










## CKJ REVIEW

# From bytes to bites: application of large language models to enhance nutritional recommendations

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## ABSTRACT

Large language models (LLMs) such as ChatGPT are increasingly positioned to be integrated into various aspects of daily life, with promising applications in healthcare, including personalized nutritional guidance for patients with chronic kidney disease (CKD). However, for LLM-powered nutrition support tools to reach their full potential, active collaboration of healthcare professionals, patients, caregivers and LLM experts is crucial. We conducted a comprehensive review of the literature on the use of LLMs as tools to enhance nutrition recommendations for patients with CKD, curated by our expertise in the field. Additionally, we considered relevant findings from adjacent fields, including diabetes and obesity management. Currently, the application of LLMs for CKD-specific nutrition support remains limited and has room for improvement. Although LLMs can generate recipe ideas, their nutritional analyses often underestimate critical food components such as electrolytes and calories. Anticipated advancements in LLMs and other generative artificial intelligence (AI) technologies are expected to enhance these capabilities, potentially enabling accurate nutritional analysis, the generation of visual aids for cooking and identification of kidney-healthy options in restaurants. While LLM-based nutritional support for patients with CKD is still in its early stages, rapid advancements are expected in the near future. Engagement from the CKD community, including healthcare professionals, patients and caregivers, will be essential to harness AI-driven improvements in nutritional care with a balanced perspective that is both critical and optimistic.

**Keywords:** artificial intelligence, chronic kidney disease, generative artificial intelligence, large language model, nutrition

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## BACKGROUND AND CURRENT PRACTICE

Medical nutrition therapy plays a vital role in the comprehensive, multidisciplinary care of patients with chronic kidney disease (CKD). Evidence-based dietary interventions, tailored to the stage of CKD and individual needs, have been shown to potentially slow disease progression [1, 2], improve blood pressure management and reduce proteinuria [3–5] and electrolyte imbalance-related complications arising from hyperkalaemia and hyperphosphataemia [6, 7]. Additionally, nutritional therapy may alleviate uraemic symptoms such as nausea and fatigue.

Providing personalized nutritional guidance is complex and multifactorial, as dietary adjustments need to address macronutrients, such as energy and protein, and micronutrients, such as potassium, sodium and phosphorus [6]. This requires a careful balance between meeting nutritional needs and managing CKD-imposed restrictions while avoiding malnutrition. Dietary recommendations must also account for restrictions from multiple comorbidities, a key factor as 96% of patients with CKD stage 3 in primary care have at least one comorbidity [8].

In today's clinical practice, access to a qualified dietitian is critical, as in-person guidance provides flexible, responsive nutritional interventions for managing each patient's evolving needs. To promote long-term dietary adherence, diets should be tailored to cultural and personal preferences and financial and time constraints. Combined with nutritional education, patients can make informed, conscious dietary choices in their everyday lives. However, dietitians may find it challenging to interpret and recommend ingredients or dishes of unfamiliar cuisines and eating habits. In addition, language barriers can impede adherence and patient safety by limiting communication, perhaps reducing the patient's understanding of dietary recommendations, and restricting dietitians' ability to assess and address patient needs.

Digital support tools and artificial intelligence (AI) solutions, including large language models (LLMs), are gaining traction in the field of CKD, with the future potential to benefit both patients and caregivers by individualizing and optimizing nutritional education and guidance. We envision LLMs, with their broad knowledge and flexibility, supporting current practices by generating personalized advice and meal plans, bridging language barriers and cultural differences and aiding in understanding of individual preferences [9]. In addition, a time-consuming task is to map the current nutritional intake, typically memorized or recorded by patients in food diaries or dish photos. The use of LLMs, leveraged by image recognition tools, could perhaps streamline this process with image-based ingredient recognition and nutritional content analysis. Figure 1 demonstrates an overview of the current workflow and potential touchpoints for LLMs to enhance dietary management. This review aims to describe current AI solutions applied to nutrition management for patients with CKD, outlining current limitations and exploring prospects.

## TECHNICAL FOUNDATIONS OF LLMS AND IMAGE RECOGNITION

LLMs are advanced AI systems designed to interpret, process and generate human language. In recent years, the public and life science community have been able to explore and enjoy accessible chatbot interfaces with back-end LLMs such as ChatGPT [10] and Gemini (gemini.google.com), with interest surging to discover potential and future applications.



**Figure 1:** The five steps (circles) of traditional workflow for nutrition support management. While application of an LLM into the nutrition management workflow can be envisioned in all five steps, it is most needed in the domains of 'develop patient specific plan' and 'implementation plan' (green circles).

Training of LLMs comprises two components: transformer architecture and reinforcement learning from human feedback. The primary task during training is next-word prediction, where the model learns to predict the next word in a sentence given the preceding words [11]. By analysing word relationships across entire contexts, LLMs capture linguistic patterns, grammar and real-world knowledge. For example, during training, the LLM observes how words like 'dialysis' and 'nutrition' are used in different contexts. When deployed and asked, 'What nutrients should dialysis patients be cautious with?', the model breaks the question into smaller units and generates a response based on patterns observed in its training dataset. If the LLM was trained on text describing nutritional guidance for patients on dialysis, it likely associates 'dialysis,' 'nutrition' and 'cautious' with 'potassium' and 'phosphorus', generating the response, 'Patients on dialysis should be cautious with foods high in potassium and phosphorous'. Thus, while LLMs seem to 'know' facts, their responses are generated based on word associations and probability, mimicking human communications derived from its training data.

Alongside the rapid advancements of text-handling LLMs, AI-powered image analysis tools like DALL-E (openai.com/index/dall-e-3), Vision AI (cloud.google.com/vision) and Azure Computer Vision (azure.microsoft.com) demonstrate impressive ability to describe images and generate images and videos from text-based instructions. Like LLMs, image analysis tools are trained on large image and text datasets, enabling recognition of objects, patterns, colours or other cues.

## AI IN NUTRITIONAL MANAGEMENT: EXISTING AND EMERGING USE CASES

### General nutritional guidance

LLMs like ChatGPT are designed to answer general inquiries, including those that are nutrition related. Recent research evaluated ChatGPT's competency in addressing common

Table 1: Overview of LLM and image recognition model use cases in supporting nutritional recommendations.

Field of focus	Summary	AI chatbot powered by LLMs
General nutritional guidance	A comparison of ChatGPT and human dietitians' answers to frequently asked nutrition questions [12].	ChatGPT
	ChatGPT was tested and successfully passed the Chinese Registered Dietitian Examination to evaluate its proficiency in evidence-based dietary advice [13].	ChatGPT, GPT 4
Recipe generation and nutritional estimation accuracy	Assessed nutritional recommendations and macronutrient (calories, carbohydrates, protein, fat) and micronutrient (phosphorus, potassium, sodium) information generated by ChatGPT for dialysis patients [14].	ChatGPT 4
	Assessed the efficacy of different AI models in discerning the potassium and phosphorus content in foods from 240 food items curated from the Mayo Clinic Renal Diet Handbook for patients with CKD [15].	ChatGPT 3.5, ChatGPT 4, Bard AI, Bing chat
	Assessed the energy intake (calories), nutrient accuracy (proteins, carbohydrates, fats and saturated fats) and meal variability generated by ChatGPT for patients with obesity, cardiovascular diseases and type 2 diabetes [16].	ChatGPT4
	Created personalized recipes tailored for individuals with food allergies [17].	ChatGPT 3
Language translation	Explored the application of ChatGPT for generating personalized dietary recommendations in various languages [14].	ChatGPT 4
Image recognition	An image recognition model based on deep learning for identifying food ingredients from images and offers nutritional guidance [13].	–
	A systematic review of AI-based digital image recognition methods for volume and nutritional content estimation [18].	–

nutritional questions by having dietitians provide their most frequently asked questions along with their own answers [12]. The same questions were asked to ChatGPT, and its responses were compared by 18 dietitians or 9 domain experts with respect to scientific accuracy, actionability and clarity. ChatGPT outperformed dietitians on five of eight questions and, notably, none of the dietitians' answers surpassed those generated by ChatGPT. In another recent study, both ChatGPT and GPT-4 successfully passed the Chinese Registered Dietitian Examination, demonstrating proficiency in providing evidence-based dietary advice [13]. ChatGPT's responses to medical nutrition questions aligned with expert advice, receiving favourable evaluations from 162 of 168 professional dietitians.

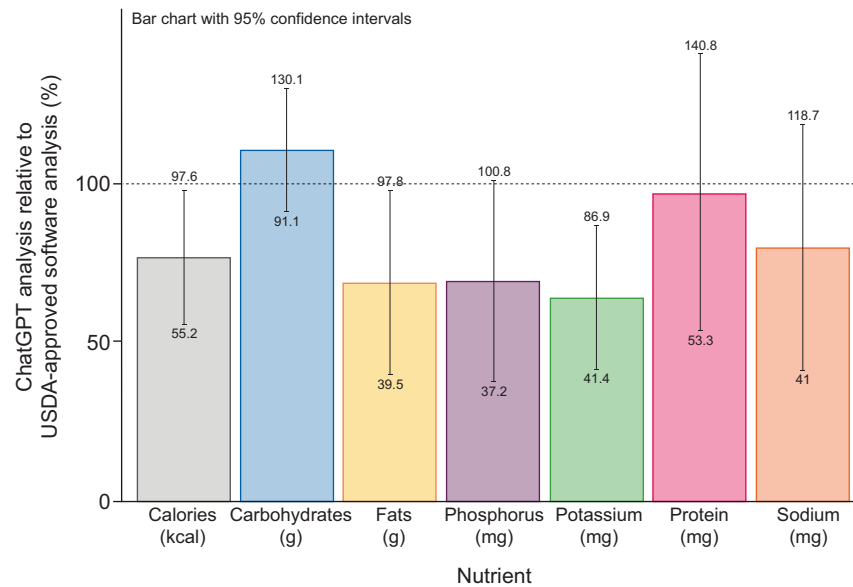
### Recipe generation and nutritional estimation accuracy

Providing personalized nutritional guidance is complex, requiring a balance between specific nutritional requirements and restrictions imposed by kidney disease and comorbidities. Many AI-aided chef solutions are available online, such as ChefGPT ([www.chefgpt.xyz](http://www.chefgpt.xyz); accessed 30 October 2024) and ChefAI ([www.chefai.net](http://www.chefai.net); accessed 30 October 2024), which generate recipes based on personalized prompts. However, none of these commercially available AI-aided chef solutions have been reviewed for CKD appropriateness.

Wang et al. [14] explored the use of ChatGPT 4 to generate personalized, kidney-friendly food recommendations. ChatGPT 4 was prompted with a fictive patient's demograph-

ics, clinical characteristics, food preferences, laboratory data and daily budget. A daily menu comprising five recipes with cooking instructions was created by ChatGPT 4 (found in [Supplementary Table S1](#)), quantifying their nutritional content accordingly. While the chatbot quantitated the carbohydrate content with reasonable accuracy (averaging 6% difference), calories were underestimated by 36% [95% confidence interval (CI) 44–88], protein by 28% (95% CI 25–167), fat by 48% (95% CI 29–81), phosphorus by 54% (95% CI 15–102), potassium by 49% (95% CI 40–68) and sodium by 53% (95% CI 14–139). Discrepancies regarding potassium and phosphorus may be partly explained by the modification of content through cooking techniques, unspecified portion sizes and limited data for ChatGPT training, possibly due to the lack of nutrition label components. Wang et al. [14] also assessed ChatGPT 4's performance in analysing the nutritional content of recipes available online (<https://www.freseniuskidneycare.com/recipes-and-nutrition>), sourced from a large dialysis organization (LDO). Interestingly, ChatGPT provided more accurate analysis of two recipes sourced from the LDO website, with differences ranging from 0 to 35% compared with the LDO's reported values. The percentage difference between the estimates provided by software from the U.S. Department of Agriculture (USDA; the reference, set to 100%) and ChatGPT's estimations of all five ChatGPT-generated and two LDO-sourced recipes are shown in Fig. 2.

Qarajeh et al. [15] demonstrated that LLMs performed better when used to predict the nutritional content for the CKD population in a dichotomized way. Potassium and phosphorus contents of foods were assessed by ChatGPT 3.5 and 4, as well



**Figure 2:** Nutritional analysis by ChatGPT 4 relative the USDA-approved nutritional software analysis. The data represents means and 95% confidence intervals. The red dotted line represents the ground truth (i.e. 100%), an analysis by a nutritional software approved by the USDA. Reproduced from Wang et al. [14].

as Bard AI and Bing Chat. ChatGPT 4 had the highest accuracy in predicting high or low phosphorus content (81%), while Bard AI had the highest (100%) accuracy in predicting whether foods had a high or low phosphate content (100%). In contrast to the study of Wang et al. [14], potassium and phosphorous contents were not quantified further [15]. To the best of our knowledge, apart from the articles by Wang et al. [14] and Qarajeh et al. [15], there are no published studies assessing the accuracy of LLMs applied for patients with kidney disease. For patients with type 2 diabetes, ChatGPT 4-generated meal plans achieved an accuracy of 96% in terms of nutrient content (proteins, carbohydrates, fat) and a mean difference of 8% in terms of energy content as compared with a knowledge-based recommender system that was used as the reference method [16].

Food allergies and intolerance are important considerations when individualizing recommendations. The ability of ChatGPT 3 to generate recipes suited for people with food allergies was explored by Niszczota et al. [17]. Most generated menus correctly excluded the allergens of interest (52 of 56 prompts). However, ChatGPT 3 incorrectly included almond milk in nut-free diets, which is particularly dangerous as nut allergies often manifest with severe consequences.

### Language translation

Miscommunication due to language barriers and illiteracy may induce inequality, reduce healthcare quality and compromise patient safety [19]. When an interpreter is unavailable, digital solutions for audio and text translation may be of help [20], such as AI-driven text and audio recognition tools like SeamlessM4T by Meta [21] or Google Translate (translate.google.com). These tools may bridge language barriers with real-time translations in >100 languages but can lack nuance in complex conversations and healthcare contexts [20, 22]. Multilingual LLMs such as BLOOM [23], excel in understanding context, although they might not be specifically designed for a clinical context. Wang et al. [14] used ChatGPT 4 to translate CKD-friendly dietary menus from English to Dutch, German, Hungarian, Mandarin and Spanish. Native speakers reviewed the translations and noted occasional issues, including grammar, omissions, word choice, context adaptation,

lexical variations and unit conversion errors. Translation quality was rated on a 5-point Likert scale (1, very poor–5, excellent), with an overall median rating of 4 (interquartile range 4–4).

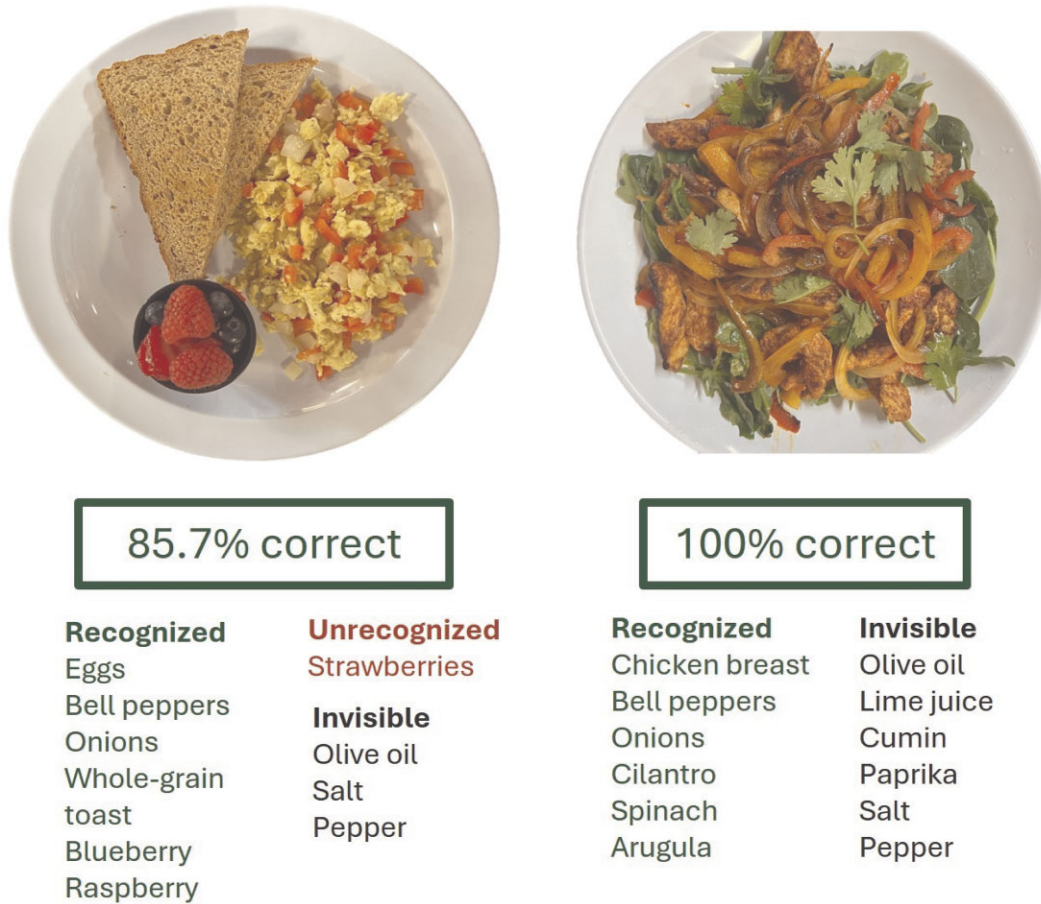
### Augmenting the use of LLMs by image recognition

Image recognition tools serve as a valuable complement to LLMs, enabling users to capture images of prepared dishes, food packages or barcodes for identification of ingredients [24, 25], portion sizes and nutritional contents, providing a convenient alternative to the manual food diary and aiding communication between patients and dietitians. Publicly available mobile applications offer a plethora of vision-based dietary support tools designed for various use cases and end users, e.g. diabetes. However, to our knowledge, no published studies have utilized vision-based tools specifically designed for dietary support of patients with CKD.

Dietary image recognition is commonly performed using machine learning techniques such as convolutional neural networks or deep learning. For example, Sun et al. [13] developed a deep learning-based image recognition model, Dino V2, to identify food ingredients. It achieved an impressive 82.5% accuracy in identifying the correct results while minimizing both false positive and false negative results. Ingredient recognition performance depends on the quality of the captured photo [26], as well as the complexity of the dish, particularly when it involves multiple mixed ingredients or unstructured layering. To state the obvious, vision-based AI systems, regardless of their sophistication, can only identify ingredients that are visible.

Like LLMs, ingredient recognition performance is dependent on the size, complexity and diversity of the pretraining dataset [27]. To date, there are limited regulatory frameworks or well-established benchmark image datasets: if these were available, they would enable head-to-head performance evaluations and aid developers and users in ensuring accurate advice and compliance with clinical standards. For example, a systematic review revealed that 22 imaging tools were trained using 37 different databases with various size and image contents [18], with the most popular used six times.





**Figure 3:** Images of meals cooked according to a recipe generated by ChatGPT. Image analysis by ChatGPT 4o identified between 85% (left) and 100% (right) of visible ingredients.

We explored the feasibility of LLMs and AI-driven image recognition to aid individualized renal dietary advice. ChatGPT 4o, an OpenAI model that provides GPT-4-level intelligence but improved capabilities across text, voice and vision, was asked to generate a daily menu. The AI-generated menus were prepared accordingly. Photos of the dishes were analysed by ChatGPT 4o. Figure 3 demonstrates ChatGPT 4o's ability to correctly identify >85% of the visible ingredients in these dishes.

To fully automate nutritional assessment of captured dishes, the tool needs to correctly identify ingredients and their quantities [28, 29]. A systematic review by Shonkoff et al. [18] examined AI recognition solutions for volume and nutritional contents estimation across 42 studies, reporting relative errors ranging from 0.1 to 38.3% for calories and 0.09 to 33% for volume estimation compared with ground truth.

Image-to-text generation can be employed to create recipes consisting of a title, ingredients and cooking instructions based on a captured image of a dish, as demonstrated by Salvador et al. [30] and Chhikara et al. [31]. The reverse example, text-to-image, can be used to visualize instructions, potentially enhancing recipe interpretability. We here demonstrate the capability of ChatGPT 4o (accessed October 2024) in generating images to illustrate cooking instructions for a four-step baked salmon recipe. Figure 4 shows a successful result with four images created as one image per instruction step. However, repeated generation showed significant errors, as illustrated in Fig. 5. Fig. 5A shows all instruction steps combined in

one image without sensible order, mislabelled ingredients and inconsistent oven temperature. In Fig. 5B ChatGPT 4o was unable to generate multiple images for each step in a sequence; instead, it generated six segmented images with incorrect step labels and content.

Instructions:

1. Preheat the oven: Set your oven to 400°F (200°C).
2. Make the marinade: In a small bowl, mix olive oil, lemon juice, garlic, Dijon mustard, honey (optional), salt, pepper and herbs.
3. Prepare the salmon: Place the salmon fillets on a baking sheet. Brush them with the marinade, coating all sides.
4. Bake the salmon: Bake in the oven for 12–15 minutes, until the salmon is flaky and opaque. Garnish with lemon slices and serve.

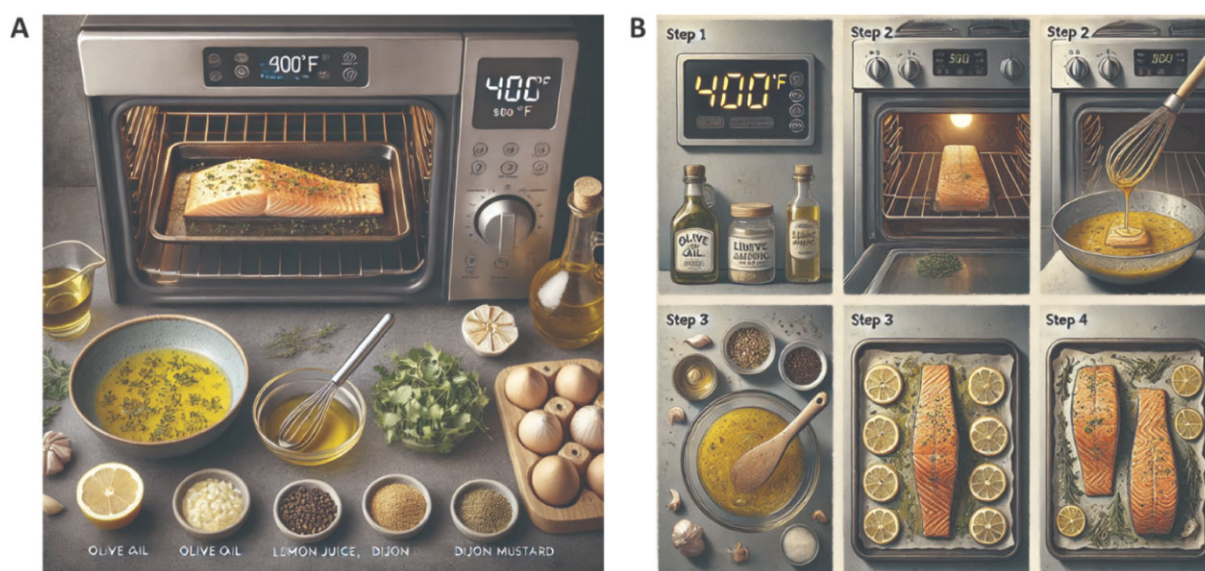
## TECHNICAL, ETHICAL, PRIVACY, REGULATORY AND SUSTAINABILITY CHALLENGES AND CONSIDERATIONS

### Technical challenges

The use of LLMs for nutritional care in CKD carries enormous potential for improvement of care [9]. Current non-LLM-driven digital dietary support tools designed for patients with CKD



**Figure 4:** Demonstration of a successfully created image. AI-generated images visualizing instructions in multiple steps, one image per step, enhancing recipe interpretability.



**Figure 5:** Demonstration of failed image creations. Both images were based on the same recipe. (A) All steps combined in one image without sensible order. (B) Six segmented images with incorrect step labels and content.

demonstrate crucial limitations in clinical applications. A recent review of 10 non-LLM CKD dietary support apps highlighted widespread inaccuracies and usability shortcomings, including high digital literacy requirements, a lack of security and interactive features and limited caregiver or family access for patient support [32]. None of the non-LLM apps investigated used the most contemporary nutrition guidelines on which to base their recommendations. To prevent inaccurate or low-quality information, LLMs can be pretrained or prompted with relevant clinical guidelines. It remains uncertain whether general LLMs like ChatGPT are sufficient or if they require specialized medical training or direct integration of clinical guidelines.

LLMs are inherently non-deterministic, producing variable outputs from identical inputs without disclosing the generation process. LLMs may be sensitive to language nuances and the user's ability to craft clear and precise prompts, impacting reliability. While creativity and flexibility are valuable assets, LLM unpredictability may pose risks in clinical settings. Safe, validated AI use requires educating both healthcare professionals and patients on proper interaction and interpretation of LLM-generated advice. For now, and the foreseeable future, AI tools can complement, not replace, existing healthcare resources. It is essential that a dietitian or another qualified nutrition expert

reviews AI-generated recommendations to ensure accuracy and suitability when designing patient menus and recipes.

### Ethical considerations

There are ethical obligations in the use of AI that include the clinician's duty to describe candidly its role, advantages and limitations and efforts to minimize biases and errors in professional curation. It is the clinician's responsibility to ensure that the advice generated is consistent and safe to the best of their knowledge. However, accountability for consequences arising from misinformation, whether it rests with the solution developer, the prescribing professional or the user, is unclear and remains a complex ethical and legal challenge.

### Privacy

Data privacy and safety are of the highest relevance when storing and handling sensitive information. Although legally binding regulations such as the Health Insurance Portability and Accountability Act in the USA and the General Data Protection Regulation in Europe exist, the risk of data breaches, misuse and privacy violations is not eliminated. Creating personalized



dietary advice with LLMs requires health records data, including sensitive medical and patient-reported information like dietary preferences, intolerances and financial or time constraints. Access to large datasets is also essential for training relevant AI tools. Beyond traditional data privacy risks, AI training and data processing may introduce additional, hypothetical vulnerabilities. For example, sensitive data may unintentionally persist in the AI model architecture and leak upon deployment, or AI tools may reidentify anonymous data by reverse engineering patterns or linking sensitive health information to indirect identifiers, such as age, location or publicly available data. Such risks, although hypothetical at this time, could threaten privacy and patient trust. As AI rapidly evolves, continuous risk analysis, explicit data consent and robust safeguards are crucial to protecting privacy and maintaining trust in clinical and research settings.

### Regulation and sustainability

Regulatory bodies are developing evolving guidance to ensure validation and accountability between healthcare providers and AI developers; however, this guidance is based on limited experience and evidence. The inherent complexity and lack of transparency in deep learning further obscure accurate and reliable oversight by both regulatory bodies and individuals, making effective regulation challenging. The US Food and Drug Administration is expected to release comprehensive regulations but has already published relevant guidance through an evolving approach. This includes the Software as a Medical Device guidelines (2013), Good Machine Learning Practices (2021) and the AI/ML Action Plan (2021). The European Union (EU) Guidelines on Trustworthy AI in 2019 was among the first frameworks that empowered more recent regulatory guidance. In January 2024, the World Health Organization released guidance on the ethics and governance of using LLMs in healthcare. In June 2024, the EU AI Act was passed, with key aspects including the establishment of an EU AI board, a risk-based classification system and penalties for non-compliance, but with exemptions for use of LLMs for scientific research and premarket development. The UK is yet to establish a regulatory body but has published guidance in association with other regulatory authorities, including the Medicines and Healthcare Products Regulatory Agency, UK General Data Protection Regulation, National Data Guidance, Equality Act 2010 and National Health Service AI Lab.

The sustainability and energy efficiency of LLMs are concerning due to their high computational demands and carbon emissions [33]. For instance, training LLaMA 2 produced 539 tonnes of carbon dioxide [34] and a single chatbot query can consume log-fold more energy than a search engine query.

### FUTURE DIRECTIONS

Generative AI, particularly LLMs, offer promising applications to enhance nutritional care for patients living with CKD. The ubiquity of smartphones and other accessible technologies unlocks new possibilities for personalized healthcare. In addition to the development of general LLMs, future improvements and refinements to a specific task are likely with the use of more advanced techniques, such as retrieval-augmented generation (RAG) for improving the capabilities of a select LLM [35]. In a RAG setup, the general knowledge of LLMs is enhanced by linking to an external database, which serves as a source to retrieve domain-specific information. This retrieved information is then added to the LLM along with the original prompt. In dietary ap-

plications, such a database could curate kidney-friendly recipes or relevant guidelines, refining the context of the prompt and improving the probability of generating relevant and accurate advice.

In-depth, personalized nutritional analysis remains time-consuming for renal dietitians and is generally being performed only once a year in the USA. In the future, AI-driven tools could emerge to aid more frequent nutritional analysis and ease continuous follow-up. In addition, generative AI could provide customized nutritional plans and recipes, tailored to individual patient profiles. These profiles could integrate factors such as food preferences, allergies, clinical health data and available budget and time to develop recipes that cater specifically to the patients' needs, e.g. generating instructional images and videos in the user's preferred language, providing step-by-step guidance that simplifies the preparation of customized, health-focused meals. In addition, food preferences and preferences of family members or tablemates can be incorporated into meal plan generation, customizing the main recipe to accommodate needs and wishes as far as possible, or by suggesting alterations for individual requests. As many LLMs are capable of memorizing conversations and preferences, integrate user feedback and provide follow-ups and reminders, interaction can be refined over time.

The flexibility of LLMs may also be beneficial in regions with limited or skewed food supplies, such as food deserts which are areas with limited access to supermarkets and affordable, healthy foods. Geographic data, such as a patient's ZIP code, could potentially be used to tailor generated recipes based on nearby supermarket locations, product availability and the user's transportation options, optimizing meal planning according to individual circumstances. For patients who order prepared meals from restaurants, LLMs could enhance their experience by identifying restaurants with healthy, kidney-friendly options. By leveraging AI-driven analysis of online restaurant menus, future applications could guide customers toward meals that align with their dietary and health needs, further supporting personalized nutrition and wellness.

### CONCLUSION

Technology continues to transform our lives, and LLMs are poised to become integral to daily routines. Specifically, LLMs offer promising tools to enhance effectiveness and efficiency in medical practice, including providing tailored nutritional guidance for patients with CKD. However, it is important to note that LLMs are capable of enhancement and aid, but cannot fully replace, the work of renal dietitians. To realize this potential, it is essential that healthcare professionals, patients and caregivers are closely involved in developing LLM-powered nutrition support tools. As a medical community, we should embrace the ways AI can improve practice, assess its readiness for clinical application and implement advancements with a critical yet optimistic approach [36].

### SUPPLEMENTARY DATA

Supplementary data are available at [Clinical Kidney Journal](#) online.

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## AUTHORS' CONTRIBUTIONS

All authors contributed to the conception, design, and development of this review. K.B. and H.Z. led the literature search. All authors drafted the initial manuscript. All authors reviewed and approved the final version.

## DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

## CONFLICT OF INTEREST STATEMENT

K.B. and H.Z. are employees of the Renal Research Institute (RRI), a wholly owned subsidiary of Fresenius Medical Care (FME). A.N.B. is a contract data analyst with the RRI. L.W. and N.G. are employees of FMC. K.B., L.W., P.K. and H.Z. are inventors of multiple patents in the kidney space. P.K. is a former employee of the RRI and holds stock in FMC. All other authors have declared no conflicts of interest.

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