DEVELOPMENT AND VALIDATION OF A MALNUTRITION RISK ASSESSMENT SCALE FOR CHRONIC KIDNEY DISEASE (CKD) PATIENTS IN SHAANXI PROVINCE, CHINA

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by

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TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF ABBREVIATIONS

ACEI	Angiotensin-Converting Enzyme Inhibitor
ARB	Angiotensin II Receptor Blockers
Alb	Albumin
ASDTH	Attitudes toward Diet Therapy Scale for Dialysis Patients
BAPEN	British Association for Parenteral and Enteral Nutrition
BMI	Body Mass Index
Ca	Expert's judgment of the project
CI	Confidence Interval
CDC	Centers for Disease Control and Prevention
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CNKI	China National Knowledge Infrastructure
Cr	Expert authority coefficient
CR	Construct Reliability
CRF	Chronic Renal Failure
CKD	Chronic Kidney Disease
CKD-MRAS	Malnutrition Risk Assessment Scale for Chronic Kidney Disease
CV	Coefficient of variation
CVI	Content Validity index
Cs	Expert familiarity with the study
DDFQ	Diet and Fluid Intake Noncompliance Questionnaire
DI	Discrimination Index
DIF I	Difficulty Index

DMS	Dialysis Malnutrition Score
eGFR	Estimated Glomerular Filtration Rate
EFA	Exploratory Factor Analysis
EPV	Events Per Variable
EQ-5D	European Five Dimensions Questionnaire
ESPEN	European Society for Parenteral and Enteral Nutrition
ESRD	End-Stage Renal Disease
ESRD-SCL	End-Stage Renal Disease Symptom Checklist
GFR	Glomerular Filtration Rate
GNRI	Geriatric Nutritional Risk Index
Hb	Hemoglobin
HIV	Human Immunodeficiency Virus
I-CVI	Item relevance CVI
KAP	Knowledge, Attitude, Practice
KDIGO	Kidney Disease: Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
KDQOL-SF	Kidney Disease Quality of Life Short Form questionnaire
KDQOL™-36	Kidney Disease Quality of Life
KMO	Kaiser-Mayer-Olkin
MCS	Mental component summary scale
KTQ	Kidney Transplantation Questionnaire
MD	Mean Difference
MIS	Malnutrition Inflammation Score
ML	Maximum Likelihood
MLR	Maximum Likelihood Estimation

MNA	Mini Nutritional Assessment
MNA(SF)	Mini Nutritional Assessment Short Form
MUST	Malnutrition Universal Screening Tool
MST	Malnutrition Screening Tool
NIS	Nutrition Impact Symptoms
NRS-2002	Nutritional Risk Screening 2002
OR	Odds Ratio
PCS	Physical component summary scale
PG-SGA	Patient-Generated Subjective Global Assessment
QoL	Quality of Life
RABQ	Renal Adherence Behaviour Questionnaire
Renal iNUT	Renal Inpatient Nutritional Screening Tool
RMSEA	Root Mean Square of Approximation
R-NST	Renal Nutrition Screening Tool
RRT	Renal Replacement Therapy
S-CVI/Ave	Scale-level Content Validity Index based on the Average method
S-CVI/UA	Scale-level Content Validity Index based on the Universal Agreement method
SD	Standard Deviation
SF-36	Short Form-36
SGA	Subjective Global Assessment
SRMR	Standardized Root Mean Square Residual
SNAQ	Short Nutritional Assessment Questionnaire
TLI	Tucker-Lewis Index
TOUS	Theory of Unpleasant Symptoms

TRF	Transferrin
UA	Universal Agreement
VIF	Variance Inflation Factor
WHO	World Health Organization
WHOQOL-BREF	World Health Organization Quality of Life-BREF
WLSMV	Weighted Least Squares Mean and Variance

LIST OF APPENDICES

PEMBANGUNAN DAN PENGESAHAN SKALA PENILAIAN RISIKO KEKURANGAN ZAT MAKANAN UNTUK PESAKIT PENYAKIT BUAH PINGGANG KRONIK (CKD) DI SHAANXI PROVINCE, CHINA

ABSTRAK

Malnutrisi kekal sebagai komplikasi utama dalam Penyakit Ginjal Kronik (CKD), yang menyumbang kepada hasil klinikal yang buruk dan penurunan kualiti hidup, namun alat yang berkesan untuk pengenalan awalnya masih terhad. Kajian semasa bertujuan untuk membangunkan dan mengesahkan Skala Penilaian Risiko Malnutrisi (CKD-MRAS) yang direka khusus untuk pesakit CKD. Dilaksanakan di Hospital Perubatan Tradisional Cina Negeri Xi’an di China, kajian ini mengikuti pendekatan berperingkat. Dalam fasa pertama, item awal untuk Skala Pengetahuan, Sikap, dan Amalan (KAP) Malnutrisi dan CKD-MRAS dibentuk melalui temu bual separa berstruktur (n=13). Item-item awal ini disempurnakan menggunakan dua pusingan kaedah Delphi yang melibatkan panel 15 pakar. Dalam fasa kedua, kajian perintis melibatkan 20 pesakit CKD dijalankan untuk memastikan kejelasan, kebolehlaksanaan, dan kesesuaian item sebelum ujian berskala besar. Selanjutnya, skala KAP Malnutrisi menjalani pengesahan pada bahagian pertama, dengan pesakit CKD (n=152) yang turut serta dalam analisis item dan analisis faktor eksploratori (EFA). Analisis item menunjukkan keperluan untuk menghapuskan item K1 kerana indeks kesukaran dan diskriminasinya yang rendah. EFA untuk domain Sikap (A) dan Amalan (P) menunjukkan muatan faktor melebihi nilai had > 0.5, menerangkan 69.87% dan 61.84% daripada keseluruhan variasi, masing-masing. Skala ini menunjukkan konsistensi dalaman yang kuat (Cronbach's alpha = 0.967, kebolehpercayaan pembahagian =

0.974). Analisis faktor pengesahan (CFA) dijalankan (n=151). Model akhir 6-item untuk domain 'K' menunjukkan kesesuaian yang baik berdasarkan beberapa indeks kesesuaian (RMSEA (90%CI) = 0.070 (0.000, 0.124), CFI=0.978, TLI=0.963, SRMR=0.061). Begitu juga, model 9-item untuk domain 'A' dan model 10-item untuk domain 'P' menunjukkan indeks kesesuaian yang sangat baik. Model pengukuran akhir terdiri daripada 25 item. Dalam bahagian kedua, regresi logistik multivariat mengenal pasti faktor risiko bebas untuk malnutrisi, termasuk Pengetahuan [AOR 0.719 (0.529-0.978), p=0.035], Sikap [AOR 0.875 (0.826-0.927), p<0.001], Amalan [AOR 0.895 (0.847-0.946), p<0.001], pendapatan bulanan per kapita isi rumah [AOR 4.658 (1.489-14.566), p=0.008], selera makan [AOR 3.575 (1.602-7.978), p=0.002], dan status gastrointestinal [AOR 8.174 (3.622-18.448), p<0.001]. CKD-MRAS mencapai nilai kawasan di bawah lengkung sebanyak 0.925 dan ketepatan keseluruhan sebanyak 92.5%. Dalam bahagian ketiga, prevalens malnutrisi di kalangan pesakit CKD didapati sebanyak 33.7%, dengan 40.7% berisiko mengikut CKD-MRAS. Selain itu, kesesuaian yang substansial diperhatikan antara CKD-MRAS dan Penapisan Risiko Nutrisi (NRS2002) (Kappa = 0.657, p < 0.001). Risiko malnutrisi menunjukkan korelasi negatif dengan pelbagai dimensi Kualiti Hidup (Nilai r antara -0.386 hingga -0.722, p < 0.001).

Kesimpulannya, CKD-MRAS adalah alat yang boleh dipercayai dan sah untuk menilai risiko malnutrisi dalam pesakit CKD, memberikan peluang untuk intervensi awal bagi meningkatkan hasil pesakit. Kajian selanjutnya perlu meneroka aplikasinya dalam populasi dan persekitaran yang pelbagai.

DEVELOPMENT AND VALIDATION OF A MALNUTRITION RISK ASSESSMENT SCALE SPECIFICALLY TAILORED FOR CHRONIC KIDNEY DISEASE (CKD) PATIENTS IN CHINA

ABSTRACT

Malnutrition remains a significant complication in Chronic Kidney Disease (CKD), contributing to poor clinical outcomes and reduced quality of life, yet effective tools for its early identification are limited. The current study aimed to develop and validate the Malnutrition Risk Assessment Scale (CKD-MRAS) tailored specifically for CKD patients. Conducted at Xi'an Provincial Hospital of Traditional Chinese Medicine in China, the study followed a multi-phase approach. In the first phase, initial items for the Malnutrition Knowledge, Attitude, and Practice (KAP) Scale and CKD-MRAS were formulated through semi-structured interviews (n=13). These initial items were refined using two rounds of the Delphi method, involving a panel of 15 experts. In the second phase, a pilot study involving 20 CKD patients was conducted to ensure clarity, feasibility, and relevance of the items before large-scale testing. Subsequently the Malnutrition KAP scale underwent validation in the first part, with CKD patients (n=152) participating in item analysis and exploratory factor analysis (EFA). Item analysis revealed the need to eliminate item K1 due to its low difficulty and discrimination index. EFA for the Attitude (A) and Practice (P) domains demonstrated factor loadings above the cut-off value of > 0.5, explaining 69.87% and 61.84% of the total variance, respectively. The scale exhibited strong internal consistency (Cronbach's alpha = 0.967, split-half reliability = 0.974). Confirmatory factor analysis (CFA) was conducted (n=151). The final 6-item model for the 'K' domain displayed good fit based on several fit indices (RMSEA (90%CI) = 0.070 (0.000, 0.124), CFI=0.978, TLI=0.963, SRMR=0.061). Similarly, the 9-item model for the 'A' domain and the 10-item model for the 'P' domain exhibited excellent fit indices. The final measurement model comprised 25 items. In the second part, multivariable logistic regression identified independent risk factors for malnutrition, including Knowledge [AOR 0.719 (0.529-0.978), p=0.035], Attitude [AOR 0.875 (0.826-0.927), p<0.001], Practice [AOR 0.895 (0.847-0.946), p<0.001], monthly per capita household income [AOR 4.658 (1.489-14.566), p=0.008)], appetite [AOR 3.575 (1.602-7.978), p=0.002], and gastrointestinal status [AOR 8.174 (3.622-18.448), p<0.001]. The CKD-MRAS achieved an area under the curve of 0.925 and an overall accuracy of 92.5%. In the third part, the prevalence of malnutrition among CKD patients was found to be 33.7%, with 40.7% at risk according to the CKD-MRAS. Additionally, substantial agreement was observed between the CKD-MRAS and Nutrition Risk Screening (NRS2002) (Kappa = 0.657, p < 0.001). Malnutrition risk demonstrated a negative correlation with various dimensions of quality of life (r value ranging from -0.386 to -0.722, p < 0.001). In conclusion, the CKD-MRAS is a reliable and valid tool for assessing malnutrition risk in CKD patients, offering an opportunity for early intervention to improve patient outcomes. Further studies should explore its application in diverse populations and settings.

CHAPTER 1

INTRODUCTION

1.1 Introduction

The first chapter primarily served to introduce this study, including the background of the study and the problem statements, to determine the main context of this study. It also introduced the research question, established the research hypothesis, established the research objectives, and finally defined the important elements of the study and explained the significance of this study.

1.2 Background of the Study

1.2.1 Chronic Kidney Disease (CKD)

Chronic kidney disease (CKD) is a progressive condition affecting roughly 10% of adults worldwide (Crews, Bello and Saadi, 2019). Presently, kidney disease significantly impacts global health, and it stands as a critical risk factor for cardiovascular disease (Bikbov *et al.*, 2020). Notably, CKD substantially contributes to the morbidity and mortality from noncommunicable diseases, ascending from the 27th to the 18th most significant global cause of death in the last two decades (Liyanage *et al.*, 2015). Since 1990, the global all-age prevalence of CKD has surged by 29.3%, paralleled by a 41.5% increase in the global all-age mortality rate (Bikbov *et al.*, 2020). Therefore, it not only inflicts personal suffering but also constitutes a significant socio-economic challenge.

At present, global CKD prevalence exhibits variations among countries and regions, reflecting diverse factors such as regional, racial, socioeconomic, and behavioral influences, along with disparities in healthcare access and quality (Levey *et al.*, 2020b). In developed nations, CKD prevalence ranges between 6.5% and 10.0% (Jha *et al.*, 2013, Bello *et al.*, 2017). The Centers for Disease Control and Prevention in the United States estimate a CKD prevalence of approximately 15.0% among American adults (Wilson *et al.*, 2021). In Asia, data from Korea indicate a CKD prevalence of 8.2% (Park, Baek and Jung, 2016). Notably, out of 697.5 million individuals with CKD worldwide in 2017, one-third hailed from China and India, accounting for 132 million in China and 115 million in India (Bikbov *et al.*, 2020). In China, CKD prevalence among adults stands notably high at 13.2%, demonstrating significant regional disparities with rates of 13.21% among urban residents and 11.9% among rural residents (Lv and Zhang, 2019), thereby imposing substantial economic and health burden (Khan *et al.*, 2018). It's pertinent to highlight that in numerous regions, individuals of lower socioeconomic status experience a heightened CKD prevalence, limited treatment access, and poorer prognoses (Crews, Bello and Saadi, 2019, Garcia *et al.*, 2019).

The primary causes of CKD encompass a spectrum of genetic diseases and environmental risk factors, prominently featuring hypertension and diabetes as the leading contributors (Correa-Rotter, Wesseling and Johnson, 2014, Köttgen *et al.*, 2022). In Western countries, diabetes mellitus stands as the primary risk factor, afflicting 30-50% (Webster *et al.*, 2017). Additionally, high blood pressure and smoking significantly elevate the risk of CKD development and hasten its progression (Webster *et al.*, 2017). Conversely, in regions like India, Asia, and sub-Saharan Africa, glomerulonephritis emerges as the foremost cause of CKD, closely followed by CKD of unknown etiology, potentially linked to heavy-metal and pesticide-contaminated soils, alongside the excessive use of herbal medicines (Fitria *et al.*, 2020). Notably, the impact of Human Immunodeficiency Virus (HIV) on CKD cannot be ignored due to direct glomerular mesangial damage by HIV itself and the considerable nephrotoxicity associated with antiretroviral therapy (Webster *et al.*, 2017). However, in certain high-burden areas worldwide, the precise etiology of CKD remains elusive (Correa-Rotter, Wesseling and Johnson, 2014).

The global burden of kidney disease continues to escalate. Strikingly, certain regions—such as Oceania, sub-Saharan Africa, and Latin America—bear a disproportionately higher burden of chronic kidney disease compared to their developmental level. Conversely, in western, eastern, and central sub-Saharan Africa, East Asia, South Asia, Central and Eastern Europe, Oceania, and Western Europe, the burden of disease appears lower than expected (Bikbov *et al.*, 2020). Despite these alarming trends, public and healthcare authorities' awareness and acknowledgment of the disease remain limited (Collaborators, 2018, Tuot *et al.*, 2016). According to the US Centers for Disease Control and Prevention (CDC), approximately 37 million individuals in the United States—equivalent to about 15% of adults—suffer from CKD (Vart *et al.*, 2020). Shockingly, 90% of adults with CKD are unaware of their condition, and even 50% of individuals with severely impaired kidney function remain undiagnosed for CKD (Schrauben *et al.*, 2020).

Due to the subtle nature of early symptoms, a considerable number of CKD patients discover severe and irreversible renal impairment during their initial clinic visit (Okparavero *et al.*, 2016). Furthermore, as the disease progresses, notable alterations in blood protein, sugar levels, and lipid metabolism occur, accompanied by an irreversible decline in renal function. This stage also witnesses an increase in protein energy consumption (Humphreys, 2018). Moreover, patients experience digestive symptoms, including loss of appetite, reduced food intake, and escalated protein and energy consumption due to uremic toxins and pro-inflammatory cytokines, thereby elevating the risk of malnutrition (Iorember, 2018). Consequently, CKD is also recognized as a nutrition-related health problem.

1.2.2 Malnutrition in CKD

CKD patients are at high risk of malnutrition due to various factors (Pérez-Torres *et al.*, 2018). According to the American Society for Parenteral and Enteral Nutrition, malnutrition is defined as "an imbalance between nutrient requirement and intake resulting in cumulative deficits of energy, protein or micronutrients that may negatively affect growth, development, and other relevant outcomes" (Becker *et al.*, 2014). This definition highlights malnutrition's components—protein and energy wastage alongside micronutrient deficiencies. Malnourished patients often change body composition and functional capacity, experiencing loss of muscle mass, reduced muscle function and strength, often characterized by weight loss, wasting, decreased fat content, and sometimes even stunted growth, leading to a sense of reduced strength (Hyun *et al.*, 2017, Fahal, 2014).

Malnutrition prevails across both developing and developed countries, correlating linearly with decreased Glomerular Filtration Rate (GFR) among CKD patients (Hyun *et al.*, 2017). A global meta-analysis investigating kidney disease patients revealed malnutrition prevalence in non-dialysis CKD stages 3-5 ranging from 11% to 54% (Carrero *et al.*, 2018). In Western countries like Italy, malnutrition incidence among CKD patients ranges from 14.1% to 22.5%, with protein-energy malnutrition reaching

30.1% (Pérez-Torres *et al.*, 2018). Moreover, studies show a startlingly high malnutrition rate exceeding 50% in stage 5 CKD patients before initiating Renal Replacement Therapy (RRT) (Hanna *et al.*, 2020). Upon progression to End-Stage Renal Disease (ESRD) and regular hemodialysis, the incidence escalates from 30% to 60% (Pérez-Torres *et al.*, 2018). Findings from a survey in China indicate a prevalent malnutrition rate of 13.3% to 50% among CKD patients (Song, Ni and Chen, 2018).

Malnutrition in CKD patients is characterized by loss of protein and energy stores associated with multiple metabolic disorders (Sabatino *et al.*, 2017). Factors contributing to this include reduced protein and energy intake, hypercatabolism, metabolic acidosis, diminished physical activity, comorbidities, and dialytic treatment, all impacting nutritional status and lean body mass, potentially leading to frailty (Sabatino *et al.*, 2017, Johansen *et al.*, 2014). Moreover, factors such as spontaneous inadequate nutritional intake, metabolic acidosis, insulin resistance, chronic inflammation, altered gut microbiota (gut ecological dysbiosis), infections, and oxidative stress also contribute to the development of malnutrition (Iorember, 2018). Moreover, inappropriate dietary restrictions or hemodialysis procedures could potentially worsen the condition (Fiaccadori *et al.*, 2021).

Alarmingly, malnutrition poses a life-threatening concern for CKD patients. Its consequences are far-reaching, negatively impacting complications, management, patient quality of life, and health economics (Ikizler *et al.*, 2013). Additionally, malnutrition as a primary contributor to major adverse clinical outcomes, linked to prolonged hospital stays, increased morbidity, and elevated mortality rates (Iorember, 2018). Furthermore, it stands as a critical risk factor for the aggressive advancement of CKD, amplifying the risks of morbidity, mortality, and overall disease burden in CKD patients (Iorember, 2018). Hence, emphasizing the nutritional status of CKD patients is vital. Doing so significantly enhances overall CKD diagnosis and treatment, delays disease progression, improves patient prognosis, and reduces medical costs (Xi *et al.*, 2023).

1.2.3 Knowledge, Attitude and Practice (KAP) About Malnutrition in Patients with CKD

Considering the widespread prevalence and risks associated with malnutrition, it's prudent to consider all hospitalized patients as potentially at risk. Despite this understanding, the detection and treatment of malnutrition often receive insufficient attention and fail to be regarded as a clinical priority (Barril *et al.*, 2022). The lack of awareness and inadequate knowledge and training appear to be significant barriers and obstacles (Carrero *et al.*, 2018). Additionally, while malnutrition in CKD patients is multifaceted, influenced by individual and socio-environmental factors, studies suggest that enhancing health-related knowledge can foster attitude changes and subsequently prompt substantial behavioral shifts (Vázquez-Espino *et al.*, 2020, Onbe and Kanda, 2018). Therefore, it's evident that a crucial step toward altering health attitudes and behaviors is to increase knowledge about malnutrition and its associated risk factors.

Knowledge encompasses an individual's understanding of disease causes, symptoms, prevention, and treatments (Razu *et al.*, 2021). Complementing this, attitude plays a crucial role in disease treatment, where a positive attitude fosters favorable practices while a negative one may lead to detrimental behaviors (Banerjee, 2020). Practice, on the other hand, reflects how individuals act to achieve health goals, drawing from their knowledge and attitudes (Razu *et al.*, 2021). These elements form a hierarchical relationship, where accurate knowledge forms the foundation, a positive attitude serves as the driving force, and healthy practices represent the ultimate goal (Rimbawan *et al.*, 2023). However, barriers such as insufficient knowledge, negative attitude, and limited practical experiences may impede effective nutrition management (Onbe and Kanda, 2018).

Most risk factors for malnutrition in CKD patients such as gender, age, weight loss, reduced food intake, dialysis, comorbidities, CKD stage, physical activity, and appetite can be prevented and controlled by developing more specific population-based prevention programs (Hyun *et al.*, 2017, Azzeh *et al.*, 2022, Xi *et al.*, 2023). However, a significant portion of malnourished CKD patients in China lack adequate knowledge and education about malnutrition (Jiang and Li, 2021). Recognizing the necessity of preventing or detecting malnutrition early on, understanding the disease, attitudes toward it, and related practices become pivotal (Dai *et al.*, 2022). Hence, to assess the risk of malnutrition in patients effectively, it is valuable to conduct a malnutrition KAP assessment in addition to evaluating the patient's risk factors. Both KAP and risk factors are important components that cannot be ignored when assessing malnutrition risk.

1.2.4 The Relationship Between Malnutrition and Quality of Life in CKD Patients

CKD is a long-term condition, and a considerable proportion of patients remain in stages 1-4 of the disease without progressing to ESRD (Baker *et al.*, 2022). Individuals in these stages often experience a high burden of symptoms, compromised physical function, and decreased levels of physical activity, which can significantly impact their quality of life (QoL) (Mackinnon *et al.*, 2018, Morishita, Tsubaki and Shirai, 2017). Furthermore, malnutrition, posing a significant health challenge, profoundly affects both daily activities and overall QoL (Norman, Haß and Pirlich, 2021). Studies highlight that nutritional aspects such as weight, diet, physical activity, and alcohol intake are linked to QoL (Salas *et al.*, 2022).

QoL has gained significant attention in research, increasingly considered a crucial outcome measure in clinical trials (Rasheed and Woods, 2013). Existing evidence recognizes the detrimental impact of malnutrition on morbidity, mortality, and QoL in various conditions, such as cancer, chronic obstructive pulmonary disease, and elderly rheumatoid arthritis patients (Polański *et al.*, 2017, Yamaya *et al.*, 2020, Nguyen *et al.*, 2019). However, there remains a scarcity of studies specifically focusing on malnutrition among CKD patients. Thus, this study aims to analyze two aspects related to malnutrition risk in CKD patients, including their KAP, and risk factors for malnutrition, and evaluate their correlation with QoL among CKD patients.

1.3 Problem Statement

Over the past decade, multiple studies have explored various malnutrition assessment tools, leading to the development of a few universally applicable malnutrition assessment scales in different countries (Detsky *et al.*, 1987, Kondrup *et al.*, 2003b, Elia, 2003). Many of these tools have been crafted based on professional or comprehensive nutritional assessments, given the absence of a definitive gold standard for malnutrition (Van Bokhorst-De Van Der Schueren *et al.*, 2014). A gold standard is crucial to establish a benchmark for accurate and consistent malnutrition diagnosis, which can guide the development and validation of more effective, population-specific tools. Without such a standard, discrepancies across existing scales may lead to inconsistent identification and management of malnutrition (Van Bokhorst-De Van Der Schueren *et al.*, 2014).

Presently, two widely employed scales are the Nutritional Risk Screening 2002 (NRS-2002) and the Subjective Global Assessment (SGA) (Sum *et al.*, 2017), both commonly used for general nutritional evaluations. Several screening tools have received endorsement from international nutrition societies. For instance, the European Society of Clinical Nutrition and Metabolism advocates for the adoption of the Malnutrition Universal Screening Tool (MUST), Malnutrition Inflammation Score (MIS), and Short-Form Mini-Nutritional Assessment [MNA(SF)], particularly for assessing the elderly (Kondrup *et al.*, 2003b, Rubenstein *et al.*, 2001b). It's important to note that while some tools are designed for broad application across populations, others are tailored for specific target groups. Additionally, there might exist numerous local tools that are neither published nor validated, which may not be widely recognized.

While the absence of a gold standard and the lack of locally developed tools in China are key gaps, the three commonly utilized tools in China—NRS-2002, SGA, and Mini Nutritional Assessment (MNA) (Xie et al., 2020b, Zhu, Zhao and Zhang, 2019) —also exhibit notable limitations when applied to CKD patients. Firstly, most existing tools were designed for general populations or specific groups like the elderly, such as the MNA and Geriatric Nutritional Risk Index (GNRI) (Bouillanne *et al.*, 2005, Guigoz, Vellas and Garry, 1997). They lack specific considerations for CKD-related malnutrition, such as metabolic disturbances, dietary restrictions, and inflammation (Van Bokhorst-De Van Der Schueren *et al.*, 2014). Secondly, tools like the SGA are time-consuming and require assessors with specialized nutritional training, making them impractical for routine clinical use in resource-limited settings (Xia, Healy and Kruger, 2016). This hinders their utility for widespread screening in CKD populations. Moreover, while some studies have compared the sensitivity and specificity of existing tools in identifying malnutrition among CKD patients, results remain inconsistent. For instance, studies highlighted discrepancies in the performance of these tools, underscoring the need for a more reliable instrument tailored to this patient group (Wang *et al.*, 2012b, Liang *et al.*, 2017). Additionally, many malnutrition assessment tools used in China are direct translations of foreign tools, often lacking proper cultural adaptation and validation for the local context (Zhu, Zhao and Zhang, 2019). This compromises their accuracy and applicability in Chinese healthcare settings. Finally, existing tools tend to overlook psychometric dimensions such as patients' knowledge, attitudes, and practices (KAP) related to nutrition, which are critical for understanding and managing malnutrition risk (Kruizenga *et al.*, 2005, Guigoz, Vellas and Garry, 1997).

As previously noted, there is a possibility that universal malnutrition assessment scales may be less accurate in evaluating malnutrition among patients with CKD due to their omission of crucial components relevant to this particular patient group. Indeed, there is no single screening tool suitable for all patients. Thus, a study is required to identify the important components related to malnutrition and subsequently to develop an appropriate screening tool to identify the risk of malnutrition for CKD patients (Van Bokhorst-De Van Der Schueren *et al.*, 2014). All of these challenges have inspired the researcher to conduct this study to devise an effective malnutrition risk assessment tool tailored specifically for the Chinese population. This tool aims to facilitate early detection of malnutrition among patients with CKD.

1.4 Significance of the Study

This study holds significant implications for understanding and addressing malnutrition risk among CKD patients. By investigating the KAP regarding malnutrition risk in CKD patients, valuable insights were gained to inform the development of the Malnutrition KAP Scale. Additionally, the identification of malnutrition risk factors facilitated the formulation of the CKD-MRAS, which serves as a vital tool for identifying CKD patients at high risk of malnutrition within clinical settings. Furthermore, this research provides valuable information for hospitals in Xi'an, Shaanxi Province, China, enabling them to effectively identify the prevalence of high malnutrition risk among CKD patients in their care. Additionally, the sensitivity and specificity of the CKD-MRAS within the CKD population were determined through comparison with the widely employed scale NRS2002, enhancing its utility and reliability in clinical practice. Finally, this study also contributes to understanding the possible association between quality of life (QoL) and malnutrition risk among CKD patients. By elucidating this relationship, it offers deeper insights into the impact of malnutrition on the well-being of CKD patients, thus informing holistic patient care strategies.

1.5 Research Questions

The research questions of this study are as follows:

1. How do patients with CKD perceive their knowledge, attitudes, and practices

(KAP) concerning malnutrition, and what do they identify as the primary risk factors contributing to their nutritional status?

2. How valid and reliable is the newly developed KAP scale in measuring malnutrition-related KAP among CKD patients?
3. What are the critical components and indicators that should be included in the development of the CKD-MRAS to accurately assess the risk of malnutrition among CKD patients?
4. What is the prevalence of CKD patients at risk of malnutrition in Xi’an, Shaanxi Province, China?
5. How does the sensitivity and specificity of the CKD-MRAS compare to the NRS2002 in identifying malnutrition risk among CKD patients?
6. Is there any association between the risk of malnutrition and QoL in the studied population?

1.6 Research Hypotheses

Null Hypothesis, Ho

1. CKD patients have limited knowledge, negative attitudes, and suboptimal practices regarding malnutrition, and they do not perceive significant risk factors contributing to malnutrition;
2. The Malnutrition Knowledge, Attitudes, and Practices (KAP) scale does not demonstrate satisfactory levels of validity and reliability;
3. The CKD-MRAS is not a valid tool for assessing malnutrition risk among CKD patients when compared to the NRS2002;
4. There is no significant association between the risk of malnutrition and QoL among CKD patients.

Alternative Hypothesis, H_A

1. CKD patients have adequate knowledge, positive attitudes, and appropriate practices regarding malnutrition, and they perceive specific risk factors to their malnutrition risk;
2. The Malnutrition Knowledge, Attitudes, and Practices (KAP) scale demonstrates satisfactory levels of validity and reliability;
3. The CKD-MRAS is a valid tool for assessing malnutrition risk among CKD patients when compared to the NRS2002;
4. There is a significant association between the risk of malnutrition and QoL among CKD patients.

1.7 Objective

1.7.1 General Objective

The general objective of this study is to develop and validate a novel Chronic Kidney Disease Malnutrition Risk Assessment Scale (CKD-MRAS) that accurately identifies the risk of malnutrition among CKD patients in Shaanxi province, China.

1.7.2 Specific Objectives

The specific objectives of this study are as follows:

Phase 1- Qualitative research

1. To explore the perceptions of CKD patients regarding their knowledge, attitude and practices (KAP) and risk factors related to malnutrition;

Phase 2- Quantitative research

2. To assess the validity and reliability of the newly developed KAP scale in measuring malnutrition-related KAP among CKD patients in Shaanxi province, China;
3. To develop a new CKD-MRAS to assess the risk of malnutrition among CKD patients;
4. To determine the prevalence of CKD patients who are at risk of malnutrition in Xi'an, Shaanxi Province, China;
5. To assess the sensitivity and specificity of the CKD-MRAS as compared to the NRS2002 in identifying risk of malnutrition among CKD patients;
6. To determine the association between the risk of malnutrition and QoL among CKD patients in Shaanxi province, China.

1.8 Operational Definition

Table 1.1: Conceptual and operational definitions

Keywords	Conceptual definition	Operational definition
Chronic kidney disease (CKD)	CKD is a general term for heterogeneous disorders affecting renal structure and function (renal impairment of more than three months) associated with or without a reduction in GFR. The symptoms are renal impairment, pathological abnormalities, or an unexplained decrease in GFR (<60 mL /min·1.73m²) over three months, with health implications (Navaneethan *et al.*, 2021).	In this study, patients aged>18 years and diagnosed with CKD were included as the participants.
Malnutrition	An imbalance between nutrient requirement and intake results in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes (Becker *et al.*, 2014).	Malnourished CKD patients with weight loss (>5% within the past 6 months, or >10% beyond 6 months), serum albumin＜35g/L, and BMI＜18.5 kg/m² (Cederholm *et al.*, 2019).

Table 1.1: Continued

Keywords	Conceptual definition	Operational definition
KAP	Knowledge encompasses an individual's understanding of disease causes, symptoms, prevention, and treatments (Razu *et al.*, 2021). A positive attitude fosters favorable practices while a negative one may lead to detrimental behaviors (Banerjee, 2020). Practice reflects how individuals act to achieve health goals, drawing from their knowledge and attitudes (Razu *et al.*, 2021).	KAP in this study refers to the KAP of CKD patients malnourished.
Risk factors	Risk factors refer to the causes or conditions that determine the development of something. In scientific experiments, the elements or causes that affect the indicators of a test are called factors (Wang *et al.*, 2021a).	The risk factors in this study referred to factors associated with malnutrition in CKD patients.
Assessment instrument	An assessment instrument refers to a particular method of acquiring data in psychological assessment such as questionnaires and scales (Yusoff, 2019).	In this study, the instrument refers to the malnutrition risk assessment scale which will be developed for patients with CKD.
Prevalence	The ratio of the number of people suffering from a disease at a given time to the average population over the same period. Mainly used in epidemiological studies of chronic diseases (e.g. cardiovascular diseases, tumors, tuberculosis, etc.) (Wang, 1998).	In this study, prevalence refers to the number of CKD patients in Xi'an, Shaanxi Province, China.
Quality of life	A person's perception of how well he or she is living in the context of the culture and value system in which he or she lives, about his or her goals, expectations, standards, and concerns (Group, 1995).	In this study, data on the participants' quality of life were obtained through the KDQOL™-36.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Background and Rationale

-Explain the importance of assessing malnutrition in CKD patients.
-Address the specific challenges and prevalence of malnutrition in CKD patients in China.

Objective of the Literature Review

This review covered six main parts, based on the following objectives. a) To review the prevalence and treatment of CKD. b) To review prevalence, risk factors and therapy of malnutrition among CKD patients. c) To review the KAP status of malnutrition among CKD patients. d) To review the KAP scale of malnutrition among CKD patients.

e) To review existing malnutrition risk assessment tools. f) To review the quality of life among CKD patients.

Search strategies

The search was conducted across five electronic databases: PubMed, Scopus, Web of Science, Embase, and China National Knowledge Infrastructure (CNKI). Search terms were systematically selected to reflect the core concepts of the study. The strategy involved combining keywords and phrases related to the research objectives, including:

a) To review the prevalence and treatment of CKD

- "Prevalence" OR "CKD prevalence" OR "Epidemiology" OR "Incidence"

- "Treatment" OR "Management" OR "Therapy"
- "CKD" OR "chronic kidney disease" OR "renal disease”

b) To review prevalence, risk factors and therapy of malnutrition among CKD patient

- "Malnutrition prevalence" OR "Prevalence" OR "Epidemiology" OR "Incidence"
- "Risk factors" OR "Factors" OR "Causes " OR "Factors influencing”
- "Treatment" OR "Management" OR "Therapy"
- "malnutrition" OR "nutrition" OR "protein-energy wasting"
- "CKD" OR "chronic kidney disease" OR "renal disease”

c) To review the KAP status of malnutrition among CKD patients

- "Knowledge, Attitude, Practice" (KAP) OR "KAP survey" OR "Nutrition awareness" OR "Dietary behavior" OR "Nutrition-related behaviors"
- "malnutrition" OR "nutrition" OR "protein-energy wasting"
- "CKD" OR "chronic kidney disease" OR "renal disease”

d) To review the KAP scale of malnutrition among CKD patients

- "Knowledge, Attitude, Practice scale" OR "KAP tool development” OR “CKD nutrition KAP scale” OR “KAP assessment” OR "KAP scale"
- "malnutrition" OR "nutrition" OR "protein-energy wasting"
- "CKD" OR "chronic kidney disease" OR "renal disease”

e) To review existing malnutrition risk assessment tools

- "Malnutrition risk assessment" OR "Risk of malnutrition assessment tools” OR "Malnutrition screening" OR "Nutrition screening tools"
- "CKD" OR "chronic kidney disease" OR "renal disease”

f) To review the quality of life among CKD patients

- "Quality of life" OR "Health-related quality of life" OR "QoL"

- "CKD" OR "chronic kidney disease" OR "renal disease"

Boolean operators (AND/OR), truncation, and MeSH terms were applied to refine the search strategy and optimize the results. The search was restricted to peer-reviewed articles published in English and Chinese, covering the period from the establishment of each database to 2024.

To align with the research objectives, the researcher conducted a literature search focusing on key topics: the prevalence and risk factors of malnutrition in CKD patients, KAP surveys related to malnutrition, and existing malnutrition risk assessment tools. Keywords like "CKD," "malnutrition," "KAP," and so on were used to identify relevant studies. The search also examined the relationship between malnutrition and quality of life, ensuring a comprehensive understanding of the issue. This strategy resulted in the inclusion of 113 studies, supporting the development of a new CKD-MRAS to the local population.

2.2 Overview of Chronic Kidney Disease (CKD)

CKD is a general term for heterogeneous disorders affecting renal structure and function (renal impairment of more than three months) associated with or without a reduction in GFR. The symptoms are renal impairment, pathological abnormalities, or an unexplained decrease in GFR (<60 mL/min·1.73m^2) over three months, with health implications (Navaneethan *et al.*, 2021). The global prevalence trend of CKD is often described as having "four highs and three lows." The "four highs" denote the high prevalence of CKD, high cardiovascular prevalence in combination with CKD, high morbidity and mortality of CKD, and high disease burden of CKD. On the other hand, the "three lows" encompass low awareness, low rates of early detection, and low control rates of CKD (Shlipak *et al.*, 2021).

Multiple genetic and environmental risk factors contribute to kidney disease, which makes it difficult to identify the underlying pathophysiologic mechanisms, therefore it is commonly referred to as “complex disease.” (Köttgen *et al.*, 2022). Environmental factors such as high salt intake, pollution exposure, obesity, and smoking are significant contributors to kidney damage (Evangelidis *et al.*, 2019, Androga *et al.*, 2017). The classification and staging of CKD are based on the Causes, GFR category (G1–G5), and Albuminuria category (A1–A3), abbreviated as CGA (Levey *et al.*, 2020a). CKD is categorized into five stages based on the degree of GFR decline (G1–G5). The diverse staging aims to offer a comprehensive assessment of the disease and bolster the early recognition and management of CKD (Alseiari, Meyer and Wong, 2016). Varied staging leads to different treatment goals and strategies, as outlined in Table 2.1 (Rovin *et al.*, 2021).

Table 2.1: Stages of CKD and Strategies for prevention and treatment

CKD Staging	GFR categories (ml/min/1.73m^2)	GFR characteristics	Prevention and treatment strategies
G1	≥90	Normal or high	Diagnosing and treating the cause and delaying the progression of CKD
G2	60-89	Mildly decreased	Delaying the progression of CKD and reducing the risk of cardiovascular disease
G3a	45-59	Mildly to moderately decreased	Delaying the progression of CKD
G3b	30-44	Moderately to severely decreased	Assessment, control of complications
G4	15-29	Severely decreased	Integrated treatment, RRT preparation
G5	＜15	Kidney failure	Timely RRT

Source: (Rovin *et al.*, 2021); CKD: Chronic Kidney Disease; GFR: Glomerular Filtration Rate; RRT: Renal Replacement Therapy.

In the early stages (stage 1-3), patients with CKD might either not show any obvious signs or exhibit mild symptoms such as loss of appetite, fatigue, and increased nocturia. As CKD progresses to more advanced stages (stage 4-5), patients may develop various clinical syndromes, including metabolite retention, water-electrolyte disturbances, and acid-base imbalance, known as Chronic Renal Failure (CRF). Further progression of CRF to stage 5 signifies the development of ESRD. Kidney failure represents the terminal phase of CKD, defined as a severe decline in renal function necessitating dialysis treatment or RRT (Wilson *et al.*, 2021). ESRD was previously referred to as uremia, at which point patients require RRT (Jörres *et al.*, 2013), encompassing treatments such as hemodialysis, peritoneal dialysis, or renal transplantation to partially replace kidney functions (Goumenos, Papachristou and Papasotiriou, 2016, Wang *et al.*, 2020).

According to a national survey conducted during 2009-2010, the prevalence of CKD in China was 10.8% (Zhang *et al.*, 2012). China thus has the largest number of people with CKD (132 million in 2017), accounting for nearly one-fifth of the global total (Zhang *et al.*, 2012). In 2018 to 2019, the prevalence of CKD was 8.2%. Among the adults with CKD, 73.3%, 25.0%, and 1.8% were at stages 1 to 2, 3, and 4 to 5, respectively (Wang *et al.*, 2023). Additionally, CKD prevalence and mortality are projected to rise to 11.7% and 17.1 per 100,000, respectively, by 2029 (Li *et al.*, 2023d). Therefore, it has become a major health and epidemiologic challenge for the general community, health professionals, and authorities in the region, especially those in low- and middle-income countries (Rovin *et al.*, 2021).

2.3 Nutritional Challenges in CKD

2.3.1 Malnutrition in CKD patients

Malnutrition is one of the complications of CKD. It is characterized by deficiencies, excesses, or imbalances in a person's intake of protein, energy, and/or other nutrients, and micronutrient deficiencies. Malnutrition can lead to reduced immune function and physical activity, increased occurrences of nutritional deficiencies such as anemia, and higher susceptibility to infection (Wright *et al.*, 2019). In addition, the average length of stay and hospitalization costs for CKD patients at nutritional risk were more than twice as high as those for patients without nutritional risk (Zhu *et al.*, 2013). What's more, malnutrition in the general population may primarily result from inadequate nutritional intake. However, malnutrition in patients with CKD cannot be explained simply by adjusting nutritional intake (Hyun *et al.*, 2017).

In Western countries such as Italy, the incidence of malnutrition in CKD patients ranges from 14.1% to 22.5, among which, the incidence of protein-energy malnutrition is 30.1% (Pérez-Torres *et al.*, 2018). Studies have reported 35% incidence of malnutrition in 489 CKD hospitalized patients in Switzerland (Muller *et al.*, 2019). Moreover, in a Nigerian investigation on the incidence of malnutrition in patients with CKD before dialysis (Oluseyi and Enajite, 2016), the incidence of malnutrition was 46.7%, and the incidence of malnutrition was higher in stage 2-5 in elderly patients, which would increase with the deterioration of renal function. While in Dai *et al.* they had conducted a nutritional survey of 1083 CKD patients in Sweden and found that 31% of CKD patients were malnourished (Dai *et al.*, 2017). The prevalence of malnutrition in end-stage CKD will rise significantly, ranging from 23% even to 75% in Italy (Rezeq *et al.*, 2018).

The pathogenesis of malnutrition in CKD patients is complex, involving a combination of factors such as inadequate dietary intake, inflammation, metabolic acidosis, hormonal imbalances, and altered gastrointestinal function. These mechanisms may vary depending on the stage of CKD, comorbidities, and treatment modalities (Carrero *et al.*, 2013). Severe renal impairment (usually recognized as a loss of GFR), not only affects water, electrolyte, and acid-base metabolism but also induces a complete change in the "internal environment", as well as specific alterations in the metabolism of proteins, amino acids, carbohydrates and lipids (Fiaccadori, Regolisti and Maggiore, 2013). Especially in its most advanced stages, may have caused various levels of metabolic disturbances, including systemic oxidative stress and mild inflammation. Acute deterioration of renal function in patients with CKD may lead to more severe metabolic alterations and consequent changes in body composition (Fiaccadori *et al.*, 2021).

Malnutrition significantly impacts CKD patients by increasing morbidity and mortality rates, with complications such as infections, cardiovascular issues, and hospitalizations being more frequent (Iorember, 2018). It contributes to protein-energy wasting, leading to muscle loss, physical frailty, and impaired daily function. The weakened immune system heightens susceptibility to infections, while delayed wound healing further complicates recovery from injuries or surgeries (Hanna *et al.*, 2020). Malnutrition also diminishes treatment effectiveness, exacerbates dialysis-related challenges, and reduces quality of life due to fatigue, psychological distress, and diminished energy levels (Ikizler *et al.*, 2013). These factors collectively lead to higher healthcare costs and underscore the importance of early nutritional screening and interventions to mitigate these adverse effects (Xi *et al.*, 2023).

CKD presents numerous nutritional challenges that significantly impact patient health and quality of life. Edema, often caused by fluid retention and altered sodium balance, can mask actual body weight and lead to challenges in nutritional assessment (Borrelli *et al.*, 2020). Weight loss due to protein-energy wasting is a common concern, as it exacerbates muscle loss and frailty, while unintended weight gain, often from fluid overload or dietary imbalances, can complicate disease management (Roth-Stefanski *et al.*, 2021). Anemia, frequently linked to reduced erythropoietin production and nutritional deficiencies like iron and vitamin B12, further undermines energy levels and physical function (Weir, 2021). Additionally, hyperkalemia, resulting from impaired potassium excretion, necessitates dietary restrictions that can limit nutrient intake and variety (Maclaughlin *et al.*, 2023). Addressing these challenges requires a multifaceted nutritional strategy tailored to the needs of CKD patients to optimize their outcomes.

2.3.2 Associated risk factors of malnutrition in CKD Patients

The causes of malnutrition in people with CKD are varied (Mak, 2016). Based on the literature review (Shengrui *et al.*, 2024), protein intake and living with family are protective factors against malnutrition. Depression, reduced appetite, comorbidities, lengthy dialysis duration, inadequate dialysis, hemoglobin (Hb), requiring feeding assistance, and age are risk factors for malnutrition (Ioannidou *et al.*, 2014), which are further explained in the following sections. The Preferred Reporting Items for

Systematic Reviews and Meta-Analyses (PRISMA) flowchart for screening the literature is shown in Figure 2.1.

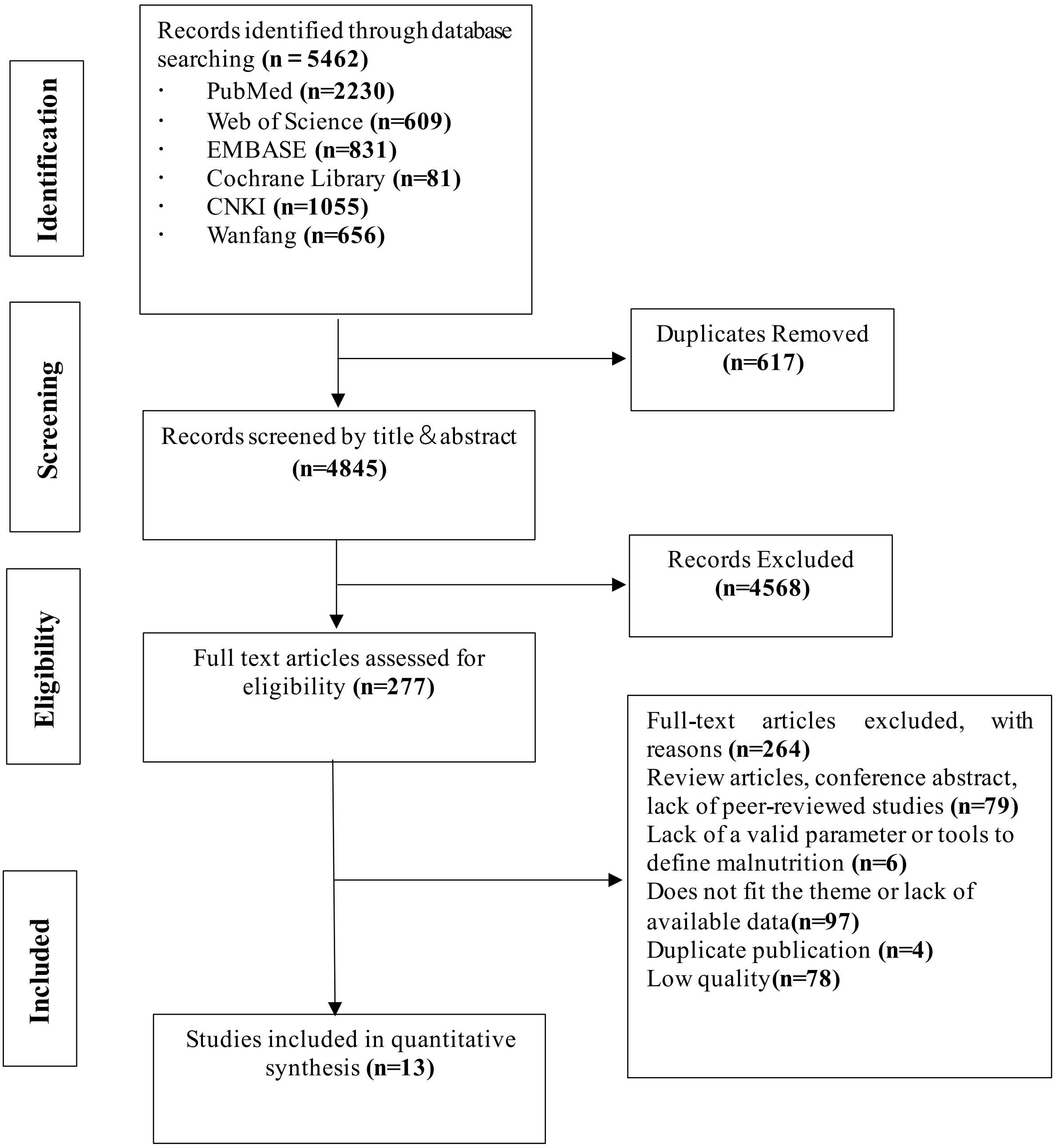

Figure 2.1 PRISMA flow chart of study selection process