Postprint of a Quality Assessment and Recommendation Comparison Study of Clinical Guidelines and Consensus Statements for Non-alcoholic Fatty Liver Disease

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Abstract

Objective To evaluate the methodological quality and reporting quality of guideline documents for non-alcoholic fatty liver disease (NAFLD) using the AGREE and RIGHT tools, summarize and compare the recommendations, and provide a reference basis for future development and reporting of NAFLD guidelines.

Methods Computerized searches were conducted in Chinese and English databases including PubMed and CNKI, with the search period from September 1, 2012 to September 1, 2022. Two trained reviewers independently used AGREE and RIGHT to evaluate the methodological quality and reporting quality of the included guideline documents, and collated and compared the recommendations from guideline documents of higher quality.

Results A total of 19 documents were included, comprising 12 guidelines and 7 consensus statements; 6 were in Chinese and 13 in English; 10 were developed using evidence-based methods. The average scores for AGREE domains were: scope and purpose (42.84%), stakeholder involvement (31.43%), rigor of development (31.25%), clarity of presentation (60.67%), applicability (32.68%), and editorial independence (37.5%). The average scores for RIGHT domains were: basic information (59.65%), background (66.12%), evidence (42.11%), recommendations (39.85%), review and quality assurance (17.11%), funding and declaration and management of conflicts of interest (18.42%), and other aspects (47.37%). Guideline documents developed using evidence-based methods had higher average scores on AGREE and higher reporting quality on RIGHT than non-evidence-based guideline documents; foreign guideline documents had

higher average scores on AGREE and higher reporting quality on RIGHT than domestic guideline documents. The main recommendations involved screening and diagnosis, assessment, management (non-pharmacological and pharmacological treatment), and surgical treatment.

Conclusion The methodological quality and reporting quality of currently published NAFLD guideline documents still need improvement, with domestic guideline documents still lagging behind international ones; the development of traditional Chinese medicine guideline documents should follow evidence-based methods. The AGREE and RIGHT international standards should be further referenced in the guideline development and reporting process. Clinically, awareness of screening for high-risk NAFLD populations should be established, a comprehensive early non-invasive diagnosis and assessment system should be established, and multidimensional treatment plans targeting lifestyle, liver function, and metabolic disorders should be provided to NAFLD patients.

Full Text

Abstract

Objective: To evaluate the methodological quality and reporting quality of guidance documents for non-alcoholic fatty liver disease (NAFLD) using the AGREE II and RIGHT tools, summarize and compare the recommendations, and provide a reference for the development and reporting of future NAFLD guidelines.

Methods: PubMed, CNKI, and other Chinese and English databases were systematically searched from September 1, 2012, to September 1, 2022. Two trained evaluators independently assessed the methodological and reporting quality of included guidance documents using AGREE II and RIGHT, respectively, and collated and compared recommendations from higher-quality guidelines.

Results: A total of 19 publications were included, comprising 12 guidelines and 7 consensus statements; 6 were in Chinese and 13 in English; 10 were developed using an evidence-based approach. The mean scores for AGREE II domains were: scope and purpose (42.84%), stakeholder involvement (31.43%), rigor of development (31.25%), clarity of presentation (60.67%), applicability (32.68%), and editorial independence (37.5%). The average reporting rates for RIGHT domains were: basic information (59.65%), background (66.12%), evidence (42.11%), recommendations (39.85%), review and quality assurance (17.11%), funding and conflict of interest declaration and management (18.42%), and other aspects (47.37%). Evidence-based guidance documents demonstrated higher mean AGREE II scores and RIGHT reporting quality than non-evidence-based documents; foreign guidance documents also outperformed domestic ones in both measures. Major recommendations addressed screening and diagnosis, assessment, management (non-pharmacological and pharmacological treat-

ment), and surgical interventions.

Conclusion: The methodological and reporting quality of published NAFLD guidance documents requires improvement, with domestic guidelines lagging behind international standards. The development of traditional Chinese medicine (TCM) guidance documents should adhere to evidence-based methods. Guideline development and reporting should further reference international standards such as AGREE II and RIGHT. Clinicians should establish screening awareness for high-risk NAFLD populations, implement comprehensive early non-invasive diagnostic and evaluation systems, and provide multidimensional treatment plans addressing lifestyle, liver function, and metabolic disorders.

Keywords: Non-alcoholic fatty liver disease, AGREE , RIGHT, Guideline, Consensus, Recommendation

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a clinicopathological syndrome characterized by hepatic steatosis exceeding 5% of hepatocytes, excluding secondary causes such as alcohol and drugs [1]. Current understanding recognizes a close association between NAFLD development and glucolipid metabolic dysfunction. The 2020 declaration proposing metabolic-associated fatty liver disease (MAFLD) [2] explicitly elaborated type 2 diabetes mellitus (T2DM) and metabolic dysfunction as essential diagnostic components, recommending MAFLD as a positive diagnostic nomenclature to replace NAFLD. (As few guidance documents use the MAFLD nomenclature and the disease connotations of NAFLD and MAFLD are largely similar, this article temporarily uses the NAFLD nomenclature.) The global prevalence is approximately 25% [3], while in China it ranges from 5% to 24% [4]. NAFLD has now replaced viral hepatitis as the most common chronic liver disease worldwide [5], and its prevalence continues to rise in the Asia-Pacific region due to changing dietary habits and lifestyles [6]. Numerous clinical practice guidelines and consensus statements on NAFLD have been published across countries and associations, yet their development and reporting quality vary considerably. The abundance of recommendations may confuse clinicians and potentially hinder clinical practice.

AGREE is currently the most recognized and widely used guideline methodological quality tool internationally, comprising 6 domains with 23 items [7]. RIGHT represents the most universal guideline reporting standard [8]. This study employs AGREE and RIGHT tools to evaluate the methodological and reporting quality of existing NAFLD clinical practice guidelines and consensus statements, providing references for quality improvement and reporting standardization, and summarizes and compares recommendations from high-quality guidelines to deliver valuable information for NAFLD prevention, diagnosis, treatment, and management.

Methods

1.1 Search Strategy

We systematically searched PubMed, CNKI, CBM, Wanfang, and VIP databases, supplemented by searches of WHO, GIN, NICE, NGC, SIGN, and Medlive databases from January 1, 2012, to January 1, 2022. Chinese search terms included: non-alcoholic fatty liver disease, non-alcoholic fatty liver, simple fatty liver, metabolic-associated fatty liver disease, guideline, expert consensus, expert opinion, and standard. English search terms included: metabolic associated fatty liver disease, nonalcoholic fatty liver disease, MAFLD, NAFLD, guideline, consensus, expert consensus, clinical practice guideline, practice guideline, recommendation, and standard. The PubMed search strategy was: #1 "metabolic associated fatty liver disease" [Title/Abstract] OR "nonalcoholic fatty liver disease" [Title/Abstract] OR "MAFLD" [Title/Abstract] OR "NAFLD" [Title/Abstract] (9,425 articles); #2 "guideline" [Title/Abstract] OR "consensus" [Title/Abstract] OR "expert consensus" [Title/Abstract] OR "clinical practice guideline" [Title/Abstract] OR "practice guideline" [Title/Abstract] OR "clinical practice" [Title/Abstract] OR "advice" [Title/Abstract] OR "recommendation" [Title/Abstract] OR "standard" [Title/Abstract] (283,785 articles); #1 AND #2 yielded 851 articles.

1.2 Inclusion Criteria

(1) Publicly published clinical practice guidelines/consensus statements/standards (hereinafter referred to as "guidance documents"); (2) Study subjects were NAFLD patients; (3) When two or more guidelines represented updated versions, only the most recent version was included; (4) Language limited to Chinese or English.

1.3 Exclusion Criteria

(1) Guideline abstracts, excerpts, interpretations, or translations; (2) Guideline development protocols, drafts, trial versions, announcements, or meeting minutes; (3) Non-Chinese or non-English guidelines.

1.4 Literature Screening and Data Extraction

Retrieved literature records were imported into NoteExpress software for deduplication. Two hepatology researchers independently screened literature and extracted data according to inclusion and exclusion criteria, with cross-checking. Discrepancies were resolved by consulting a third expert. Corresponding authors were contacted to supplement missing information when possible. Based on AGREE and RIGHT items, we designed a data extraction form covering: guideline title, corresponding author, publication/update date, developing country/association, evidence-based development method, evidence quality grading method, funding support, and conflict of interest.

1.5 Methodological and Reporting Quality Assessment

Two evaluators independently assessed methodological and reporting quality using AGREE and RIGHT tools after receiving professional training to ensure consistent evaluation criteria. AGREE comprises 6 domains with 23 items, each scored from 1 (lowest) to 7 (highest). The standardized percentage score for each domain was calculated as: (actual score - minimum possible score) / (maximum possible score - minimum possible score) × 100%. The sum of scores from both evaluators for each domain was calculated, then expressed as actual total score / total maximum possible score × 100% (rounded to two decimal places). Guidelines were graded as: Grade A (all six domains $ $60%)− "recommended for clinical use" ; Grade B (any domain <60% but $ $3 domains $ 30 $3 domains <30%)− "not recommended" [9].

RIGHT comprises 7 domains with 22 items, each rated as "completely reported (Y)," "partially reported (P)," "not reported (N)," or "not applicable (I)." For quality evaluation, "Y" was assigned 2 points, "P" 1 point, and "N" or "I" 0 points. The total reporting rate was calculated as actual total score / total maximum possible score × 100% (rounded to two decimal places).

1.6 Quality Control

Before formal evaluation, three guidance documents were randomly selected for pilot assessment. Intraclass correlation coefficient (ICC) was used to test AGREE reliability using SPSS 23.0. When ICC $ $0.75, evaluators were re-trained; formal evaluation began when ICC >0.75. Discrepancies in RIGHT evaluation were resolved by consulting a third expert.

1.7 Summary of Major Recommendations

Major recommendations from Grade B and above NAFLD guidance documents were summarized according to screening and diagnosis, assessment, management (non-pharmacological and pharmacological treatment), and surgical treatment. For evidence-based guidance documents, recommendation strength and evidence level were extracted according to GRADE standards (see Table 1). If other grading systems were used, hepatology experts converted them to GRADE standards based on content. When recommendation strength and evidence level were not explicitly stated, research team experts assigned them according to GRADE standards and documented original content.

Results

2.1 Literature Search Results

A total of 2,026 articles were retrieved (1,168 Chinese, 858 English). After importing into NoteExpress 3.5 and deduplication, 1,817 articles remained. Following title, abstract, and keyword screening, 1,780 articles were excluded; after

full-text review, 18 more were excluded, leaving 19 articles [10-28]. The literature screening flowchart is shown in Figure 1 [Figure 1: see original paper].

2.2 Basic Characteristics of Included Literature

Nineteen NAFLD-related guidance documents were included: 12 guidelines [10,13,16-20,23-24,26-28] and 7 consensus statements [11-12,14-15,21-22,25]; 6 in Chinese [10-15] and 13 in English [16-28]; 10 developed using evidence-based methods [10,15-19,23,25-26,28]. Basic characteristics are shown in Table 2 .

2.3 Methodological Quality Assessment

Three guidance documents were randomly selected; ICC values for AGREE evaluation exceeded 0.8, indicating good consistency. The mean standardized percentages across AGREE ' s six domains for the 19 guidelines were: scope and purpose (42.84%), stakeholder involvement (31.43%), rigor of development (31.25%), clarity of presentation (60.67%), applicability (32.68%), and editorial independence (37.50%), with an overall actual/total maximum score of 46.36%. No Grade A documents were identified; 12 were Grade B [10,15-19,22-26,28] and 7 were Grade C [11-14,20-21,27]. Detailed scores are shown in Table 3 .

Scope and Purpose: Only three documents [15-16,26] described expected benefits; all lacked descriptions of comparator measures; none completely described basic characteristics of target populations, disease conditions, or exclusion criteria.

Stakeholder Involvement: All documents lacked complete descriptions of guideline development members' names, research fields, institutions, addresses, and roles; only two [16-17] collected perspectives from target populations during development.

Rigor of Development: Only two documents [16-17] provided complete evidence search methods and strategies; only one [15] clearly described evidence selection criteria. Five documents [16-18,24,28] underwent external expert review before publication but provided no reviewer information. Seven documents [10,14,16,18-19,24,26] stated future updates would occur but described no methods, cycles, or timelines.

Clarity of Presentation: Five documents [11-14,22] did not highlight recommendations, creating difficulty in locating them.

Applicability: Nearly half [11-14,20-22,27-28] did not mention facilitators or barriers to application. Almost none provided adequate implementation tools or resources. Nearly half [14,18,20,22-24,27-28] did not consider potential resource requirements. One document [26] provided no monitoring criteria for recommendations.

Editorial Independence: Six documents [17,19,22-23,25,26] clearly stated sponsor views did not influence recommendations. Six documents [10-14,20] did

not document developer conflicts of interest.

2.4 Reporting Quality Assessment

RIGHT evaluation revealed generally low reporting quality among included NAFLD guidance documents. Only one document [16] achieved a total reporting rate >80% (85.71%). Guidelines demonstrated superior reporting quality compared to consensus statements. TCM guidance documents showed particularly low quality, all with total reporting rates <40%. The average total reporting rate for all 19 documents was 46.47%. Domain-specific average reporting rates were: Domain 1 (basic information) 59.65%, Domain 2 (background) 66.12%, Domain 3 (evidence) 42.11%, Domain 4 (recommendations) 39.85%, Domain 5 (review and quality assurance) 17.11%, Domain 6 (funding and conflict of interest declaration and management) 18.42%, and Domain 7 (other aspects) 47.37%. Domains 1 and 2 showed higher reporting quality, while Domains 5 and 6 were notably deficient, primarily because most documents did not report external expert review or quality assessment, and provided incomplete funding source and conflict of interest declarations. No documents reported fund usage processes. Detailed reporting quality scores are shown in Table 4 .

2.5 Summary and Comparison of High-Quality Guideline Recommendations

Major recommendations from the 12 Grade B documents [10,15-19,22-26,28] were summarized, with strength and evidence levels for the 10 evidence-based Grade B documents [10,15-19,23,25-26,28] compiled according to GRADE standards (see Figure 2 [Figure 2: see original paper]). The summary of major recommendations from Grade B documents is presented in Table 5 , with strength and evidence grading shown in Table 6 .

Recommendations addressed screening and diagnosis, assessment, management (non-pharmacological and pharmacological treatment), and surgical treatment. Screening and diagnosis recommendations focused on high-risk population characteristics, recommended diagnostic tools, alternative diagnostic tools, and differential diagnosis tools. Screening recommendations primarily included blood liver enzymes (ALT, AST, GGT), overweight/obesity, T2DM, and metabolic syndrome. Diagnostic recommendations mainly comprised abdominal ultrasound, liver biopsy, and genetic testing. Assessment recommendations included serum markers, abdominal ultrasound, CT, MRI/MRS, and VCTE.

For screening, recommendations were relatively consistent and predominantly strong for using overweight/obesity, T2DM, and metabolic syndrome as screening targets. However, one document [28] did not recommend NAFLD screening for obesity and diabetes patients in primary care settings, citing lack of clear treatment protocols and long-term beneficial evidence.

Non-pharmacological recommendations centered on low-calorie diets and exercise. Two documents [10,19] suggested moderate coffee consumption

may benefit NAFLD patients, both with strong recommendations. Six documents [10,15-17,19,28] recommended strict alcohol restriction, predominantly with strong recommendation grades. Since no FDA-approved drugs for NAFLD treatment currently exist [29], pharmacological recommendations were numerous and varied, generally targeting liver function and metabolic disorders, including ACEI/ARB, metformin, pioglitazone, statins, ω-3 fatty acids, GLP1-RA, SGLT-2 inhibitors, and UDCA. Recommendations for vitamin E, ω-3 fatty acids, pioglitazone, and UDCA were inconsistent: eight documents [10,16-19,23,25,28] recommended vitamin E while one [14] did not; four [10,18,23,28] recommended ω-3 fatty acids while one [16] did not; eight [10,16-19,23,25-26] recommended pioglitazone while one [28] did not; one [23] recommended UDCA while two [17,28] did not, with low evidence grades for ω-3 fatty acids and UDCA recommendations. Surgical recommendations focused on bariatric (metabolic) surgery for obese patients unresponsive to non-pharmacological and pharmacological therapy, and liver transplantation for cirrhosis, decompensated cirrhosis, and HCC, predominantly with strong recommendation grades.

Discussion

3.1 Overview of NAFLD Guidance Documents

NAFLD is among the most common chronic liver diseases causing abnormal liver function, encompassing simple fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), and related cirrhosis and hepatocellular carcinoma (HCC) [30]. With the proposal of the "metabolic-associated fatty liver disease (MAFLD)" nomenclature [2], the role of metabolism-related factors in hepatic steatosis has gained increasing attention. Among the 19 included guidance documents, 16 used the NAFLD nomenclature [10-18,20-24,27-28] and 3 used MAFLD [19,25-26]. The three MAFLD-named documents were published in 2020 [26], 2021 [19], and 2022 [25], indicating the MAFLD nomenclature has been increasingly adopted in recent guideline development, with all three focusing on metabolic factors' influence on fatty liver pathogenesis. By development method, the 19 included publications comprised 12 guidelines [10,13,16-20,23,24,26-28] and 7 consensus statements [11,12,14,15,21,22,25], with 10 developed using evidence-based methods [10,16-19,23,26,28]. One document [15] provided screening and treatment recommendations specifically for T2DM patients with NAFLD. Regarding treatment recommendations, three documents [12-14] provided TCM-related treatment opinions but without supporting efficacy evidence, suggesting insufficient evidence for TCM treatment of NAFLD and highlighting the need for high-quality TCM clinical trials to provide an evidence base for TCM guideline development.

3.2 Methodological Analysis of NAFLD Guidance Documents

Among the 19 included guidance documents, 6 were Chinese [10-15] and 13 English [16-28]. Of the 6 Chinese documents, 2 were Grade B [10,15] and 4

Grade C [11-14]; among the 13 English documents, 10 were Grade B [16-19,22-26,28] and 3 Grade C [20-21,27]. Domestic guidance documents showed lower methodological quality compared to international ones, with TCM guidelines demonstrating particularly insufficient methodological quality—all rated Grade C, with low recommendation levels and none following evidence-based methods. AGREE evaluation revealed that the 10 evidence-based guidance documents [10,16-19,23,26,28] achieved significantly higher standardized scores than non-evidence-based documents in total score, scope and purpose, rigor of development, and editorial independence, demonstrating that evidence-based methods substantially improve guideline quality [31]. Average standardized scores across stakeholder involvement, rigor of development, applicability, and editorial independence domains were all below 40%, primarily due to incomplete participant information, absent or incomplete description of search methods and evidence inclusion/exclusion criteria, inadequate description of factors influencing recommendation implementation, supporting tools, and resource usage, and failure to disclose sponsorship and conflicts of interest. Guideline companion documents or implementation suggestions can facilitate clinical application, making complete and referenceable tools crucial for dissemination and implementation. Additionally, among the 6 domestic guidance documents, 5 [10-14] scored 0 in editorial independence, indicating domestic guidelines should pay attention to collecting and disclosing sponsorship and conflict of interest information during development.

3.3 Reporting Quality Analysis of NAFLD Guidance Documents

RIGHT evaluation revealed low overall reporting quality among the 19 included guidance documents. Only one document [15] exceeded 80% total reporting rate, and only two [16-17] exceeded 60%. Guidelines demonstrated significantly better reporting quality than consensus statements. Domain 1 (basic information) and Domain 2 (background) scored higher, while Domain 5 (review and quality assurance) and Domain 6 (funding and conflict of interest declaration and management) scored lower, primarily because most documents did not report independent external expert review or quality assessment, and provided incomplete funding source and conflict of interest declarations. No documents reported fund usage processes. Therefore, guideline developers should receive standardized reporting training to enhance awareness, follow RIGHT tool requirements during development, and conduct structured reporting according to RIGHT items.

3.4 Analysis of NAFLD Guidance Document Recommendations

NAFLD guidance document recommendations primarily addressed screening and diagnosis, assessment of hepatic fat and fibrosis severity, management (non-pharmacological and pharmacological treatment), and surgical treatment. Patients with persistently abnormal liver enzymes should undergo NAFLD screening, though enzyme abnormalities are not recommended as diagnostic compo-

nents. NAFLD has become the most common chronic liver disease worldwide [5]. With promotion of the "multiple-hit"hypothesis [32], overweight/obesity, T2DM, and metabolic syndrome populations have become priority screening targets. Genetic testing may help assess genetic susceptibility to NAFLD, steatohepatitis, cirrhosis, and HCC. Abdominal B-ultrasound is the recommended imaging diagnostic method for NAFLD; ultrasound, CT, MRI, MRS, and VCTE can assess hepatic steatosis; serum fibrosis markers, FIB-4, and NFS scores can evaluate hepatic fibrosis and cirrhosis; HOMA-IR can assess insulin resistance in normal populations. Since plasma ALT levels and AST/ALT ratio remain questionable for evaluating steatohepatitis [33-34], NASH diagnosis strictly depends on liver biopsy. As NAFLD is a diagnosis of exclusion [2], confirmation requires ruling out alcoholic liver disease, autoimmune liver disease, and other causes of hepatic steatosis. However, in MAFLD-named guidance documents [19,25-26], diagnostic criteria have changed to non-exclusive positive diagnostic standards: evidence of hepatic steatosis via imaging, blood biomarkers, or histology, plus overweight/obesity, T2DM, or at least two metabolic risk factors. Although current disease connotations under both nomenclatures are largely similar, MAFLD as an inclusive diagnosis allows coexistence of dual or multiple etiologies causing hepatic steatosis, making it more suitable for clinical practice, while NAFLD strictly excludes other liver diseases, making it more appropriate for clinical trials with strict inclusion/exclusion criteria. These diagnostic standard changes may impact future clinical practice and research. Based on recommendations from included Grade B guidance documents, a clinical practice flowchart for MAFLD was developed (see Figure 2 [Figure 2: see original paper]).

Non-pharmacological recommendations focused on diet and exercise. Overweight/obese patients should restrict caloric intake, which, despite implementation difficulties, demonstrates good clinical efficacy [35]. Mediterranean diet-based low-carbohydrate and low-fructose dietary patterns are recommended, with strict alcohol avoidance. Ketogenic diets show beneficial effects on hepatic inflammation and fibrosis [36] and can rapidly reduce hepatic fat accumulation when combined with low-calorie diets [37], showing potential for future NAFLD treatment. Aerobic or resistance exercise is recommended, with at least 7%-10% weight loss suggested. Two guidance documents [10,19] recommended moderate coffee consumption for NAFLD patients, possibly related to caffeine and other major coffee components reducing hepatic fat content and stiffness and improving metabolism [38].

Currently, no FDA-approved drugs exist to definitively slow, halt, or reverse NAFLD and NASH. Recommended pharmacological therapies primarily target related metabolic disorders. Vitamin E, metformin, pioglitazone, and statins were most frequently recommended. Vitamin E 800 IU/day and pioglitazone 30-45 mg/day are reference doses for steatohepatitis. Metformin is recommended for isolated insulin resistance or T2DM. GLP1-RA improves obesity and reduces blood glucose by decreasing satiety and food intake [39], suggesting appetite regulation may be a therapeutic mechanism. ACEI/ARB drugs are

first-line antihypertensives for patients with comorbid hypertension. Statins are recommended for dyslipidemia, and ω-3 fatty acids may be used for hypertriglyceridemia. PCSK9 inhibitors [40] and liraglutide [41] have proven effective in significantly reducing serum LDL cholesterol and cardiovascular events in NAFLD patients, suggesting potential applications for dyslipidemia. Recommendations for vitamin E, ω-3 fatty acids, pioglitazone, and UDCA were inconsistent: opposing views on vitamin E, ω-3 fatty acids, and pioglitazone were based on lack of efficacy evidence in the specific patient populations studied in those guidelines [15-16,28]; UDCA opposition stemmed from ineffectiveness for NASH and NAFLD/NASH-related fibrosis [17] and lack of efficacy evidence [28]. TCM guidance documents provided available herbal prescriptions, but no TCM recommendations appeared in other guidelines. For obese NAFLD patients unresponsive to management or NASH patients, bariatric (metabolic) surgery is recommended (excluding decompensated cirrhosis), but patients' cirrhosis and decompensation risks must be strictly assessed, with no consensus on BMI thresholds.

Regarding evidence, few high-quality evidence-based guidance documents provided complete supporting evidence, while most showed incomplete evidence presentation. Pharmacological treatment recommendations generally had lower evidence strength than other aspects, likely because no single drug has clear evidence for improving NAFLD hepatic steatosis. This partly demonstrates NAFLD is not simply a "two-hit" disorder from hepatic lipid deposition, insulin resistance, and oxidative stress [42], but rather a "multiple-hit" disorder involving genetics and multiple pathway-mediated metabolic dysfunctions [2]. This explains why liver-centered treatments are often ineffective, suggesting new drug development should target multiple pathways and improve NAFLD-related metabolic disorders from various angles.

Conclusion

The methodological and reporting quality of NAFLD-related guidance documents requires improvement. Methodology should focus on stakeholder involvement, rigor of development, applicability, and editorial independence. Reporting standardization should emphasize review and quality assurance, funding, and conflict of interest declaration and management. Guideline development should follow AGREE requirements, and reporting should be structured according to RIGHT standards. Domestic guidance documents should improve methodological quality during development, and TCM guidance documents should adopt evidence-based methods to strengthen methodological quality.

This study summarizes major recommendations from higher-quality NAFLD guidance documents, providing some clinical guidance. Clinicians should establish screening awareness for overweight/obese, T2DM, metabolic syndrome, and non-obese populations with high insulin resistance, and implement comprehensive early non-invasive diagnostic and evaluation systems. Clinicians should provide NAFLD patients with lifestyle recommendations beyond diet and ex-

ercise, and select guideline-recommended drugs based on metabolic disorders, liver dysfunction, or inflammatory manifestations.

This study has limitations. Literature was limited to Chinese and English languages, and journal publication space constraints may have limited the number of documents and information included. While AGREE and RIGHT are internationally recognized tools, they have overlapping evaluation scopes, insufficient content coverage, heavy workload, dependence on complete guideline reporting, and limited effectiveness for evaluating non-evidence-based guidance documents. Future studies should expand language scope and explore more suitable evaluation tools for comprehensive quality assessment.

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Conflict of Interest Statement: All authors declare no conflicts of interest.

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Table 1: GRADE Evidence Quality and Recommendation Strength Grading

Table 2: Essential Features of Included Guidelines

Table 3: Methodological Quality Scores of Included Guidelines (AGREE Tool)

Note: Figure translations are in progress. See original paper for figures.