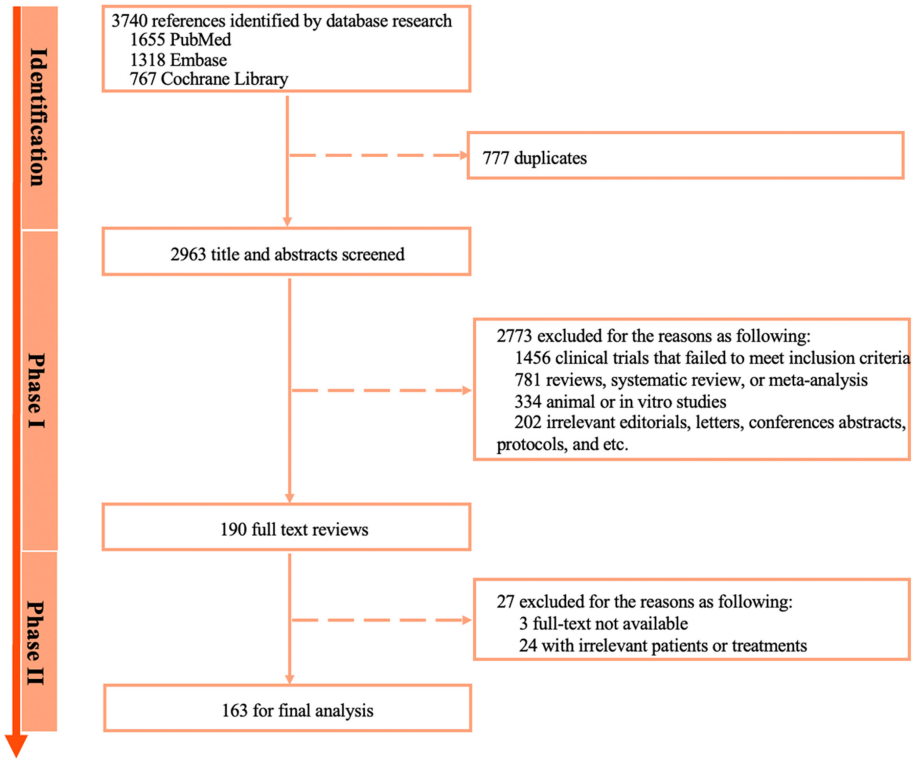

FIGURE 1 | Flow diagram of the studies selection process.

microbiotherapy and their definitions. Responses were given on a five-point scale from 0 to 4 (0 = Strongly disagree, 1 = Disagree, 2 = Neutral, 3 = Agree, 4 = Strongly agree). For each item, the pre-established threshold was reached when the overall agreement (strongly agree or agree) rate was ≥80%. All items below 80% of the agreement were revised and rated again in a further round of voting. After rating, the experts provided comments regarding the items or suggestions for improvement. Finally, the refined consensus was reached for all items after anonymous voting and editing.

2.5 | Data Analysis

All analyses were carried out using IBM SPSS Statistics 23.0 and GraphPad 8.0. The characteristics of included studies were evaluated using proportions for categorical variables. Comparisons between groups for skewed continuous variables were performed using the Mann–Whitney U test or Kruskal-Wallis test with Dunn's multiple comparisons test as a post-test, and Chi-Square test or Fisher's exact test for categorical variables. The difference was considered statistically significant when $p < 0.05$.

3 | Results

3.1 | Literature Analysis

The flow chart of the studies selection process was shown in Figure 1. The search strategy identified 3740 records through the three databases. A total of 163 studies were included in the

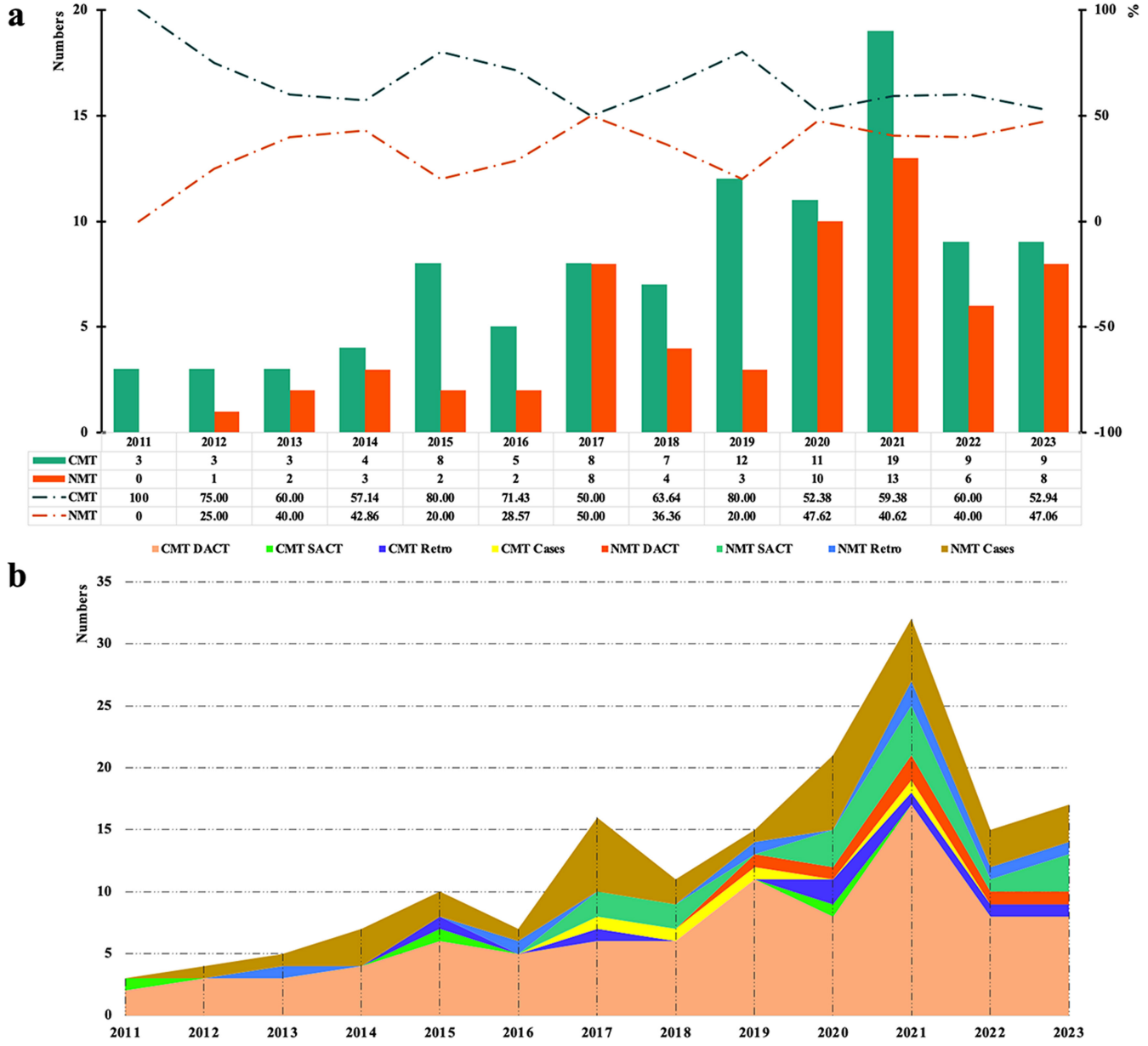

FIGURE 2 | Research trends of microbiotherapy in oncology studies from 2011 to 2023. Abbreviations: DACT, double-arm clinical trial; SACT, single-arm clinical trial; Retro, retrospective study; Cases, case report/series. CMT, studies of culture-based microbiotherapy; NMT, studies of non-culture-based microbiotherapy.

systematic review for final analysis after careful screening, with 101 CMT and 62 NMT. Solid tumors were the most common tumor type (114 studies) treated by microbiotherapy, followed by hematological tumors (40 studies).

The annual research trends of microbiotherapy in oncology were shown in Figure 2. In total, 127 related articles were published from 2017 to 2023, accounting for 78.91% of the total publications over the past 13 years. The proportion of NMT increased from 0.0% in 2011 to 47.06% in 2023, which was comparable to CMT. The proportion of case report/series gradually decreased, while the proportion of more rigorous design research increased, especially in NMT studies (Figure 2b).

As shown in Figure 3, only 39.3% ($n=64$) of the included studies received a score of 10, followed by 27.6% ($n=45$) with a score of 9 and 15.3% ($n=25$) with a score of 8. The minimum number of items reported in all studies was 4. Subgroup analysis showed that the double-arm clinical trial had higher PRIM scores than the case report/series [9 (8–10) vs. 8 (7–9), adjust $p=0.0026$; Figure 3a]. The PRIM scores of CMT were significantly higher than those of NMT ($p=0.018$; Figure 3b).

As shown in Table 2, of the 10 items, safety, state, and dosage were the top three missing items in all the studies, as well as in CMT studies. State, classification and safety were the top three missing items in NMT studies. The missing rates of classification and state in NMT were significantly higher than those in CMT studies (classification: 35.5% vs. 3.0%, Chi-square test, $p<0.001$; state: 40.3% vs. 13.9%, Chi-square test, $p<0.001$; Table 2). In terms of safety, the missing rate of NMT tended to be lower than that of CMT studies (29.0% vs. 43.6%, Chi-square test, $p=0.064$).

As shown in Figure 4, the application of CMT differed from that of NMT. Postoperative complications were the most common indications of CMT ($n=29$), followed by side effects of chemotherapy ($n=20$), cancer comorbidities ($n=13$), and radiotherapy and/or chemotherapy-induced oral diseases ($n=10$). While NMT was mainly used in CDI ($n=19$), other common

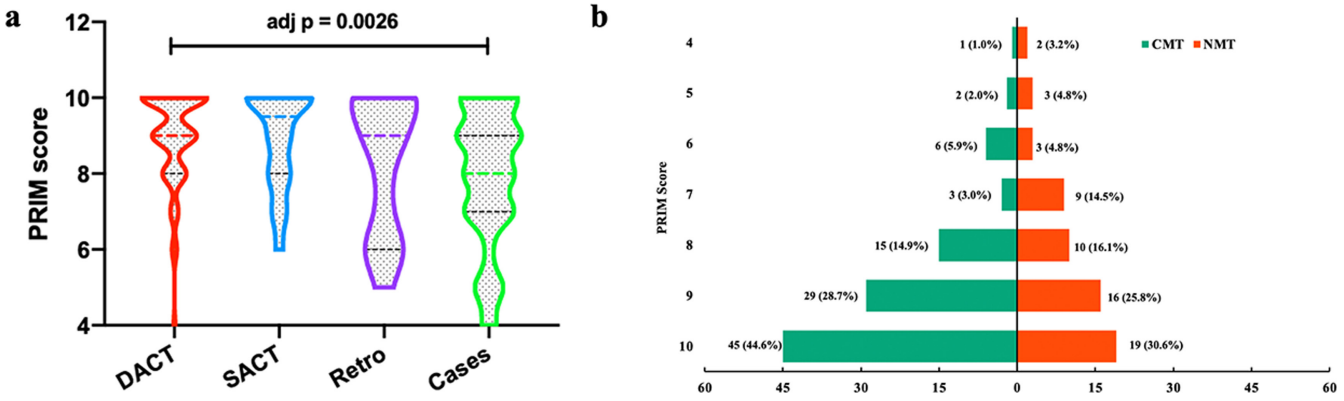

FIGURE 3 | The PRIM scores of the included studies. (a) The PRIM scores of different research types were compared using the Kruskal-Wallis test with Dunn's multiple comparisons test as a post-test. (b) The PRIM scores between CMT and NMT were compared using the Mann–Whitney U test. $p<0.05$ was considered statistically significant. Abbreviations: DACT, double-arm clinical trial; SACT, single-arm clinical trial; Retro, retrospective study; Cases, case report/series; CMT, studies of culture-based microbiotherapy; NMT, studies of non-culture-based microbiotherapy.

TABLE 2 | The missing items of the included studies based on the initial PRIM.

Items	Total (N = 163)	CMT (*N* = 101)	NMT (*N* = 62)	*p*
Diagnosis	0 (0.0)	0 (0.0)	0 (0.0)	—
Delivery route	11 (6.7)	5 (8.1)	6 (5.9)	0.749
Source	17 (10.4)	13 (12.9)	4 (6.5)	0.193
Preparation	0 (0.0)	0 (0.0)	0 (0.0)	—
Classification	25 (15.3)	3 (3.0)	22 (35.5)	**< 0.001**
Dosage	29 (17.8)	15 (14.9)	14 (22.6)	0.210
State	40 (24.5)	14 (13.9)	25 (40.3)	**< 0.001**
Concomitant treatment	27 (16.6)	13 (12.9)	14 (22.6)	0.105
Efficacy	0 (0.0)	0 (0.0)	0 (0.0)	—
Safety	62 (38.0)	44 (43.6)	18 (29.0)	0.064

Abbreviations: CMT, studies of culture-based microbiotherapy; NMT, studies of non-culture-based microbiotherapy.

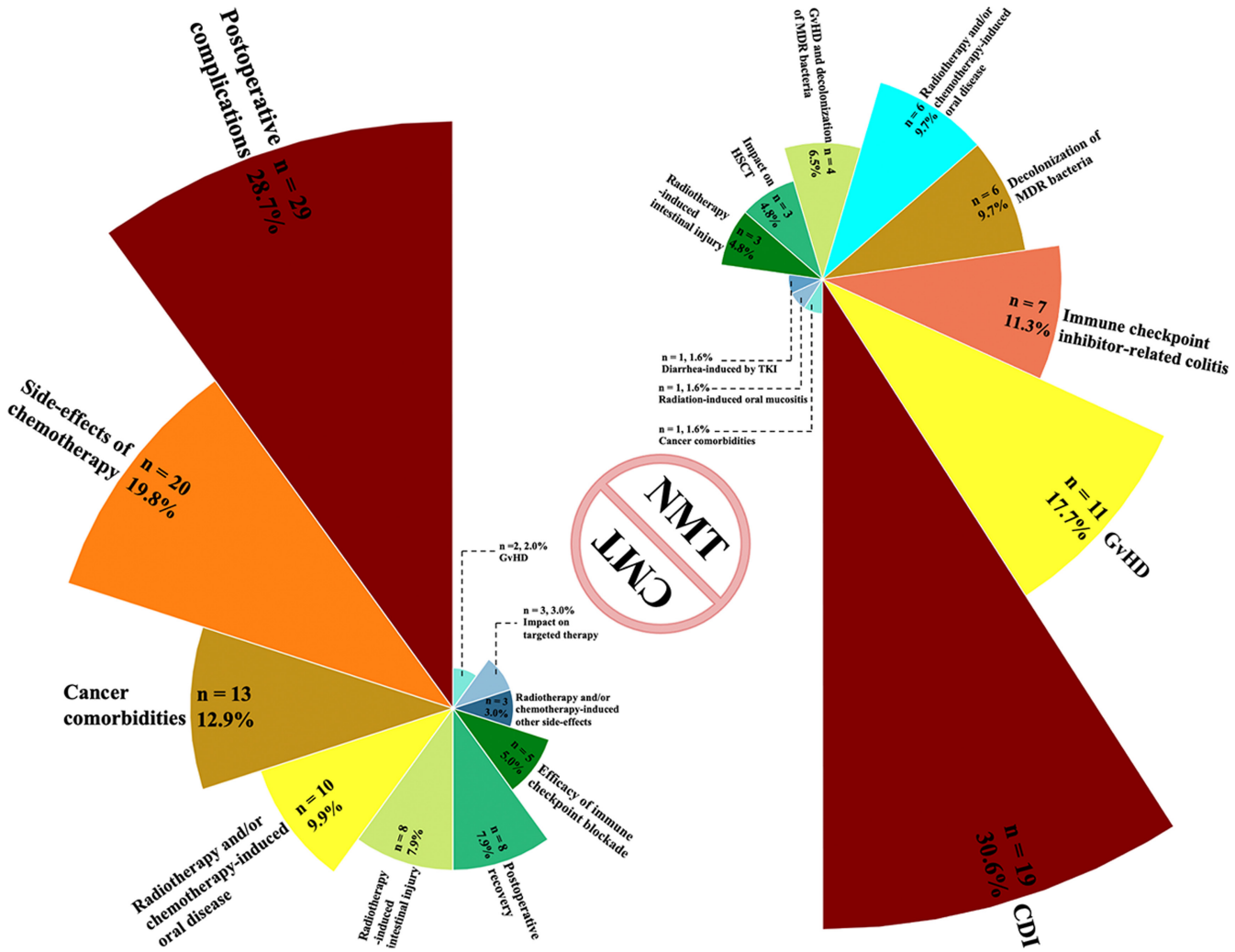

FIGURE 4 | The application of CMT and NMT in oncology studies. Abbreviations: CDI, *Clostridioides difficile* infection; GvHD, graft-versus-host disease; HSCT, hematopoietic stem cell transplantation; MDR bacteria, multidrug-resistant bacteria.

indications included graft-versus-host disease ($n = 11$), immune checkpoint inhibitor-related colitis ($n = 7$), and decolonization of multi-drug resistant bacteria ($n = 6$).

3.2 | The Delphi Consensus Recommendation on the PRIM 2024 Guidelines

The panel group was formed by 22 experts in the field of microbiotherapy from 20 hospitals in 8 countries (America, Australia, Canada, China, India, Italy, Japan, Singapore) from North America, Australia, Asia, and Europe. In the first round of Delphi process, the anonymous voting achieved threshold of 80% support for all of the 10 statements and the refined PRIM checklist with 18 points; i.e. these items need to be clearly presented in a research report (Table 3). Less than 80% of all items of the PRIM list (i.e. 14 points in the current version of PRIM) is considered a low-quality research report. Then, the feedback and opinions from experts are compiled and summarized to create a draft report, which is sent to all experts once again to independently evaluate and provide further comments before finalizing the PRIM checklist (PRIM 2024 guidelines).

4 | Statements, Discussion and Conclusions

Statement 1. *The detailed documentation of indication with microbiotherapy includes the disease and condition using standard diagnostic criteria.*

Comment. The reproducibility of research findings in clinical practice depends on targeting the same patient population. Randomized controlled trials (RCTs) provide the high quality of evidence for clinical practice, however, it has been noted that participants in RCTs often do not adequately represent the patient population of interest, especially in a severe or advanced disease or condition [21]. Our systematic review found NMT was more likely utilized in those instances, and in the forms of single-arm studies, retrospective studies, and case reports. And they provided the important real-world experience to guide and inform the microbiotherapy in vulnerable and underrepresented patient groups.

Statement 2. *The delivery route of microbiotherapy includes capsule, gastroscopy, mid-gut tube, colonic transendoscopic enteral tube (TET), colonoscopy, enema, skin, atomization, nasal*

TABLE 3 | The checklist of items for PRIM 2024 guidelines.

Items	Description	Score
Indication	Diagnosis according to international disease classification or guideline.	1
	Disease condition: severity, comorbidity, etc.	1
Delivery route	Oral (capsule, tablet, powder, suspension), gastric (gastroscopy, nasogastric tube), mid-gut (duodenoscopy, mid-gut tube), lower gut (colonic transendoscopic enteral tube, colonoscopy, enema), skin, atomization, nasal lavage, intravenous injection, intraperitoneal injection, etc.	1
Source	Autologous, allogenic, human-origin, food, environment, etc.	1
Preparation for products	Screening methods: donor screening (age, gender, history, tests, etc.), strain screening (toxicity, stability etc.).	1
	Producing methods: fecal microbiota transplantation (manual preparation of fecal microbiota, washed microbiota, spores), bacteria, fungus, phages, virome, engineered bacteria, etc.	1
Classification	Legal and ethical statement.	1
	Classification for the products: medication, investigational new drug, medical therapy, food.	1
Dosage	Dose: bacteria count, colony forming unit, plaque forming unit, unit, volume, weight, etc.	1
	Frequency: time, course, timeline of courses.	1
Formulation	State: storage (fresh, frozen, refrigerated, lyophilized), pasteurized, live, dead, etc.	1
	Subsidiary material: vehicle, protectant, additive, etc.	1
Concomitant treatment	Patient preparation: antibiotics, acid inhibitors, prokinetic agents, colon cleaning, etc.	1
	Treatments affecting the outcome: details on medications, diet, prebiotics, postbiotics, fiber, etc.	1
Efficacy	Definition: cure, remission, improvement, survival, non-response, etc.	1
	Rate or data available for the rate calculation.	1
Safety	Severity and relevance of adverse events, management for the adverse events, short-term, long-term, etc.	1
	Rate or data available for the rate calculation.	1

lavage, intravenous injection, intraperitoneal injection and others should be reported.

Comment. The distribution and concentration of microbes in human organs varies widely, and the microbial cell mass culminates in the lower gut (10^{14}) since transit in the colon is over a dozen times longer than that in the small intestine (10^{7}–10^{11}) [22]. Hence, the crosstalk of microbiota-host would vary at different sections of the intestine. The incidence of FMT delivery-related adverse events varied: colonic TET (6%), colonoscopy (15%), enema (26%), capsule (29%), mid-gut tube (29%) and gastroscopy (32%) in a systematic review including reports from 2000 to 2020 [23]. In adults or children with serious intestinal mucosal injury (serious intestinal erosive/ulcerative lesions, immunocompromised, or critically ill), the delivery route of microbiotherapy via small intestine should be weighted against potential complications such as aspiration, bacterial translocation and sepsis [23, 24]. Therefore, the delivery route is a crucial element to report to explore its impact on efficacy, safety, and microbe-host interactions.

Statement 3. *The sources of matter for microbiotherapy include various possible options, such as autologous, allogenic, human-origin, food, environment, cultured bacteria, etc.*

Comment. The isolation of probiotic strains can come from natural foods, feces, breast milk, the vagina, etc. Bacteriophages may originate from sewage or clinical samples. All this information on sources should be clearly included in the methods of study, and how it complies with the legal regulations of the respective country. If ethical review is required, the reports should state that the approval has been obtained from the human ethics committee. The use of gene-edited microbes in clinical research is subject to different review requirements in different countries. When FMT is considered as a trial related to investigational new drug, the source of FMT should be transparent. When FMT is considered a medical technique rather than a drug produced by pharmaceutical entities, only clinical settings that have the legal qualifications (outpatient clinic setting and hospital setting) can prepare and provide FMT [2, 13, 25].

Statement 4. *The description of the preparation for products includes the screening and producing methods for microbiotherapy need to be described*.

Comment. The inclusion and exclusion criteria (age, sex, medical history, high risk behaviors etc. for FMT, vaginal microbiota transplantation [26–28], nasal microbiota

transplantation [29], and other microbiota transplantation) as well as tests used in donor screening for NMT, and strain screening (toxicity, stability, efficacy etc.) for CMT need to be described. FMT can be prepared by manual methods, automatic filtration, and washing process, and spores preparation. With the washing procedure, metabolites with pro-inflammatory effects in the fecal microbiota supernatant, such as leukotriene B4, corticosterone, and prostaglandin G2 were removed. This might be the reason for the fever after FMT being significantly decreased from 19.35% to 5.15% in automatic preparation of fecal microbiota [30].The manufacturing methods of products may affect the clinical findings, however, the specific ways in which process impacts the therapy is still under investigation. Currently, the understanding of the substances contained in feces for FMT is insufficient. Important microorganisms such as fungi and bacteriophages [31] have hardly been considered in the transplantation process. Therefore, it is necessary to meticulously record the preparation and handling process of FMT samples to infer the potential impact on the substances that may be present.

Statement 5. *The classification for microbiotherapy includes the regulation statement (legal and ethical statement) and the specific classification statement (licensed medications, investigational new drugs, ethically approved medical therapies, and food supplements).*

Comment. Transparent regulations and ethical statements can reduce illegal research and medical services. The regulations on microbiotherapy vary from country or area worldwide. The mainstream of the category FMT is that it is classified as both a pharmaceutical and a medical technique service, coexisting under a dual-track system [2]. Despite lots of challenges in standardizing FMT policies, reporting this items would be helpful in transparency of legal management, protecting patients and ultimately realization of non-conflict between region and countries.

Statement 6. *It is essential to describe the dose (such as bacterial count, colony forming unit, plaque forming unit, unit, volume, weight, etc.) and frequency (such as time, course of treatment, timeline of courses, etc.) in detail.*

Comment. The dose and frequency of administration may influence the efficacy of microbiotherapy. Lower dose and less frequent dosing may improve the feasibility in practice. However, the minimal dose or ideal frequency of administration to treat a particular condition remain to be determined. Higher doses may improve response rate; for example, the clinical response rate in irritable bowel syndrome was higher using 60 g FMT than that in 30 g FMT over 1 month (85.5% vs. 75.9%, $p < 0.001$) after FMT [32]. FMT is effective for CDI, and the course of FMT needs to be determined according to the severity of CDI [33, 34]. The colony forming unit or bacterial count should be reported where applicable.

Statement 7. *The description of formulation includes the state of microbial materials (fresh, frozen, lyophilized, pasteurized, live, dead, etc.), the subsidiary material (vehicle, protectant, additive, etc.) and storage methods (refrigeration, freezing, lyophilization, and anaerobic storage) should be included.*

Comment. The state might be correlated with the clinical outcomes of microbiotherapy. In one study, the cure rate of CDI was higher in fresh FMT compared with lyophilized products (100% vs. 78%, $p = 0.022$) [35]. Pasteurized *Akkermansia muciniphila* improved insulin sensitivity, and reduced insulinemia compared to placebo, but live *A. muciniphila* did not in a preliminary study [36]. Subsidiary materials may affect the safety of microbiotherapy. For example, certain preservatives or stabilizers added to microbial products might potentially cause allergic reactions in some individuals, thereby affecting the safety of the therapy.

Statement 8. *Concomitant treatment with microbiotherapy includes the methods for patient preparation (colon cleaning, fasting, antibiotics, acid inhibitors, prokinetic agents, etc.) and the use of combination treatments aiming at treating diseases or preventing adverse events (medication, nutritional elements, prebiotics, postbiotics, fiber, diet, etc.) should be reported.*

Comment. The bowel cleansing introduces an instant and substantial change of the intestinal microbiota from the findings of microbiome in the collected defecated stool [37] and ileocecal stool in situ [38]. The impact of bowel cleaning on microbiotherapy is not well studied, but it is an important aspect to report to ensure reproducibility of studies. Other important concomitant therapies to report include steroids, dietary intervention, and other treatments that may affect efficacy or safety. 57.1% of patients (8/14) with steroid-dependent ulcerative colitis (UC) achieved clinical improvement and were able to discontinue steroids following step-up FMT (regular steroids based on FMT) [39]. FMT with an anti-inflammatory diet effectively induced deep remission in mild–moderate UC which was sustained with an anti-inflammatory diet over 1 year [40]. A synbiotic preparation of three lyophilized *Bifidobacteria* strains and three prebiotic compounds (SIM01) was effective in alleviating multiple symptoms of post-acute COVID-19 syndrome [41]. An RCT study demonstrated that a single-dose oral FMT combined with daily low-fermentable fiber supplementation improved insulin sensitivity in patients with severe obesity and metabolic syndrome [42]. The impact of concomitant medications and dietary intake on clinical outcomes remains unknown if the information on combined treatments is not fully described.

Statement 9. *Efficacy is the core outcome measured in microbiotherapy studies, encompassing cure, remission, improvement, survival, non-response, etc.*

Comment. Each type of efficacy should be clearly defined, and the rate of efficacy or data available for the rate calculation should be shown in the study. For rigorously designed clinical studies, the outcome measurements should be clinically relevant and pre-defined. It should be noted that effective results are rarely unpublished, while ineffective results are seldom reported as scientific articles. Research publication bias occurs when trials showing negative or no effect are not published; outcome reporting bias occurs when authors fail to report unfavorable data [43].

Statement 10. *Safety includes the rate and the description (severity, relevance, management, prognosis, short-term, long-term, etc.) of the adverse events.*

Comment. The safety item in probiotics research is largely missing. This issue has been pointed out that the theoretical risks of probiotics have not been clearly described [44]. FMT as the typical microbiotherapy was reported with high safety and few self-limited adverse events in short-term or long-term clinical practice [45], thus researchers may ignore the safety in their reports. It can be difficult to understand how microbial manipulation impacts disease risk given all of the potential confounders described above. Therefore, the short- and long-term safety of associated therapies is important to track and monitor.

In conclusion, the proposed PRIM 2024 framework provide a clear and practical guide for reporting on microbiotherapy in the field of microbiota medicine across medical disciplines. The originality of PRIM deserves arousable attention of microtherapy applicable to patients in need. This will further promote transparency in this field of research to ultimately benefit patients, whether the treatment involves microbiotherapy via gut, vaginal microbiota transplantation, nasal microbiota transplantation, or phages therapy.

Conflicts of Interest

Faming Zhang conceived the concept of GenFMTer and transendoscopic enteral tubing and the devices (FMT Medical, China) related to them. Siew C Ng received patent royalties through her affiliated institutions and is named inventors of patent applications held by The Chinese University of Hong Kong and Microbiota I-Center that cover the therapeutic and diagnostic use of microbiome. Siew C Ng is a founder member and shareholder of GenieBiome Ltd. Gianluca Ianiro has received personal fees for acting as speaker for Biocodex, Danone, Sofar, Malesci, Metagenics, Illumina, and Tillotts Pharma, and for acting as consultant/advisor for Ferring Therapeutics, Giuliani, Metagenics and Tillotts Pharma. Dr. Sunny H Wong and Dr. Jingnan Li are Editorial Board member of JGH and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication. The other authors have no potential competing interest to disclose.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.