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Nutritional Value of Pulses and Whole Grains

Edited by
Christopher P. F. Marinangeli

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About the Editor

Christopher P. F. Marinangeli

Dr. Marinangeli has a PhD in food and nutrition science and is a registered dietitian. He is a scientist and food industry professional with over 12 years of experience across the consumer packaged goods and the Canadian agriculture sectors. As a recognized expert in national and international food regulations and the effects of dietary components on cardiometabolic health, his expertise includes human nutrition sciences, regulatory affairs, and the use of consumer insights and equity for developing effective strategies and tactics for dietary integration of healthy food options. Currently, Dr. Marinangeli leads the Regulatory Centre of Excellence at Protein Industries Canada. Prior positions include senior nutritional and regulatory positions at Pulse Canada and Kellogg Canada. He has served on numerous advisory committees, including a board member for the Canadian Federation of Dietetic Research (CFDR) and member of the Canadian Advisory Committee for ILSI North America. He currently serves on the Scientific Advisory Committee for CFDR and jury member for Agriculture Agri-food Canada's Food Waste Reduction Challenge: Novel Technologies.

Preface to "Nutritional Value of Pulses and Whole Grains"

Pulses and whole grains are well known components of healthy dietary patterns. It is also well known that these two foods continue to undergo study in the context of human health. However, the opportunity to lead this Special Issue of *Nutrients* on the *Nutritional Value of Pulses and Whole Grains* provided a platform to present research across a broad array of outcomes, in addition to health, that highlight their benefits on an individual and societal level. The broad scope of research presented in this book underscores the need for data continuity across the food system to foster the adoption of healthy and sustainable dietary patterns with the use of these two foods. Obvious touchpoints include health, but also regulatory, policy, economic and consumer analysis that are also critical to effective dietary change. It is hopeful that this compendium of manuscripts can help facilitate and expedite the expansion of datasets aimed at increasing the use pulses and whole grains, and other healthy foods, across the food sector for meaningful integration into dietary patterns that deliver on enhanced health and wellbeing.

My sincere appreciation to all of the authors for their thoughtful and innovative contributions to this body of work. I would also like to thank the support staff at MDPI.

Christopher P. F. Marinangeli
Editor

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Editorial

The Special Issue on "The Nutritional Value of Pulses and Whole Grains": A Continued Endeavor to Delineate Their Benefits for Today and Addressing the Challenges of the Future

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Dietary patterns are increasingly focusing on the interplay between nutritional adequacy, reduction of chronic disease, and environmental sustainability. While both pulses and whole grains have a rich history as part of healthy and sustainable dietary patterns [1,2], there is ongoing interest in the use of these foods, and their ingredient derivatives, to delineate effects on multiple aspects of human health and quantify their individual and societal benefits. Both pulses and whole grains are considered to be nutrient dense foods, with fibre and micronutrients being common nutritional attributes that are promoted in dietary guidelines [3]. Pulses contain considerably higher levels of protein compared to whole grains [3]. However, amino acid complementarity between these foods is an additional value proposition, as pulses are leveraged in diets that index higher on plant protein sources and can be an efficient means of replacing animal-derived proteins with those from plants [4].

This Special Edition of Nutrients, "The Nutritional Value of Pulses and Whole Grains" provides a series of papers that touch on various topics and themes that are relevant to a changing food landscape aimed at incorporating more pulses and whole grains into diets. In addition to identifying near and future benefits of these foods, the provided analysis underscores some of the underlying challenges around their incorporation into diets and examination of benefits, which could be critical for using whole grains and pulses in a manner that aligns with global dietary objectives.

Whole grains and pulses are a common thread in healthy dietary patterns. Whether emphasized by specific dietary guidelines in a jurisdiction, as a pattern of eating based on shared attributes across a region, such as the Mediterranean diet, or to tackle societal challenges across metrics of health and sustainability, both pulses and whole grains are touted for their nutritional contributions. Low consumption of whole grains and pulses (and other legumes) are associated with well over 3 million deaths, primarily due to cardiovascular disease [5]. On its own, diets low in dietary fibre have been associated with $\geq$1million deaths from cardiovascular disease and diabetes and $\geq$20 million disability-adjusted life years globally [5]. Studies have reviewed the effects of pulses and whole grains on reducing risk factors for cardiometabolic diseases, such as lipids, blood pressure, and glycemic response [6–8]. Two reviews published as part of this compendium offer an update and summation of data linking whole grain and pulse (lentil) on markers of inflammation and post-prandial glycemic response, respectively.

The review by Milesi et al. [9] provides a systematic assessment of whole grain consumption on inflammatory biomarkers using criteria that aligns with an accepted definition of whole grains in adults. Analysis of 31 randomized clinical trials (RCTs) showed that overweight/obese individuals and those with pre-existing health conditions demonstrated a reduction in markers of inflammation, primarily CRP [9]. The study by Clark et al. [10] showed that at least 110 g lentils is required to generate a relative reduction in post-prandial glycemic response by 20%, with effects most strongly correlated with levels of

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protein (r = 0.5513) and fibre (r = 0.3326). Low glycemic response and glycemic index foods have been promoted for reducing risk of cardiometabolic diseases and diabetes management [11–14]. Using the diabetic rat model, the study by Ren et al. [15] investigated mechanisms for hypoglycemic effects of foxtail millet, a cereal grain that is cultivated across 26 countries. 16S RNA sequencing revealed a correlation between abundance of Lactobaccillus and Ruminococcus_2 and lower fasting and post-prandial glycemic levels. Molecular analysis demonstrated activation of the P13K/AKT signaling pathway, leading to decreased gluconeogenesis and increased glycolysis; and inflammation was suggested given the observed down regulation of NFκB. Collectively, these studies strengthen the importance of carbohydrate quality in food choices, which encompasses "whole food" constituents, low glycemic response and glycemic index foods, and dietary fibre [16]. Carbohydrate quality is increasingly emphasized as a value proposition for consumers to choose foods with significant effects on dietary quality and reduced risk factors for chronic disease [17,18]. The information disseminated in this Special Issue brings new perspectives and data to support the use of pulses and whole grains as healthy carbohydrate foods.

As briefly discussed above, the global burden of disease reports have been effective at translating the societal costs of unhealthy dietary patterns. Over the last decade, additional analyses have aimed to assign a "cost-of-illness" as a novel perspective by evaluating potential healthcare savings when a proportion of a population adopts a healthy diet. In the past, various diets [19], and their components, including, pulses, and whole grains have been associated with significant direct and indirect healthcare cost savings by estimating putative associations with constipation, cardiovascular disease, and cancer in Canada [20,21] and the US [22,23]. In this issue, this analysis was expanded to Australia and Finland. Abdullah et al. [24] showed that increasing whole grain consumption to a 48 g/day target across 5 to 100% of the population could decrease healthcare costs associated total and colorectal cancer by 126.2 M to 1.37 B AUD over 20 years. Similarly, Martikainen et al. [25] used 3 theoretical scenarios (1. 10% unit increase in the Finnish population consuming at least one whole grain serving per day; 2. Increase consumption of one or more whole grain food servings per day among adults already consuming at least one whole grain serving per day; 3 a combination of scenarios 1 and 2) for increasing servings whole grains to estimate potential reductions healthcare costs associated with type 2 diabetes in Finland [25]. Despite already high consumption rates of whole grains compared to other countries in the EU, 286 M€ to 989 M€ in healthcare and productivity cost savings were projected over 10 years, respectively, across scenarios 1–3. Over 30 years, modeled savings increased from over 1.2 B€ to 4.2 B€ and generated 44,237 to 154,094 quality-adjusted life years [25]. In addition to better health, these and other data support top-down dietary guidelines and policies in the context of a balanced and healthy diet to drive broad societal benefits.

One cannot ignore current and future challenges for expanding consumption of both pulses and whole grains. While promoted in dietary guidelines, consumption of these two foods remains relatively low relative to recommendations [1]. The analysis of 6 cycles of NHANES by Mitchell et al. [26] from this collection demonstrated no significant trend in pulse consumption from 2003–2014 with per capita consumption ranging between 19.3 and 24.9 g/day. Although pulse consumers reported higher intakes of dietary fibre, folate, potassium, iron, and protein at intakes $\geq$69.4 g/day compared to non-pulse consumers, only 27% of adults consumed pulses on one of the two days of the survey [26]. These low consumption rates of pulses mirror previous analysis of the NHANES [27] and the Canadian Community Health Survey [28]. This is corroborated by other data demonstrating that pulses are relatively minor contributors to total protein intakes of diets in Canada [29], the US (~1.3%) [30], France (<1%) [31,32], and the UK (not reported as a significant source of protein) [33]. While consumers are somewhat more familiar with whole grains, in some regions, such as the US, only a fraction of the recommended level of intake have been shown to be consumed on any given day [34].

Over the last decade however, there has been significant growth in the number of manufactured food products that are leveraging whole grains and pulses as ingredients to bolster their actual or perceived nutritional density. The study by Bielefeld et al. [35] demonstrated that the number of legume food products grew from 312 products in 2019 to 610 in 2021 across four major grocery retail outlets in Sydney Australia. Furthermore, legume-formulated snack foods showed the greatest increase (n = 88), with the legume chip category growing by 357%. Nutrient content claims represented the most prominent type of claim used across foods, with most claims promoting foods as a source of dietary fibre (n = 246), gluten free (n = 216), and source of protein (n = 208) [35]. Claims identifying legume foods as clean label (no artificial colours, flavours or preservatives) (n = 252), vegetarian/vegan (n = 232), and organic (n = 115) were also prominent in the 2021 food audit. However, the analysis of nutritional quality of whole grain cereal-based products within the Italian retail market suggested that, without a harmonized legal definition of whole grains, the presence of whole grains cannot be used as a stand alone marker of nutritional quality [36]. Levels of dietary fibre were similar between foods formulated entirely or partially with whole grain ingredients, with these foods containing more sodium than refined grain products. These results speak to some of the consumer challenges in food innovation, with varying motivations and priorities of food attributes across consumer segments [36]. In the same regard, the study by Sajdakowska et al. [37] evaluated consumer motivations and perceptions of pasta and pasta with added fibre. Results segmented consumers as quality, sensory, convenience, or neutral-oriented, with health and fibre promoting statements scoring highest in the quality-oriented segment compared to other groups. Sensory-oriented individuals also indicated that pasta with added fibre has a less appealing taste and visual appearance compared to other groups. These results align with other consumer analysis where taste and price have been the top two purchase drivers in the US over the last 10 years [38]. Overall results corroborate various initiatives to enhance the nutritional profile of manufactured foods, where pulses and whole grains, can underpin such efforts. However, deliverance on those functional drivers will be required for these foods to support adoption of healthy dietary patterns, but likely cannot be achieved without understanding consumer attitudes and motivations toward food choices.

Finally, the final two articles target some of the ongoing challenges for facilitating and understanding the impacts of whole grains and pulses on dietary patterns. The first was led by members of the Whole Grain Initiative; a global consortium comprised of members of academia, government, and industry with a focus on promoting whole grain consumption [39]. The consortium stresses that lack of consensus on a definition of whole grains, and a whole grain food, creates inconsistencies for consumers achieving evidenced-based benefits from whole grain consumption [39]. Recall, that using an acceptable definition of whole grain foods was used by Melesi et al. [9] to summarize the association between whole grain intake and markers of systemic inflammation and the study by Dall'Asta et al. [36] suggested that not having a legal definition of whole grains has created a heterogeneous food environment in Italy with inconsistent nutritional attributes around whole grain foods. In this regard, van der Kamp et al. [39] suggest that only foods containing a minimum of 25% whole grain ingredients (based on dry weight) be eligible for a front-of-pack whole grain claim. Given the breadth of experts establishing proposed definitions for whole grain foods, the proposed definitions and labelling requirements could be used by regulatory agencies for the development of nutritional policies.

The remaining paper by Mitchell et al. [40] discusses the limited data that is available for evaluating intakes of pulses and pulse-derived ingredients. As mentioned previously, consumption levels of pulses are low in many developed jurisdictions that acquire populational food intake data through national surveys. However, given that pulses are legumes, but not all legumes are pulses, pulse consumption is often measured as part of a broader legume food group [40]. This presents some challenges, as pulses have unique nutritional attributes and patterns of consumption compared to other legumes, such as soy and peanuts. The editorial by Mitchell et al. [40] highlights this challenge in the context of the US, where, not until the 2020–2025 Dietary Guidelines for Americans" had the term "pulse" been recognized. With a global focus on enhancing consumption of pulses as part of healthy and sustainable dietary patterns, using the specific terminology to identify pulses in epidemiologic databases is required for generating optimal consumption rates and to create more robust data sets regarding the effects of pulses on nutrient intakes and chronic disease outcomes.

This Special Issue of Nutrients provides a snapshot of interesting developments in the value of pulses and whole grains in healthy dietary patterns. These foods and their ingredients can be useful for bolstering the nutritional value of manufactured food products. However, understanding the expectations of consumers could be critical for offering foods that deliver on individual and societal benefits. At the same time, a judicious examination of policies, regulations, and research methods could be a meaningful exercise to further delineate and ascertain benefits from using these foods more liberally in the food system. Whole grains and pulses continue to be dietary assets that align with global dietary objectives across various nutrition, health, and economic goals.

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Review

Whole Grain Consumption and Inflammatory Markers: A Systematic Literature Review of Randomized Control Trials

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Abstract: Whole grain foods are rich in nutrients, dietary fibre, a range of antioxidants, and phytochemicals, and may have potential to act in an anti-inflammatory manner, which could help impact chronic disease risk. This systematic literature review aimed to examine the specific effects of whole grains on selected inflammatory markers from human clinical trials in adults. As per the Preferred Reporting Items for Systematic Reviews (PRISMA) protocol, the online databases MEDLINE, Embase, Cochrane, CINAHL, and Scopus were searched from inception through to 31 August 2021. Randomized control trials (RCTs) $\geq$ 4 weeks in duration, reporting $\geq$1 of the following: C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor (TNF), were included. A total of 31 RCTs were included, of which 16 studies recruited overweight/obese individuals, 12 had pre-existing conditions, two were in a healthy population, and one study included participants with prostate cancer. Of these 31 RCTs, three included studies with two intervention arms. A total of 32 individual studies measured CRP (10/32 were significant), 18 individual studies measured IL-6 (2/18 were significant), and 13 individual studies measured TNF (5/13 were significant). Most often, the overweight/obese population and those with pre-existing conditions showed significant reductions in inflammatory markers, mainly CRP (34% of studies). Overall, consumption of whole grain foods had a significant effect in reducing at least one inflammatory marker as demonstrated in 12/31 RCTs.

Keywords: whole grain; refined grain; inflammation; inflammatory markers; C-reactive protein; tumor necrosis factor; interlukin-6

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1. Introduction

Whole grains are defined by Food Standards Australia and New Zealand (FSANZ), to be ' ... intact, dehulled, ground, cracked or flaked grains where the components–endosperm, germ and bran are present in substantially the same proportions as they exist in the intact grain' and includes wholemeal [1]. More recently, a consensus definition of whole grain as a food and as an ingredient was published with the aim of assisting in nutrition education and food labeling, but this also provides useful guidance for research [2]. Foods containing whole grains are both higher in nutrients and dietary fiber, as compared to refined grain alternatives, and in observational studies, diets higher in whole grains positively impact chronic disease, such as type 2 diabetes mellitus [3], cardiovascular disease (CVD) [4], certain cancers [4] including colorectal cancer [5–8], and other influencing risk factors, such as weight [9], and markers for CVD, such as triglyceride and cholesterol levels [10]. In addition, the nutrient bundle within whole grains contains potential anti-inflammatory properties, which is of importance as elevated levels of inflammatory biomarkers are linked to an increase in chronic disease risk [2,3]. The benefits of whole grain foods, including pseudo grains, quinoa, buckwheat, and amaranth, have been known for several decades, and included in the Australian Dietary Guidelines since 1979 [11].

Chronic disease was responsible for 9 out of 10 deaths in Australia in 2018, and 61% of the total burden of disease in Australians in 2017 [12], indicating the potential importance of improved dietary guidance and dietary patterns. However consumption of whole grain foods continues to remain at a low level, with Australian adults only consuming 21 g/day, less than half of the 48 g daily target intake (DTI) [11,13]. Furthermore, diets low in whole grains have been identified as the second greatest dietary risk factor for mortality in the Global Burden of Disease studies [14], highlighting the importance of dietary patterns.

The anti-inflammatory effects of whole grains can be examined via inflammatory markers, such as C-reactive protein, (CRP), interleukin-6, (IL-6), and tumor necrosis factors (TNF), and can potentially downregulate an inflammatory response [15]. Inflammatory markers change in response to a cascade of internal metabolic processes, where chronic inflammation can lead to chronic disease [15].

There is a growing body of evidence linking whole grain consumption with overall health benefits; however, the specific influence of whole grains on inflammatory markers is conflicting [11,16]. To date, systematic reviews of randomized controlled trials (RCTs) have focused on the consumption of whole grains and their association with individual chronic health diseases, such as CVD or T2D [17]. Others have focused specifically on dietary fiber levels in whole grains and associated effects; however, there is no current summation of the literature focusing solely on the consumption of whole grains and their direct effect on inflammatory markers. Although there are two previously published systematic reviews in this area [17,18], an update was necessary that focused only on adults, with a strict criteria for whole grain to meet the accepted definition and to clarify other discrepancies. This systematic literature review aimed to examine the specific effects of whole grains on inflammatory markers from human clinical trials in adults. The intent was to investigate whether the consumption of whole or pseudo grains, over refined grains, resulted in changes in inflammatory markers, based on results in human subjects in studies $\geq$ 4 weeks duration.

2. Materials and Methods

This systematic literature review of RCT was performed to assess the effect of whole grain consumption on inflammatory markers following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. This study was registered with the International Prospective Register of Systematic Reviews (CRD: pending).

2.1. Eligibility and Exclusion Criteria

The research question 'Is there an effect of whole grain consumption on measures of inflammation?' was developed using the Population, Intervention, Comparator, Outcome (PICO) format (Figure S1). Publications needed to meet the following inclusion criteria: (a) RCT, parallel, or cross-over design; (b) studies conducted on humans aged $\geq$18 years; (c) studies $\geq$ 4 weeks in duration; (d) studies with interventions including both whole grain and pseudo grain diets, where whole grains included: cereal grains; wheat; including spelt, emmer, einkorn, Khorasan or kamut, durum, and faro; oats, corn/maize, rice, teff, canary seeds, Job's Tears, barley, sorghum, rye, millet and triticale, and pseudo-cereal grains; amaranth, buckwheat, quinoa, and wild rice; (d) reporting $\geq$1 of the following serum inflammatory markers: interleukin-6, (IL-6), C-reactive protein, (CRP), tumor necrosis factor (TNF). Full search terms can be found in Table S2.

The following exclusion criteria were applied; (a) studies conducted on humans < 18 years; (b) study intervention arms not randomized; (c) studies < 4 weeks in duration. Although inflammatory markers were examined by both Jenkins et al. [19] and Kristensen et al. [20], the intervention diet included several foods, not just whole grain foods; therefore, these studies were excluded from the current review.

2.2. Search Strategy

The following online databases were searched: Medline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL). Available online: https://ovidsp.ovid.com/ (accessed on 13 December 2021), and CINAHL. Available online: https://www.ebsco.com/ (accessed on 13 December 2021), from database inception until 31 August 2021. In addition, reference lists of eligible studies were scanned and PubMed. Available online: https://pubmed.ncbi.nlm.nih.gov/ (accessed on 13 December 2021).

Was searched manually for any additional studies. The search strategy was designed in Medline and translated for other databases (Table S2). Grey literature, abandoned trials, and any journals published in languages other than English were excluded from the search strategy.

2.3. Study Selection, Data Extraction, and Quality Assessment

Reviewer G.M extracted all citations into EndNote X9, with duplicates removed manually. Reviewer G.M independently double screened all titles and abstracts, with any uncertainty and assistance from S.G. Following title and abstract screening, a full-text screen was completed on the remaining articles by two independent reviewers (S.G. and G.M.). Reviewers met and resolved any discrepancies, with any remaining uncertainty resolved by a third reviewer (A.R.).

A data extraction form was created in a Microsoft® Excel® spreadsheet (Microsoft 365 MSO Version 2109.14430.20306 Redmond, WA, USA) to facilitate the retrieval and storage of relevant data. Extracted data included study design (parallel or cross-over), study duration, participant characteristics, number of participants, control and intervention diet, outcomes measured, and results obtained (baseline, endpoint data, and *p*-value).

The included studies were reviewed for risk of bias using the Cochrane Risk of Bias tool (Rob2) for RCTs [21]. Reviewer G.M assessed studies to determine if each study had low, some concerns, or high risk of bias. Assessment criteria included risk of bias arising from recruitment of subjects, the randomization process, deviations from the interventions, missing data, measurement of outcome, or selection of the reported result. A second reviewer (S.G.) was consulted over any uncertainties.

2.4. Data Analysis

Tabulation of studies including reported mean ± SD of baseline and endpoint data and statistical significance (*p*-value) for within-group and between-group intervention changes for each study, and for studies with multiple intervention arms was performed. Within the included studies, outcomes were considered statistically significant when $p < 0.05$. The outcome measures were maintained as per the study units due to the differences in the various experimental methods used. Studies were then categorized into population groups based on the authors' description of participants: healthy individuals, overweight or obese individuals, individuals with pre-existing conditions, and others (prostate cancer).

3. Results

3.1. Search Results and Study Selection

The initial search, conducted on 31 August 2021, returned a total of 730 studies. An additional four studies were identified from the reference list of eligible studies and manual searches from PubMed. After the removal of duplicates, 397 were screened for the title and abstract, with a further 312 studies excluded. A full-text review was completed on the remaining 85 records, with 47 removed due to the type of study, study did not have an adult population, or length of the RCT < 4 weeks. The remaining 38 studies were further assessed, with six removed as the control or intervention diet was not whole or refined grains and one measured inflammation in fecal matter, not from blood serum. A remaining total of 31 RCTs met the inclusion criteria and were included in the systematic review (Figure 1).

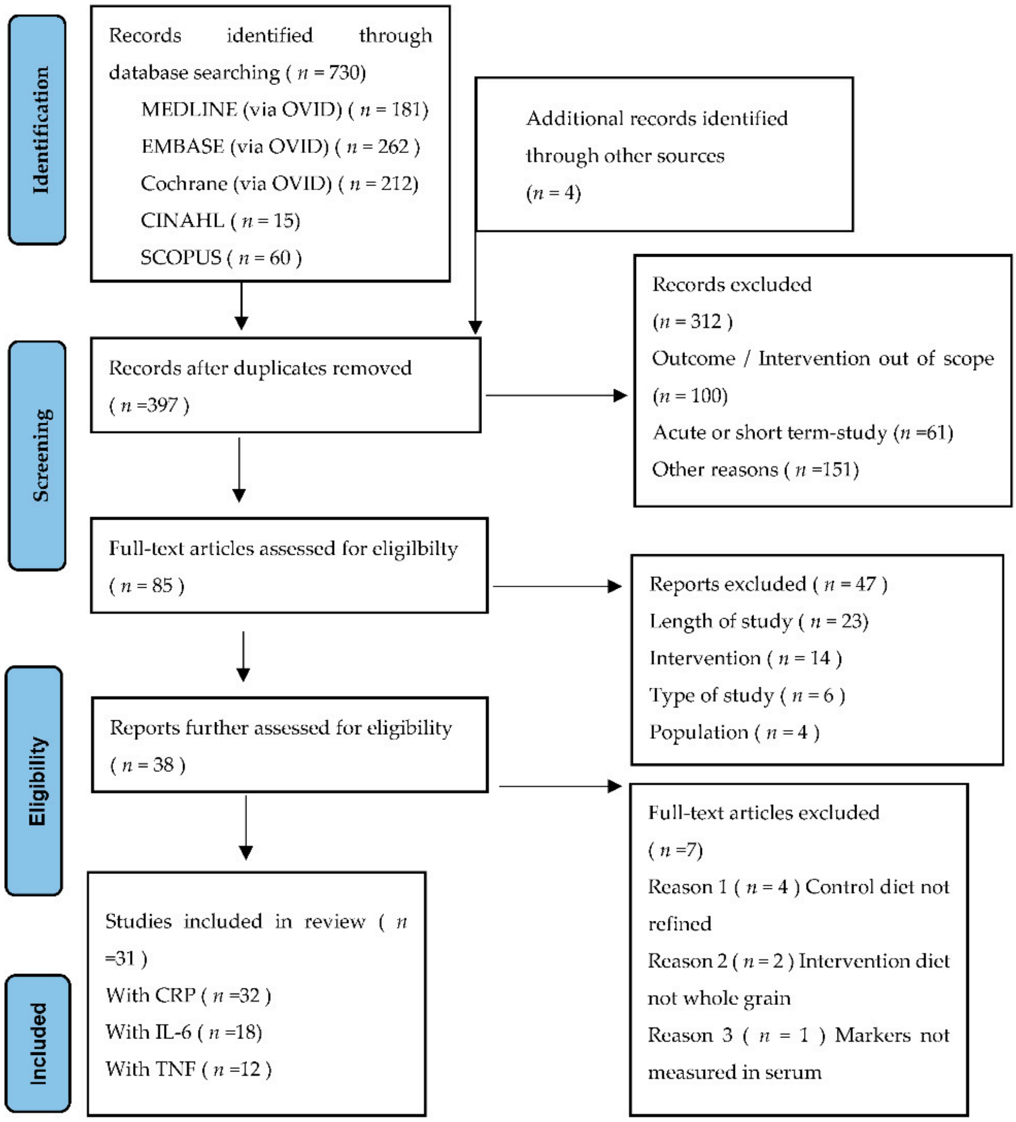

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram for study selection.

3.2. Study Characteristics

Of the 31 studies included in analysis, 16 were parallel RCTs and 15 were crossover trials. Of these studies, three RCTs included two intervention arms, and thus were split into a further three studies [22,23]. Table 1 displays the study characteristics. Two studies comprised whole grain interventions in healthy populations, 16 studies overweight or obese, 12 pre-existing conditions, and one reviewing another disease state: prostate cancer. The studies had a total of 2047 participants, with a mean age of 49.7 (range 20–80 years old) and the mean duration of the study was 12.5 weeks (range 4–24 weeks).

Table 1. Characteristics of studies examining whole grain consumption and inflammatory markers.

Study	Design and Duration	N (I/C)	Characteristics	(M/F)	Age (Years)	Intervention Diet	Control Diet
Ampatzoglou et al. 2016 [24]	Cr 6 weeks	33 (33/33)	Healthy	(12/21)	48.8 ± 1.1	WG > 80 g/day	RG diet; <16 g/day WG
Andersson et al. 2007 [25]	Cr 6 weeks	30 (30/30)	Overweight	(8/22)	59 ± 5	Various WGs = 112 g/day	Various RGs-111 g/day
Brownlee et al. 2010 [22]	P 16 weeks	266 (85/81/100)	Overweight	(133/133)	G1: 45.9 ± 10.1; G2: 45.7 ± 9.9; G3: 45.6 ± 1.0	G1: WG 60g/day; G2: 60 g/day 8 weeks + 120 g/day 8 weeks	Same diet as prior WG < 30 g/day
Connolly et al. 2011 [26]	Cr 16 weeks	32 (16/16)	Glucose intolerant or mild to moderate hypercholesterolamic	(12/20)	23–64	WG: 45 g WG/day as breakfast cereal	RG: 45 g/day as breakfast cereal
Giacco et al. 2013 [27]	P 12 weeks	123 (61/62)	Metabolic syndrome	N/A	40–65	WG or WW foods to replace RG	RG foods only for breads, pastas, cereals
Harris Jackson et al. 2014 [28]	P 12 weeks	50 (25/25)	Metabolic syndrome	(25/25)	35–45	187 g WG/day	RG, WG = 0 g/day
Hoevenaars et al. 2019 [29]	P 12 weeks	50 (25/25)	Overweight and obese	(19/31)	45–70	98 g WG/day	98 g RG/day
Iversen et al. 2021 [30]	P 12 weeks	242 (121/121)	Overweight and obese	(95/147)	30–70	Rye 53–60 g/day	Wheat 66 g/day
Joo et al. 2020 [31]	P 12 weeks	49 (26/23)	Metabolic syndrome	(38/11)	44.3 ± 6.1	Black rice powder 60 g/day	White rice powder 60 g/day
Katcher et al. 2008 [32]	P 12 weeks	50 (25/25)	Obese with metabolic syndrome	(25/25)	WG 45.4 ± 8; RG 46.6 ± 9.7	WG: 5, 6, 7 serves on hypocaloric diet	No WG foods in hypocaloric diet
Kazemzadeh et al. 2014 [33]	Cr 14 weeks	35 (20/15)	Overweight and obese	(0/35)	32.6 ± 6	Brown rice 150 g/day	White rice 150 g/day
Kirwan et al. 2016 [34]	Cr 8 weeks	33 (33/33)	Overweight and obese	(6/27)	39 ± 7	WG 93 ± 19 g/day	RG, WG = 0 g
Kondo et al. 2017 [35]	P 8 weeks	28 (14/14)	Type 2 Diabetes	(18/10)	40–80	Brown rice (250 cal = 182 g) to replace 10/21 meals/week	White rice (250 cal = 153 g) to replace 10/21 meals/week

Table 1. *Cont.*

Study	Design and Duration	N (I/C)	Characteristics	(M/F)	Age (Years)	Intervention Diet	Control Diet
Kopf et al. 2018 [36]	P 6 weeks	31 (17/14)	Overweight and obese	N/A	WG:39.2 ± 13.5 RG:27.6 ± 5.9	Whole grains 3.4 ± 0.2 serves/day	Refined grains 7.1 ± 0.7 serves/day
Li et al. 2018 [37]	Cr 8 weeks	30 (15/15)	Overweight and obese	(30/0)	36–70	20 g quinoa flour/day in form of 160 g bread roll	20 g refined flour/day in form of 160 g bread roll
Ma et al. 2013 [23]	P 30 days	199 (65/71/63)	Type 2 Diabetes & Metabolic Syndrome	(84/115)	20–65	WG1: 50 g oat germ/day WG2: 100 g oat germ/day	Usual diet Usual diet
Malik et al. 2019 [38]	Cr 14 weeks	113 (55/58)	Overweight BMI > 23	(62/51)	25–65	Brown rice 182 g/day	White rice 175 g/day
Meng et al. 2018 [39]	Cr 13 weeks	11	Overweight and obese	(4/7)	50–80	Unrefined carbohydrate 19.5 g fiber/day	Refined carbohydrate 9.6 g fiber/day
Munch Roager et al. 2019 [40]	Cr 16 weeks	50 (25/25)	Overweight and obese	(18/32)	20–65	WG 157.9 ± 35 g/day	RG diet; WG 6 ± 4.8 g/day
Navarro et al. 2018 [41]	Cr 4 weeks	80	Healthy	(40/40)	18–45	Whole grain foods 55 g fiber/day	Refined grain foods 28 g fiber/day
Pavadhgul et al. 2019 [42]	Cr 8 weeks	24	Hypercholesterolamic	(12/12)	30–60	Whole grain oat porridge 70 g/day	Rice porridge 70 g/day
Pavithran et al. 2020 [43]	P 24 weeks	80 (40/40)	Type 2 diabetes	(52/28)	LGI: 54.43 ± 7.57 Control: 51.93 ± 7.43	LGI: whole wheat, red rice	Usual diet
Pourshahidi et al. 2020 [44]	Cr 12 weeks	40	Overweight and obese	(12/28)	57.68 ± 6.15	15g quinoa biscuits (60 g flour/100 g)	Control iso-energetic biscuits
Saglam et al. 2018 [45]	P 4 weeks	24 (12/12)	Type 2 Diabetes	(0/24)	40.29 ± 6.81	Whole grain bread 270 cal/ 35.32 g fiber/day	Whole wheat bread 227 cal/7.39 g fiber/day
Schutte et al. 2018 [46]	P 12 weeks	50 (25/25)	Overweight	(31/19)	WG: 61 [51–70] RG: 61 [4–69]	WG 98 g/day	RG 98 g/day

Table 1. *Cont.*

Study	Design and Duration	N (I/C)	Characteristics	(M/F)	Age (Years)	Intervention Diet	Control Diet
Tighe et al. 2010 [47]	P 12 weeks	136 (73/63)	Overweight	(68/68)	WG1: 51.6 ± 0.8; RG: 51.8 ± 0.8 WG2: 52.1 ± 0.9; RG: 51.8 ± 0.8	WG1: 3 servings (70-8 0g WG bread + 30-40 g WG cereal) WG2: 1 serve of whole wheat foods + 2 serving of oats	Refined cereals and white bread Refined cereals and white bread
Vetrani et al. 2016 [48]	P 12 weeks	40 (21/19)	Metabolic syndrome	(16/24)	WG 57.2 ± 1.9; RG 58.4 ± 1.6	WG products plus a small portion of endosperm rye bread 40.2 ± 1.2 g fiber/day	Commercial refined grain cereal products 22.1 ± 0.9g fiber/day
Vitaglione et al. 2015 [49]	P 8 weeks	68 (36/32)	Overweight and obese	(0/68)	WG 40 ± 2; RG 37 ± 2	100% WG, 70 g/day	RG products, 60 g/day
Whittaker et al. 2015 [50]	Cr 24 weeks	22	Acute Coronary Syndrome	(13/9)	61 (47-75)	Khosoran Semolina 62 g/day Khosoran flour 140 g/day	Control Semolina 62 g/day Control Flour 140 g/day
Whittaker et al. 2017 [51]	Cr 24 weeks	21	Type 2 Diabetes	(7/14)	64.4 ± 10.9 w	Khosoran Semolina 62 g/day Khosoran flour 140 g/day	Control Semolina 62 g/day Control Flour 140 g/day
Zamaratskaia et al. 2020 [52]	Cr 24 weeks	17	Prostate cancer	(17/0)	73.5 ± 4.6	WG foods 485 g/day	RG foods 485 g/day

Abbreviations: Crossover (Cr); Parallel (P); Number of participants (*n*); Intervention (I); Control (C); Male (M); Female (F); Whole Grain (WG); Whole Wheat (WW); Refined Grain (RG); Group (G).

3.3. Risk of Bias

A summary of the within-study risk of bias is shown in Figure 2. The included studies were assessed against the predetermined criteria of the Cochrane RoB2 tool for randomized control and crossover trials [21]. Within Domain 1: Randomization Process, there were five studies with some concerns of bias [24,28,30,31,43], with the remaining studies ($n = 26$) with a low risk of bias. In Domain 2: Deviations from intended intervention, there was one study with a high risk of bias [22], one with some concern [31], and the remainder with a low risk of bias ($n = 29$). Three studies had some risk of bias for Domain 3: Missing outcome data, [28,41,45], and the remainder had a low risk of bias ($n = 28$). Two studies had some risk of bias for both Domain 4: Measurement of the outcome [25,47] and Domain 5: Selection of the reported result [26,31], with the remainder having a low risk of bias ($n = 29$).

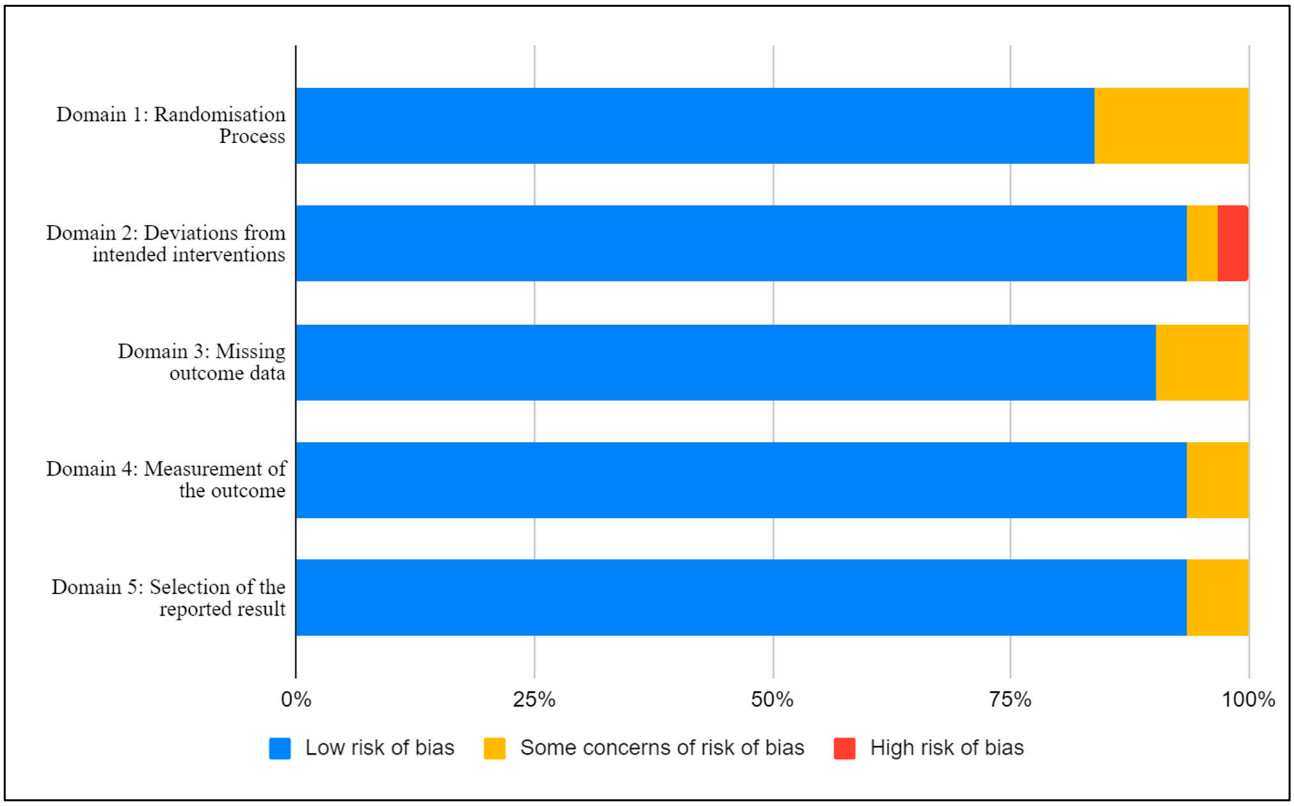

Figure 2. Risk of bias assessment using the revised Cochrane risk-of-bias (RoB 2).

3.4. Effect of the Intervention on the Outcome

3.4.1. Healthy Individuals

Two studies measured the effect of whole grain consumption on healthy individuals, who had a BMI < 25 and with no pre-existing conditions [23,40]. Within these studies, two measured CRP, while only one measured IL-6 and TNF. No marker for the studies looking at healthy individuals showed any level of statistical significance. The details are displayed in Table 2.

Table 2. Effect of whole grain consumption on inflammatory markers in healthy individuals between the intervention and control diet.

Study	N (I/C)	CRP Baseline	CRP Endpoint	*p*-Value
Ampatzoglou et al. 2016 [24]	I (*n* = 33) C (*n* = 33)	2.2 (0.5) ng/L 1.7 (0.3) ng/L	1.6 (0.4) ng/L 1.8 (0.3) ng/L	0.099
Navarro et al. 2019 [41]	I (*n* = 40) C (*n* = 40)	1.5 ± 2.7 mg/L 1.5 ± 2.7 mg/L	n.d n.d	0.19
Study	**N (I/C)**	**IL-6 Baseline**	**IL-6 Endpoint**	***p*-Value**
Ampatzoglou et al. 2016 [24]	I (*n* = 33) C (*n* = 33)	1.2 (0.2) ng/L 1.3 (0.2) ng/L	1.6 (0.1) ng/L 1.4 (0.2) ng/L	0.702
Study	**N (I/C)**	**TNF Baseline**	**TNF Endpoint**	***p*-Value**
Ampatzoglou et al. 2016 [24]	I (*n* = 33) C (*n* = 33)	10.8 (0.4) ng/L 10.5 (0.5) ng/L	10.8 (0.6) ng/L 10.7 (0.5) ng/L	0.381

Abbreviations: Number of participants (N); Intervention (I); Control (C); C-Reactive Protein (CRP); Interlukin-6 (IL-6); Tumor Necrosis Factor (TNF); *p*-value between groups unless stated; *p*-value < 0.05; baseline and endpoint data presented as mean ± S.D, mean (range) or mean (SE) as per raw data, where S.D is standard deviation and SE = standard error.

3.4.2. Overweight or Obese Individuals

Among the 16 studies in the overweight and obese populations (BMI 25–35), two had two intervention arms [22,47], resulting in 18 studies within this category (Table 3). All 18 studies measured CRP levels, with six of these (33%) observing a statistically significant reduction in CRP levels following whole grain consumption [29,30,32,33,38,40]. Nine of the studies measured IL-6 levels, with one observing a statistically significant change in IL-6 levels after consumption of whole grain foods [40]. A further two of the five total studies measuring TNF also observed a statistically significant change in inflammatory marker levels [32,49].

Table 3. Effect of whole grain consumption on inflammatory markers in overweight and obese individuals.

Study	N (I/C)	CRP Baseline	CRP Endpoint	*p*-Value
Andersson et al. 2007 [25]	I (*n* = 30) C (*n* = 30)	2.03 ± 1.62 mg/L 2.86 ± 2.96 mg/L	2.38 ± 2.29 mg/L 2.34 ± 1.57 mg/L	0.55
Brownlee et al. 2010 [22]	I1 (*n* = 85) C (*n* = 100)	2.4 ± 9.9 mg/L 2.4 ± 2.3 mg/L	3.1 ± 4.3 mg/L 2.9 ± 3.5 mg/L	>0.05
Brownlee et al. 2010 [22]	I2 (*n* = 81) C (*n* = 100)	3.2 ± 4.6 mg/L 2.4 ± 2.3 mg/L	3.2 ± 5.9 mg/L 2.9 ± 3.5 mg/L	>0.05
Hoevenaars et al. 2019 [29]	I (*n* = 20) C (*n* = 20)	5.29 ± 8.14 μg/mL 2.58 ± 2.70 μg/mL	2.16 ± 1.82 μg/mL 5.24 ± 14.1 μg/mL	0.03 **
Iversen et al. 2021 [30]	I (*n* = 121) C (*n* = 121)	1.45 (1.21; 1.73) mg/L 1.44 (1.19; 1.74) mg/L	1.12 (0.93; 1.36) mg/L 1.58 (1.29; 1.92) mg/L	0.001 **
Katcher et al. 2008 [32]	I (*n* = 121) C (*n* = 121)	1.45 (1.21; 1.73) 1.44 (1.19; 1.74)	1.12 (0.93; 1.36) mg/L 1.58 (1.29; 1.92) mg/L	0.001 **
Kazemzadeh et al. 2014 [33]	I (*n* = 20) C (*n* = 15)	G1: 2.0 ± 1.3 mg/L G2: 1.5 ± 1.2 mg/L G1: 2.0 ± 1.3 mg/L G2: 1.5 ± 1.2 mg/L	G1: 1.9 ± 1.9 mg/L G2: 0.9 ± 1.1 mg/L G1: 1.9 ± 1.9 mg/L G2: 0.9 ± 1.1 mg/L	0.012 **
Kirwan et al. 2016 [34]	I (*n* = 33) C (*n* = 33)	3.7 ± 3.3 mg/L 5.9 ± 7.1 mg/L	0.8 (−1.1, 2.6) mg/L −2.3 (−4.8, 0.1) mg/L	0.06
Kopf et al. 2018 [36]	I (*n* = 17) C (*n* = 14)	0.8 ± 0.6 mg/mL 0.6 ± 0.4 mg/mL	0.8 ± 0.4 mg/mL 0.7 ± 0.5 mg/mL	0.89

Table 3. *Cont.*

Study	N (I/C)	CRP Baseline	CRP Endpoint	*p*-Value
Li et al. 2018 [37]	I (*n* = 28) C (*n* = 28)	3.7 ± 3.3 mg/L 3.7 ± 3.3 mg/L	3.7 ± 3.3 mg/L 3.7 ± 3.3 mg/L	0.197
Malik et al. 2019 [38]	I (*n* = 55) C (*n* = 58)	4.1 ± 2.8 mg/L 4.1 ± 2.8 mg/L	0.03 ± 2.12 mg/L 0.63 ± 2.35 mg/L	0.04 **
Meng et al. 2019 [39]	I (*n* = 11) C (*n* = 11)	n.d n.d	2.1 (0.7–4.7) mg/L 2.0 (0.6–4.6) mg/L	0.84
Munch Roager et al. 2019 [40]	I (*n* = 25) C (*n* = 25)	6.3 ± 14.0 mg/L 3.1 ± 2.6 mg/L	4.2 ± 6.8 mg/L 5.0 ± 5.8 mg/L	0.003 **
Pourshahidi et al. 2020 [44]	I (*n* = 20) C (*n* = 20)	156 ± 195 μg/dL 156 ± 195 μg/dL	142 ± 115 μg/dL 171 ± 254 μg/dL	0.265
Schutte et al. 2018 [46]	I (*n* = 25) C (*n* = 25)	5294 ± 8140 ng/mL 2575 ± 2702 ng/mL	2162 ± 7260 ng/mL 2555 ± 1658 ng/mL	0.064
Tighe et al. 2010 [47]	I1 (*n* = 85) C (*n* = 100)	3.3 (0.5, 2.3) mg/L 1.4 (0.7, 2.7) mg/L	0.9 (0.5, 1.9) mg/L 1.1 (0.6, 3.0) mg/L	0.349
Tighe et al. 2010 [47]	I2 (*n* = 81) C (*n* = 100)	1.0 (0.4, 1.6) mg/L 1.4 (0.7, 2.7) mg/L	1.0 (0.6, 2.3) mg/L 1.1 (0.6, 3.0) mg/L	0.349
Study	**N (I/C)**	**IL-6 Baseline**	**IL-6 Endpoint**	***p*-Value**
Andersson et al. 2007 [25]	I (*n* = 30) C (*n* = 30)	14.8 ± 32.2 mg/L 15.9 ± 32.4 mg/L	15.2 ± 33.2 mg/L 15.8 ± 30.9 mg/L	0.79
Hoevenaars et al. 2019 [29]	I (*n* = 20) C (*n* = 20)	1.17 ± 1.26 pg/mL 1.09 ± 0.81 pg/mL	1.13 ± 0.89 pg/mL 1.46 ± 1.58 pg/mL	0.73
Katcher et al. 2008 [32]	I (*n* = 121) C (*n* = 121)	3.2 ± 6.3 pg/mL^6 2.2 ± 1.3 pg/mL^6	2.3 ± 3.6 pg/mL^6 2.1 ± 0.4 pg/mL^6	Group 0.94 ^ Time 0.57
Kopf et al. 2018 [36]	I (*n* = 17) C (*n* = 14)	4.4 ± 1.9 mg/mL 2.9 ± 1.5 mg/mL	5.2 ± 1.3 mg/mL 3.2 ± 1.7 mg/mL	0.89
Meng et al. 2019 [39]	I (*n* = 11) C (*n* = 11)	n.d n.d	0.6 (0.4–0.8) pg/L 0.6 (0.4–0.8) pg/L	0.77
Munch Roager et al. 2019 [40]	I (*n* = 20) C (*n* = 15)	1.6 ± 1.2 mg/L 1.2 ± 0.7 mg/L	1.4 ± 1.1 mg/L 2.0 ± 2.0 mg/L	0.009 **
Tighe et al. 2010 [47]	I1 (*n* = 85) C (*n* = 100)	1.3 (0.8, 2.3) pg/L 1.1 (0.8, 1.7) pg/L	1.4 (1.0, 2.4) pg/L 1.1 (0.8, 1.6) pg/L	>0.05
Tighe et al. 2010 [47]	I2 (*n* = 81) C (*n* = 100)	1.2 (0.9, 1.9) pg/L 1.1 (0.8, 1.7) pg/L	0.9 (0.5, 1.9) pg/L 1.1 (0.8, 1.6) pg/L	>0.05
Vitaglione et al. 2015 [49]	I (*n* = 36) C (*n* = 32)	57.5 ± 7.5 pg/mL 65.5 ± 11.4 pg/mL	46.9 ± 4.0 pg/mL 60.2 ± 7.2 pg/mL	0.06
Study	**N (I/C)**	**TNF Baseline**	**TNF Endpoint**	***p*-Value**
Hoevenaars et al. 2019 [29]	I (*n* = 20) C (*n* = 20)	3.07 ± 1.85 pg/mL 2.26 ± 1.43 pg/mL	2.90 ± 1.89 pg/mL 2.29 ± 1.38 pg/mL	0.26
Katcher et al. 2008 [32]	I (*n* = 121) C (*n* = 121)	1.2 ± 0.3 pg/mL^6 1.3 ± 0.4 pg/mL^6	1.1 ± 0.3 pg/mL^6 1.2 ± 0.2 pg/mL^6	Group 0.04 **^ Time 0.80
Kopf et al. 2018 [36]	I (*n* = 17) C (*n* = 14)	26.7 ± 4.17 pg/mL 23.8 ± 5.9 pg/mL	21.4 ± 2.9 pg/mL 23.4 ± 6.6 pg/mL	0.11
Munch Roager et al. 2019 [40]	I (*n* = 20) C (*n* = 15)	1.7 ± 0.8 pg/mL 1.7 ± 0.9 pg/mL	1.7 ± 0.08 pg/mL 1.7 ± 0.9 pg/mL	0.87
Vitaglione et al. 2015 [49]	I (*n* = 36) C (*n* = 32)	341.9 ± 25.5 pg/mL 321.9 ± 52.1 pg/mL	26.8 ± 3.2 pg/mL 329.8 ± 5.06 pg/mL	0.04 **

Abbreviations: Number of participants (N); Intervention (I); Control (C); C-Reactive Protein (CRP); Interlukin-6 (IL-6); Tumor Necrosis Factor (TNF); *p*-value between group unless stated; *p*-value < 0.05 (**); baseline and endpoint data presented as mean ± SD, mean (range) or mean (SE) as per raw data, where SD is standard deviation and SE = standard error; ^ *p*-value Group vs. Time.

3.4.3. Individuals with Pre-Existing Conditions

In the 12 studies that reviewed individuals with pre-existing conditions, which included type 2 diabetes [23,35,43,45,50], metabolic syndrome [27,28,31,48], type 2 diabetes and metabolic syndrome [23], acute coronary syndrome [50], and hypercholesterolaemia [42], one study had two intervention arms included in this SLR [23] (Table 4). Of the 11 studies measuring CRP, four observed a statistically significant change [23,31,42,43]. Seven studies measured IL-6 levels, with only one showing a significant change [42]. These seven studies also reviewed TNF levels, with three observing an increase in the level of change between the intervention and the control group, which was statistically significant [28,42,51].

Table 4. Effect of whole grain consumption on inflammatory markers in individuals with pre-existing conditions.

Study	N (I/C)	CRP Baseline	CRP Endpoint	*p*-Value
Connolly et al. 2011 [26]	I (*n* = 16) C (*n* = 16)	1.69 ± 0.35 mg/L 1.8 ± 0.47 mg/L	2.45 ± 0.92mg/L 2.36 ± 0.49 mg/L	0.934
Giacco et al. 2013 [27]	I (*n* = 61) C (*n* = 62)	1.95 (0.74; 4.12) mg/dl 1.95 (0.96; 2.56) mg/dl	1.36 (0.62; 3.34) mg/dl 1.74 (1.04; 2.95) mg/dl	0.16
Harris Jackson et al. 2014 [28]	I (*n* = 17) C (*n* = 25)	3.0 (2.0, 4.6) mg/L 2.1 (1.4, 3.1) mg/L	2.4 ± 0.5 mg/L 1.5 ± 0.4 mg/L	>0.05
Joo et al. 2020 [31]	I (*n* = 26) C (*n* = 23)	0.205 (0.183) mg/dL 0.137 (0.165) mg/dL	0.101 (0.028) mg/dL 0.154 (0.025) mg/dL	0.03 **
Kondo et al. 2017 [35]	I (*n* = 14) C (*n* = 14)	0.09 ± 0.12 µg/L 0.04 ± 0.03 µg/L	0.05 ± 0.05 µg/L 0.05 ± 0.06 µg/L	0.063
Ma et al. 2013 [23]	I1 (*n* = 65) C (*n* = 63)	3.65 (2.45) mg/L 3.76 (1.99) mg/L	3.13 (2.61) mg/L 3.81 (2.21) mg/L	>0.05
Ma et al. 2013 [23]	I2 (*n* = 71) C (*n* = 63)	3.46 (2.55) mg/L 3.76 (1.99) mg/L	2.26 (2.12) mg/L 3.81 (2.21) mg/L	<0.05 **
Pavadhgul et al. 2019 [42]	I (*n* = 24) C (*n* = 24)	2.7 ± 2.1 mg/L 2.7 ± 2.1 mg/L	2.2 ± 2.1 mg/L 2.9 ± 2.9 mg/L	<0.05 **
Pavithran et al. 2020 [43]	I (*n* = 40) C (*n* = 40)	3.38 ± 3.83 mg/L 2.79 ± 4.20 mg/L	1.46 ± 1.04 mg/L 3.16 ± 4.61 mg/L	0.026 **
Saglam et al. 2019 [45]	I (*n* = 12) C (*n* = 12)	n.d n.d	n.d n.d	>0.05
Vetrani et al. 2016 [48]	I (*n* = 21) C (*n* = 19)	2.52 ± 0.5 mg/dL 2.27 ± 0.4 mg/dL	2.44 ± 0.5 mg/dL 2.39 ± 0.4 mg/dL	0.693
Study	**N (I/C)**	**IL-6 Baseline**	**IL-6 Endpoint**	***p*-Value**
Connolly et al. 2011 [26]	I (*n* = 16) C (*n* = 16)	4.13 ± 1.47 pg/mL 4.09 ± 1.71 pg/mL	5.88 ± 1.78 pg/mL 7.16 ± 3.46 pg/mL	0.925
Giacco et al. 2013 [27]	I (*n* = 61) C (*n* = 62)	1.42 (1.01; 2.32) pg/mL 1.41 (0.84; 2.21) pg/mL	1.54 (1.12; 2.23) pg/mL 1.43 (1.07; 2.11) pg/mL	0.52
Harris Jackson et al. 2014 [28]	I (*n* = 23) C (*n* = 23)	1.8 (1.5, 2.2) pg/mL 1.7 (1.4, 2.0) pg/mL	2.1 ± 0.2 pg/mL 1.8 ± 0.2 pg/mL	>0.05
Pavadhgul et al. 2019 [42]	I (*n* = 24) C (*n* = 24)	150 ± 57.9 pg/L 150 ± 57.9 pg/L	123 ± 44.5 pg/L 145 ± 54.0 pg/L	<0.01 **
Vetrani et al. 2016 [48]	I (*n* = 21) C (*n* = 19)	1.84 ± 0.2 pg/mL 1.69 ± 0.3 pg/mL	2.23 ± 0.3 pg/mL 1.7 ± 0.3 pg/mL	0.161
Whittaker et al. 2015 [50]	I (*n* = 22) C (*n* = 22)	2.26 (1.50–3.03) pg/mL 3.16 (1.51–4.81) pg/mL	1.53 (1.16–1.90) pg/mL 3.30 (1.24–6.37) pg/mL	0.698
Whittaker et al. 2017 [51]	I (*n* = 21) C (*n* = 21)	2.76 ± 2.01 pg/mL 2.15 ± 1.57 pg/mL	2.16 ± 1.21 pg/mL 1.70 ± 1.24 pg/mL	0.9

Table 4. *Cont.*

Study	N (I/C)	TNF Baseline	TNF Endpoint	*p*-Value
Connolly et al. 2011 [26]	I (*n* = 16) C (*n* = 16)	20.2 ± 4.0 pg/mL 46.3 ± 26.0 pg/mL	36.5 ± 15.7 pg/mL 42.2 ± 14.8 pg/mL	0.519
Giacco et al. 2013 [27]	I (*n* = 61) C (*n* = 62)	0.73 (0.50; 0.96) pg/mL 0.62 (0.43; 1.05) pg/mL	0.68 (0.50; 0.94) pg/mL 0.63 (0.41; 0.90) pg/mL	0.84
Harris Jackson et al. 2014 [28]	I (*n* = 24) C (*n* = 24)	1.2 (1.0, 1.3) pg/mL 1.4 (1.2, 1.7) pg/mL	1.2 ± 0.1 pg/mL 1.3 ± 0.1^5 pg/mL	<0.05 **
Pavadhgul et al. 2019 [42]	I (*n* = 24) C (*n* = 24)	49.5 ± 26.4 pg/L 49.5 ± 26.4 pg/L	39.83 ± 15.9 pg/L 47.4 ± 24.1 pg/L	<0.01 **
Vetrani et al. 2016 [48]	I (*n* = 21) C (*n* = 19)	1.71 ± 0.6 pg/mL 1.07 ± 0.4µg/mL	1.50 ± 0.6 pg/mL 1.31 ± 0.5 pg/mL	0.232
Whittaker et al. 2015 [50]	I (*n* = 22) C (*n* = 22)	4.54 ± 3.32 pg/mL 6.5 (2.9–9.9) pg/mL	3.9 (1.4–6.4) pg/mL 4.6 (0.9–8.2) pg/mL	0.798
Whittaker et al. 2017 [51]	I (*n* = 21) C (*n* = 21)	4.54 ± 3.32 pg/mL 4.36 ± 4.09 pg/mL	4.74 ± 3.09 pg/mL 4.84 ± 4.07 pg/mL	0.04 **

Abbreviations: Number of participants (N); Intervention (I); Control (C); C-Reactive Protein (CRP); Interlukin-6 (IL-6); Tumor Necrosis Factor (TNF); *p*-value between group unless stated; *p*-value < 0.05 (**); baseline and endpoint data presented as mean ± SD, mean (range) or mean (SE) as per raw data, where SD is standard deviation and SE = standard error.

3.4.4. Individuals with Other Conditions

One study had a population that fit outside of the other population groups: males with prostate cancer [52] (Table 5). This study measured CRP and IL-6 levels and whilst the data was not prepared in accordance with other measures, the study observed no statistical level of significance for either.

Table 5. Effect of whole grain consumption on inflammatory markers in individuals with other conditions.

Study	N (I/C)	CRP Baseline	CRP Endpoint	*p*-Value
Zamaratskaia et al. 2020 [52]	I (*n* = 17) C (*n* = 17)	n.d	n.d	>0.05
Study	**N (I/C)**	**IL-6 Baseline**	**IL-6 Endpoint**	***p*-Value**
Zamaratskaia et al. 2020 [52]	I (*n* = 17) C (*n* = 17)	6.3 (5.3–7.5) pg/mL 5.8 (4.8–6.9) pg/mL	n.d	>0.05

Abbreviations: Number of participants (N); Intervention (I); Control (C); C-Reactive Protein (CRP); Interlukin-6 (IL-6); *p*-value between group unless stated; *p*-value <0.05; baseline and endpoint data presented as mean ± SD, mean (range) or mean (SE) as per raw data, where SD is standard deviation and SE = standard error.

4. Discussion

Consumption of whole grains in preference to refined grains is known to have improved health benefits, with the broad range of benefits often attributed solely to the presence of dietary fiber [10,53]; however, other components, phytochemicals, fatty acids, amino acids, vitamins, and minerals are all likely to play a role. This review of 31 RCTs found that consumption of whole grain foods had a moderate effect on reducing inflammatory markers, with five of the possible 15 crossover studies [33,38,40,42,50], and seven of 16 parallel studies demonstrating statistically significant changes [23,29–32,43,49]. Within the population groups studied, the reduction in markers was most often observed in obese and overweight populations, and among those with pre-existing conditions, compared with studies of healthy populations, although there were only two studies in this category.

Previous systematic reviews and meta analyses, performed by Rahmani et al. [17] and Hajihashemi et al. [18] utilising publications up until 2019, found little evidence of a relationship between whole grain consumption and inflammatory markers. The current review included a total of 13 papers not included in the aforementioned reviews [17,18], six of which were published outside the timeframe utilized by the previous authors [30,31,41,43,44,52], and a further seven were included in the current review due to a variation in the search strategy [23,29,37,39,42,45,51].

While the findings of the current study provide some indication that whole grain consumption leads to a downregulation of inflammation, the wide variety of foods classed as whole grain included in the intervention diets varied between studies, from commercially available whole grain products to a specific dose allocated via food items provided by the research group. Of the 31 studies reviewed, 27 provided the intervention foods; however, the remaining four studies [25,32,36,43] only provided guidelines or instructions of which foods to purchase, adding a significant burden for study participants in sourcing and selecting the correct food types, which is a known issue for consumers [54]. Blind compliance checks are problematic and alkylresorcinol levels were only utilized by Harris Jackson et al. [28]; however, this test is only relevant for whole grain wheat and rye [55,56]. Despite this limitation, such biomarkers have been suggested in research to help support dietary assessment of consumption [56].

Only three of the 31 studies noted that subjects were instructed to maintain weight for the duration of the study [27,29,42], and only one study controlled for weight in their analysis [50], with all others showing a slight decrease in weight or no data mentioned. In addition, only eight studies recorded or mentioned physical activity or exercise, with six asked to maintain [23,25,27,30,33,41], one asked to record any exercise [32], and one asked to refrain completely [29]. A change in weight either through diet or exercise could be a possible confounder, as it becomes difficult to isolate the changes in inflammatory status as a result of the consumption of whole grain or as a result of the weight (fat) loss [57]. Despite the focus of papers based on the overweight and obese population, only 16 of 30 RCTs measured body fat mass [22,24,25,27,30,31,34,35,37,38,40,41,45,46,48,49], with no consistency in the method or type of body fat measured between studies, making comparisons between studies difficult. Furthermore, the more favorable results within studies of overweight populations are likely due to higher inflammatory marker levels at baseline in comparison to healthy populations. This finding is of particular importance as dietary interventions that result in a reduction in inflammation are important due to the link with reduced risk of chronic diseases [58].

As inflammation is known to increase with age [59] and the average age of the participants was 50 years (20–80 years), future studies could look at potential differences in age groups, or alternatively study a larger population sample segmenting by age, health status, or gender. This would enable the identification of population groups where the diet prescription may be most efficacious.

Chronic disease remains one of the largest cost contributors to the global burden of disease, with overweight contributing 8.7% of the annual cost of the total burden of disease in Australia in 2019 [12]. On a population level, swapping from refined grains to whole grains has the possibility of reducing the risk of chronic disease, in turn lowering the costs related to the burden of disease. A recent nutrition economics analysis found that a swap to whole grain from refined grain foods could provide significant healthcare cost savings for cardiovascular disease, type 2 diabetes, and cancer, particularly colorectal cancer, for the Australian population [60,61].

Further studies investigating the relationship between consumption of whole grain foods over comparable refined grain products and the influence on inflammatory markers are needed to confirm the presence and strength of the relationship. Studies with standardized diets where the single focus of the dietary intervention was whole grain foods compared with refined grain foods would help to narrow the possibility that the intervention diet was responsible for the change in the inflammatory response. Previous research has emphasized the need to accurately assess and record the whole grain content of foods in participant diets, with a minimum DTI of 48 g of whole grain, rather than using the weight of the whole grain food to allow for a more accurate dose assessment [56]. Products in the Australian market can claim a whole grain content from as little as 8 g per manufacturer serve or 25% whole grain and these may be consumed alongside products that are 100% whole grain, such as oats or brown rice. The recently proposed global definition for whole grains as an ingredient and as a whole grain food provides further guidance for research to assist with comparison between studies [2]. Studies also need to consider that the health outcomes from various whole grain food products may not be homogeneous, with potential differences between types of whole grains, for example, wheat versus rye versus oats versus brown rice; differing proportions of dietary fiber, and within that, soluble to insoluble fiber content; and also consideration of other components, such as beta-glucan. This has been discussed in a previous systematic review regarding cardiovascular risk factors, where whole grain oats were found to be more effective than other grains in reducing cholesterol, and brown rice was more effective in reducing triglycerides.

A strength of this analysis was the study design, clarifying the discrepancies in previously published systematic reviews. For example, the careful inclusion of only adult RCTs, and the removal of quasi-experimental studies including only those utilizing blood measures of cytokines (not faecal measures) and those with test diets that included whole grain rather than the fiber component from whole grain sources. The collection of data from the differing population groups enabled categorization and comparison between study population types, highlighting differences between healthy and unhealthy population groups, a potential consideration for future research.

5. Conclusions

With obesity rates continuing to grow in Australia and globally, coupled with the link to a higher risk of chronic disease, dietary interventions that investigate simple food changes, such as exchanging refined grain for whole grain, are of particular interest. This study further contributes to increasing current knowledge, pointing to future research considerations, particularly the need to conduct research with individual whole grain food types, discern potential differences, accurately account for the dose of whole grain, and measure compliance.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nu14020374/s1, Table S1: PICO Framework, Table S2: Search Terms, Figures S1 and S2: Results of Risk of Bias Assessment.

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Review

A Review of the Relationship between Lentil Serving and Acute Postprandial Blood Glucose Response: Effects of Dietary Fibre, Protein and Carbohydrates

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Abstract: Pulse consumption has been shown to confer beneficial effects on blood glucose and insulin levels. Lentil consumption, in particular, consistently lowers acute blood glucose and insulin response when compared to starchy control foods. The mechanism by which lentils lower postprandial blood glucose response (PBGR) and insulin levels is unclear; however, evidence suggests that this effect may be linked to macronutrients and/or the amount of lentils consumed. This review attempts to consolidate existing studies that examined lentil consumption and glycemic and/or insulinemic responses and declared information on macronutrient composition and dietary fibre content of the foods tested. Collectively, these studies suggest that consumption of lentils reduces PBGR, with the minimum effective serving being ~110g cooked to reduce PBGR by 20%. Reductions in PBGR show modest-to-strong correlations with protein (45–57 g) and dietary fibre (22–30 g) content, but has weaker correlations with available carbohydrates. Increased lentil serving sizes were found to moderately influence relative reductions in peak blood glucose concentrations and lower the area under the blood glucose curve (BG AUC). However, no clear relationship was identified between serving and relative reductions in the BG AUC, making it challenging to characterize consistent serving–response effects.

Keywords: lentil; glycemic response; insulin; protein; dietary fibre; carbohydrates; human trials

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1. Introduction

Type 2 diabetes (T2D) is characterised by impaired fasting blood glucose (BG) levels and is associated with increased risk for coronary heart disease, stroke, and a two-fold increase in overall mortality [1]. Chronic elevation of BG was also linked to obesity, hypertension, and coronary heart disease, even in persons without a history of diabetes [1]. As such, the Canadian clinical practice guidelines for diabetes stresses the importance of dietary approaches, including the increased use of pulses, for achieving optimal glycemic control in persons with T2D [2,3]. Lentils are dry harvested grains containing significant amounts of resistant, slow and rapidly digestible starches, with a range of protein depending on the variety [4]. These pulses also contain many polyphenolic compounds, with a majority being flavonoids, that contribute to health-promoting properties such as antioxidant activity and delayed glucose and lipid digestion, which could contribute to improved glycemic control and reduced risk for obesity [5]. Incorporation of pulses into daily meal consumption was shown to improve glycemic control partly due to their low glycemic index (GI), and this effect may vary between lentil varieties [6–9]. For example, a meta-analysis of non-oilseed pulse intervention studies showed that regular consumption of chickpeas, beans, peas and lentils improved glycemic control in both healthy and diabetic participants [9]. However, lentil dosage varied significantly amongst the various studies, with a major problem being that dry and wet weights are not regularly reported in published articles. Varying reductions in area under the blood glucose response curve (BG AUC) were observed in study participants who consumed lentils ranging from as much as 715 g per serving [10] to as little as 50 g [11]. As such, the minimum effective serving of lentil required to significantly and consistently lower BG has not yet been determined. An important feature of the latter effect is that this amount of lentils should be easily consumed by the average adult. In addition, there is a need to ascertain whether a serving–response relationship exists between lentil consumption and BG lowering. At present, it is unclear whether consuming larger quantities of lentils results in a larger attenuation effect on glycemic response or improved glycemic control.

The BG-lowering effects of lentil consumption have been independently attributed to carbohydrate composition and protein content [9]. In a regression analysis of pulse consumption in low-GI or high fibre diets, dietary carbohydrates accounted for 22% of the variation in fasting blood glucose (FBG) while proteins accounted for 14% [9]. However, this analysis also found that the quantity of either protein or carbohydrate did not differentially alter the effect of non-oil-seed pulses on glycosylated blood proteins or FBG [9]. It was suggested that the source of carbohydrates used in control foods (starch, glucose or sucrose) is the most important factor in determining whether a protein-containing treatment is capable of impacting BG and insulin responses in nondiabetic participants [12]. Furthermore, in that analysis, up to 40% of the variation in fasting blood insulin concentrations could be explained by fiber content of pulses [9]. In contrast, results of meta-analyses suggest that the BG-lowering effects of pulses were not attributed to fibre content; rather, pulses independently reduced FBG and glycosylated proteins in T2D patients [9,13]. More recently, ingestion of β-glucan, a soluble fibre, was reported to reduce postprandial BG AUC and insulin levels in healthy and diabetic individuals [6]. Clearly, the contribution of dietary fibre, protein and carbohydrates towards the attenuation of postprandial BG AUC is not fully understood. It is important that this relationship be delineated for regulatory purposes, and to guide the manufacture of pulse and lentil-based functional foods.

The objectives of this review are: (i) to attempt to establish a minimum effective serving for lentils to lower BG concentrations; (ii) to determine whether there is a serving–response relationship between the amount of lentils consumed and PBGR, and (iii) to attempt to identify the dietary component responsible for the glucose-lowering effect of lentils.

2. Materials and Methods

This review examined data from published research on effects of lentil consumption on both diabetic and non-diabetic participants. A systematic search and reporting of data was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [14].

2.1. Study Selection

Literature searches were conducted using PubMed, Scopus, CABI Global Health, Google Scholar, Canadian Agricultural Library, and the University of Guelph Library databases for relevant studies published from 1980 until 4 March 2021. The following search terms and Boolean operators were used: "lentil AND blood glucose AND diabetes AND postprandial AND acute". In order to retrieve published studies involving healthy participants, the term "AND diabetes" was removed. The search was restricted to acute human studies; those that measured only chronic responses to lentil consumption or concurrent interventions with other pulses were excluded. All studies included in this analysis needed to have had BG and insulin concentrations measured within the first two hours following lentil consumption, and these measures were defined as an "acute" or "postprandial" response.

2.2. Data Extraction

The relevant data, study characteristics and outcomes were independently extracted by three investigators (S.S., D.G.R., G.C.F.). The total amount of lentils consumed by participants in each study was recorded as the cooked weight. Raw weights provided by these studies were converted to cooked weights using the average moisture content of green lentils (68.4%), as gathered from our previous research (unpublished data). The cooked weight was calculated as follows: (dry weight/% solids) × 100, where % solid = 100–68.4. Macronutrient profiles including protein, available carbohydrates (CHOav) and total carbohydrate, as well as dietary fibre content of the lentil treatments were also recorded, if included in the publication. If total carbohydrate data were not provided, it was calculated by adding CHOav and dietary fibre values. Time and value of the maximum BG concentration (BG Cmax) were recorded for lentil and control treatment groups. Glycemic response or AUC, was also extracted, if available; if not, absolute differences and percent reductions in AUC between lentil and control treatments were calculated. Insulin data, maximum insulin concentration (insulin Cmax), area under the blood insulin response curve (iAUC), and the absolute difference between peaks were also recorded.

2.3. Data Analysis

Relationships between glycemic response and dependent variables of lentil serving size, protein, dietary fibre, and total carbohydrates were explored using linear regression and multiple regression analyses. Linear, exponential, logarithmic, and quadratic correlations were assessed. An appropriate line of best fit for each specific outcome was chosen by comparing the correlation coefficient and standard error of the mean, as well as a visual inspection of each plot. From these assessments, AUC was noted as either an absolute value or relative reduction. If not provided in the study, relative reductions in AUC were calculated manually by using $[(AUC_{CONTROL} - AUC_{LENTIL})/AUC_{CONTROL}] \times 100\%$. For studies that provided AUC in different units (e.g., mg × h/dL), measurements were converted to mmol × min/L by standard conversion factors (e.g., 1 mg/dL glucose = 0.05551 mmol/L glucose). For studies that represented data only in graphical formats, Plot Digitizer (Ver. 2.6.8; Source Forge; accessed on 7 January 2022; http://plotdigitizer.sourceforge.net) was used to digitise functional data from plots, and the average of three estimates for each data point was used to obtain the reported value. Graphing and data analysis was carried out using GraphPad Prism (Ver. 9.2; GraphPad Software, San Diego, CA, USA). The Pearson coefficient (r) was calculated for linear relationships, while Spearman's rank correlation coefficient (r_s) was used for describing non-linear relationships. A value of $p < 0.05$ was considered to be indicative of a significant relationship.

3. Results

A total of twelve studies that measured BG and/or insulin responses to various lentil treatments in healthy participants were identified (Table 1), and an additional six studies involved diabetic participants (Table 2). However, several studies did not provide all the variables relevant to this review, such as the lentil serving size and the amount of CHOav. Some studies only provided BG concentrations, and not the AUC. In addition, six studies included data on insulin; four with healthy participants and two with diabetic participants. While there were insufficient number of studies to clearly define correlations, some trends between lentil serving and the corresponding beneficial impacts on AUC and insulin responses were observed in healthy participants.

3.1. Lentil Serving Size

Among healthy participants, BG AUC displayed a quadratic relationship with increasing lentil serving size (Figure 1). As control treatment servings increased, BG AUC tended to increase at a nearly exponential rate; this was expected given that there would be a concomitant increase in CHOav. At nearly equivalent servings, BG AUC tended to be lower with lentil treatments than controls. For lentil treatments, AUC increased at a slower rate compared to controls, reached a lower peak and began to trend towards a decrease in AUC at higher servings. A quadratic model best fitted the lentil (r_s = 0.6201; n = 10; *ns*) and control data (r_s = 0.7212; n = 10; $p < 0.05$) for BG AUC according to serving size. As such, the minimum effective serving of cooked lentil for reducing blood glucose AUC appears to be between 100 and 120 g. There did not appear to be an association between lentil serving size and relative reduction in AUC compared to control foods (Figure 2); however, servings between 100 and 120 g lentils resulted in relative reductions of BG AUC that were similar to servings of between ~350 and 450 g. The large variation in the relative reduction in AUC by lentil at servings between 300 and 500 g is suggestive of the need for more carefully controlled acute feeding trials involving human participants.

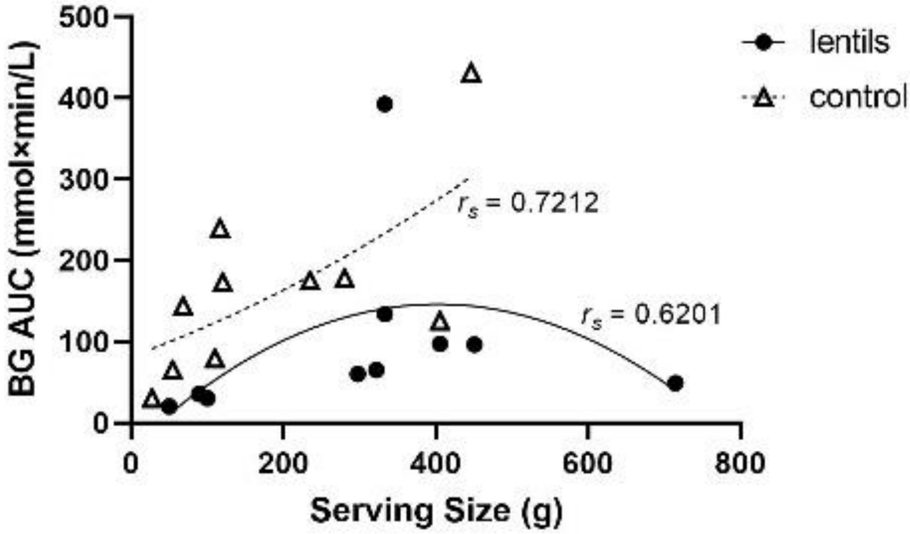

Figure 1. Area under the blood glucose response curve (BG AUC) for various lentil and control serving sizes (g). A quadratic model best fit the lentil (r_s = 0.6201; n = 10; *ns*) and control data (r_s = 0.7212; n = 10; $p < 0.05$).

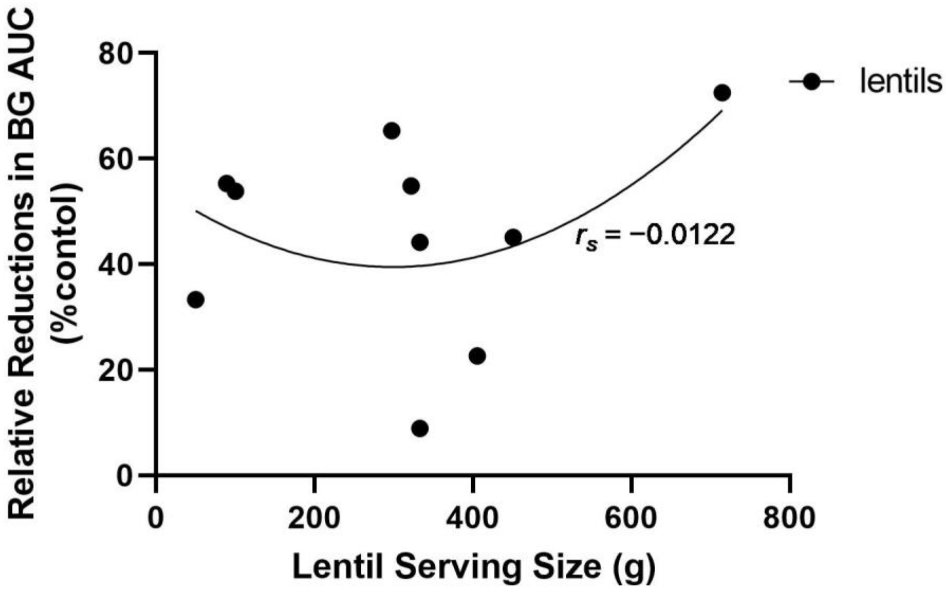

Figure 2. Relative reductions (%) in area under the blood glucose response curve (BG AUC) according to lentil serving sizes (g) with reference to controls. Relative reduction was calculated using the formula: ((Lentil BG AUC–Control BG AUC)/Control BG AUC) × 100. A quadratic curve best fit this data (r_s = −0.0122; n = 10; *ns*).

3.2. Protein

Analysis of the available data suggest that there may be a quadratic relationship between protein content of test meals and BG AUC, with both low and high protein intakes being associated with lower BG AUC (lentil r_s = 0.0365; n = 11; *ns*; control r_s = 0.4384; n = 11, *ns*; Figure 3). At higher protein content values, BG AUC was lower for both lentil treatments and controls, although lentil treatments resulted in lower BG AUC at similar protein content of control foods. The relationship between increased protein content and lower BG AUC within lentil treatments followed a similar quadratic trend to that of the BG AUC lowering effect noted with increased lentil serving size. However, it is unlikely that protein content is the sole determinant of BG AUC reduction associated with lentil consumption; it appears that portion size may contribute to this effect. As an example, a study that examined a lentil-based breakfast with 57 g of protein in a 387 g total meal serving size resulted in a mean (±SEM) BG AUC of 49 ± 13 mmol × min/L, whereas the control meal with the same protein content and 643 g meal serving size produced a BG AUC of 178 ± 34 mmol × min/L [10]. A similar finding was observed when two studies with similar protein content were compared. The first study investigated a 50 g serving size of green lentils containing 4.94 g of protein, and this led to a BG AUC of 20 ± 5 mmol × min/L [11]. The second study used a control diet of instant potato flakes containing 5.0 g of protein with 50 g of equivalent CHOav, and this led to a BG AUC of 268 ± 40 mmol × min/L [15]. Despite treatments being nearly equivalent in protein content, the BG AUC of participants consuming lentil treatments were notably lower than that of the control treatments. The amount of total protein and serving size both appear to have notable impacts and may each have important roles in the BG AUC lowering effect of lentil treatments.

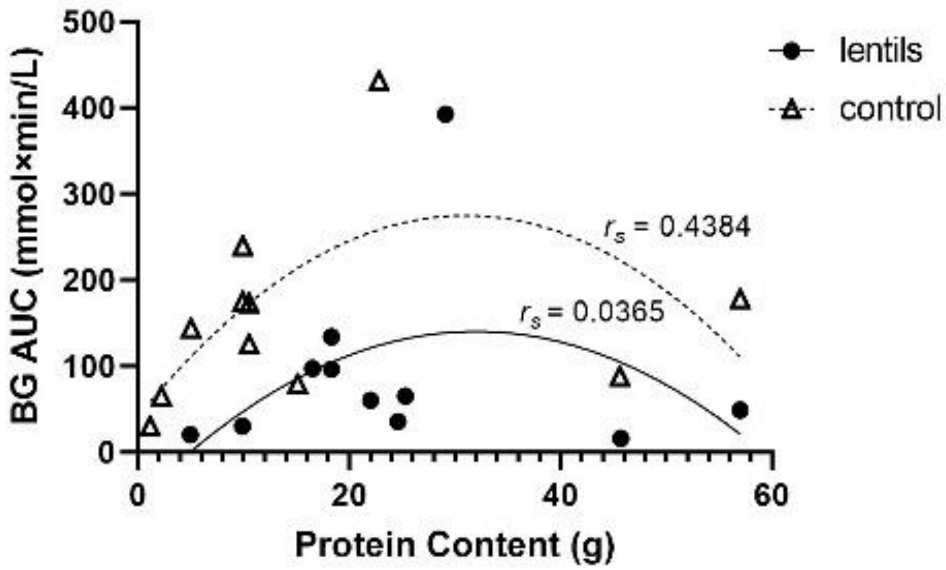

Figure 3. Relationship between area under the blood glucose response curve (BG AUC) and protein content (g) in lentil treatments and controls. Quadratic models for both lentil (r_s = 0.0365; n = 11; *ns*) and control treatments (r_s = 0.4384; n = 11; *ns*) best fit the data.

3.3. Dietary Fibre

Lentil treatments generally had more dietary fibre content compared to corresponding controls, and this was associated with lower BG AUC values (Figure 4). Lower BG AUC values (<100 mmol × min/L) were reported at both low (<10 g) [16] and high levels (>20 g) [10,15,17] of fibre, following a trend similar to that of protein content. While BG AUC initially increased with increasing fibre content, it quickly reached a peak and started to decrease as the fibre content of the treatments increased. The BG AUC followed a quadratic model for protein content of lentil treatments (r_s = 0.2278; n = 11, *ns*), while controls followed an exponential trend (r_s = 0.5872, n = 11, *ns*).

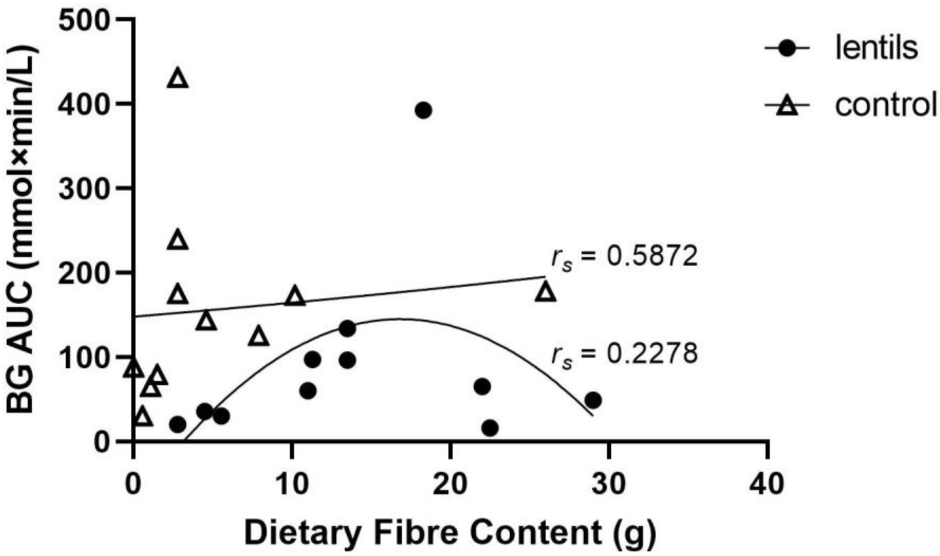

Figure 4. Area under the blood glucose response curve (BG AUC) according to dietary fibre content (g) in lentil treatments and controls. Lentil data best fit a quadratic model (r_s = 0.2278; n = 11; *ns*), and control data followed an exponential trend (r_s = 0.5872; n = 11; *ns*).

3.4. Available Carbohydrates (CHOav)

The relationship between BG AUC and CHOav appeared to be linear for lentil treatments (r = 0.5325, n = 8; *ns*; Figure 5), while controls followed an exponential trend (r_s = 0.6347; n = 8; *ns*). For both lentil treatment and control groups, an increase in CHOav provoked a progressive increase in AUC. In general, participants who consumed lentil treatments had lower BG AUC values compared to controls prepared from starchy foods (potatoes, bread, or pasta), and this trend was apparent at all levels of CHOav. Even at low levels of carbohydrate intake such as that observed in a study with green lentils (6.91 g CHOav), the BG AUC was significantly lower (20 ± 5 mmol × min/L) than a white potato control with 6.14 g of CHOav (BG AUC 42 ± 5 mmol/L × min, $p < 0.001$) [11].

When macronutrients (protein, CHOav) and dietary fibre in the lentil treatments were compared separately, all showed positive correlations with BG AUC, although the correlation coefficients were relatively small (Figure 6): CHOav had a moderate linear relationship (r = 0.5325; n = 8; *ns*), while a quadratic model best fit protein (r_s = 0.0365; n = 11; *ns*) and dietary fibre (r_s = 0.2278; n = 11; *ns*). The magnitude of relative reduction of BG AUC decreased with increasing levels of CHOav and dietary fibre (Figure 7). The BG AUC reduction with lentil treatment relative to control was greatest with increasing protein content in a quadratic model (r_s = 0.5513; n = 11, *ns*). Although moderate, this correlation was greater than that between BG AUC relative reduction and CHOav (r = 0.1161; n = 8; *ns*; linear model) or dietary fibre (r_s = 0.3326; n = 11; *ns*; quadratic model).

3.5. Maximum Blood Glucose Concentrations

BG Cmax also followed a quadratic trend with lentil serving size (r_s = 0.5968, n = 11, *ns*). BG Cmax was not remarkably different when high and low lentil serving sizes were compared, as values of 4.7–5 mmol/L were obtained with sservings as low as 50 g and as high as 715 g of cooked lentils (Table 1; Figure 8). The latter serving size appeared to skew this relationship; when removed there was a significant linear relationship between BG Cmax and lentil serving (r = 0.779; n = 10; $p < 0.01$). The relative reduction in BG Cmax also had a quadratic correlation with lentil serving size (r_s = 0.4419; n = 11; *ns*; Figure 9); as the serving size increased, so did the relative reduction in BG AUC compared to controls.

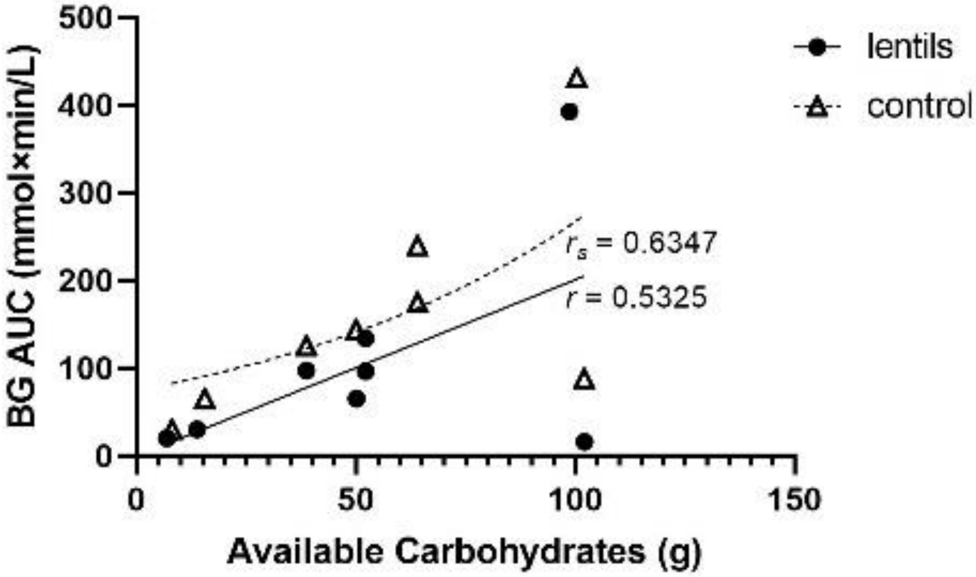

Figure 5. Area under the blood glucose response curve (BG AUC) response at various amounts of available carbohydrates (CHOav) in the lentil treatment or control. A linear model best fit the lentil data (r = 0.5325; n = 8; *ns*), and the control data followed an exponential trend (r_s = 0.6347; n = 8; *ns*).

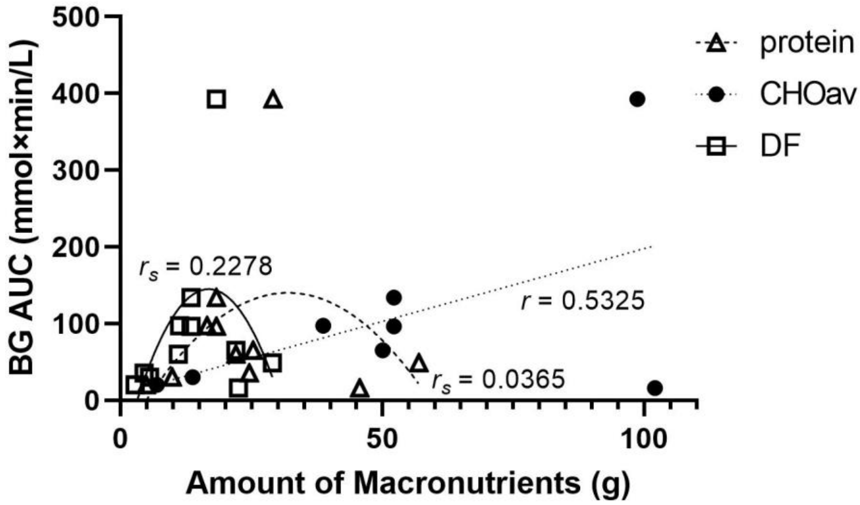

Figure 6. Area under the blood glucose response curve (BG AUC) according the amount of macronutrients or dietary fibre (g) per lentil treatment serving. This plot combines the lentil data of Figures 3–5. Quadratic modeling best fit protein (r_s = 0.0365; n = 11; *ns*) and dietary fibre (DF) (r_s = 0.2278; n = 11; *ns*), and a linear model best fit available carbohydrates (CHOav; r = 0.5325; n = 8; *ns*).

3.6. Macronutrients, Dietary Fibre and BG Cmax

Protein (r_s = 0.1404; n = 12; *ns*), CHOav (r_s = 0.4939; n = 10; *ns*) and dietary fibre (r_s = 0.2947; n = 12; *ns*) all displayed quadratic relationships with BG Cmax (Figure 10); however, their relative abundance in test meals varied, with dietary fibre having the lowest and CHOav having the highest range of values. Dietary fibre had a weak correlation with BG Cmax, and increased dietary fibre content in the test meals was associated with reduced BG Cmax, even at low levels of intake. With respect to relative reduction of BG Cmax (% control), CHOav (r_s = 0.4134; n = 10; *ns*) and dietary fibre (r_s = 0.6900; n = 12; $p < 0.02$) both displayed quadratic relationships, while protein demonstrated a linear relationship (r = 0.5623; n = 12; *ns*; Figure 11). The relationship between BG Cmax reduction and dietary fibre was significant, and both dietary fibre and protein content had relative reductions in BG Cmax with increased content. On the other hand, the impact of CHOav content on relative reductions in BG Cmax was inconsistent across studies. A maximum relative reduction in BG Cmax (41.5%) was achieved at 50 g CHOav, and relative reductions in BG Cmax of 22.2% and 28.5% were recorded from studies containing 105 g and 102 g of CHOav respectively. In contrast, there was only a minimal relative reduction in BG CMax (>3%) in a study that contained 98.7 g of CHOav in the lentil meal.

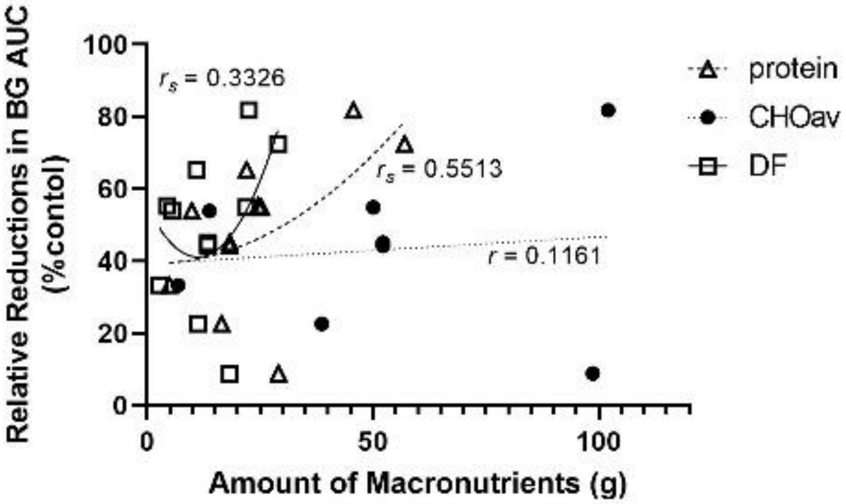

Figure 7. Relative reductions (%) of area under the blood glucose response curve (BG AUC) according to the amount of macronutrients or dietary fibre (g) in the lentil treatment group with respect to the control group. Quadratic modeling best fit protein (r_s = 0.5513; n = 11; *ns*) and dietary fibre (DF; r_s = 0.3326; n = 11; *ns*), and a linear model best fit available carbohydrates (CHOav; r = 0.1161; n = 8; *ns*).

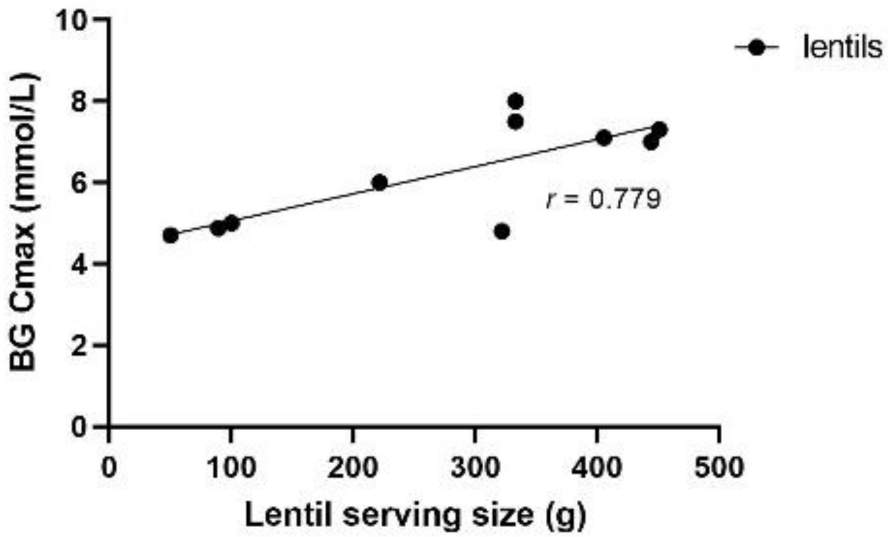

Figure 8. Maximum BG concentration (Cmax, mmol/L) according to lentil serving size (g). The linear trend best represented data (r = 0.779; n = 10; $p < 0.01$). The largest serving size investigated (715 g) was removed from this plot.

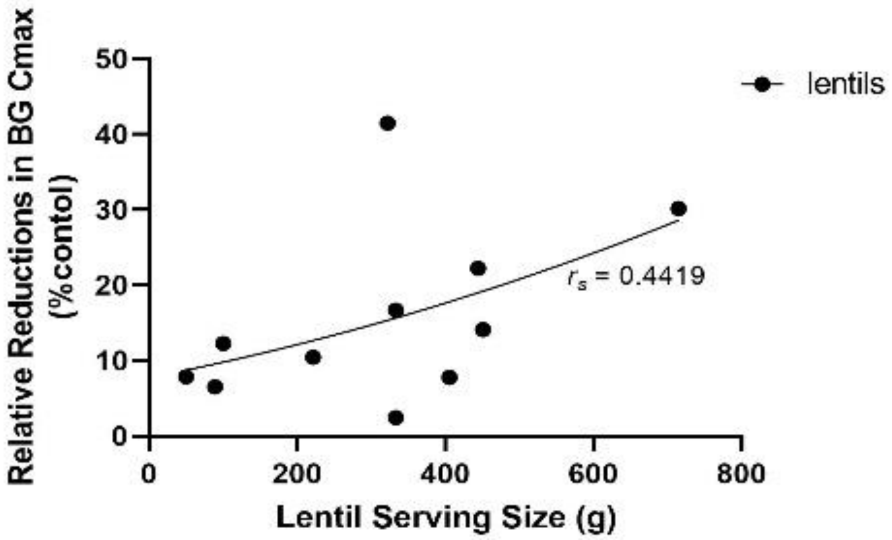

Figure 9. Relative reductions (%) of blood glucose maximum concentration (BG Cmax) according to the lentil serving size (g) in the lentil treatment group with respect to the control group. A quadratic model best fit this data ($r_s = 0.4419$; $n = 11$; *ns*).

3.7. Studies Involving Diabetic Participants

Trends were more difficult to elucidate with diabetic participants as most studies included in this review did not provide BG AUC. Although it is usually expected that persons with diabetes have an exaggerated glycemic response, the relative difference in BG AUC and BG Cmax should give some indication of the efficacy of lentils. Upon assessment of the studies listed in Table 2, the available data show that relative reduction in BG AUC, following lentil treatments, ranged from approximately 24% to 68%, which is a clinically significant effect. Further, it is clear that lentil treatments also resulted in reduction of BG Cmax of between 20% and 76%, with the mean (SD) relative reduction being 51.7 ± 25.4%.

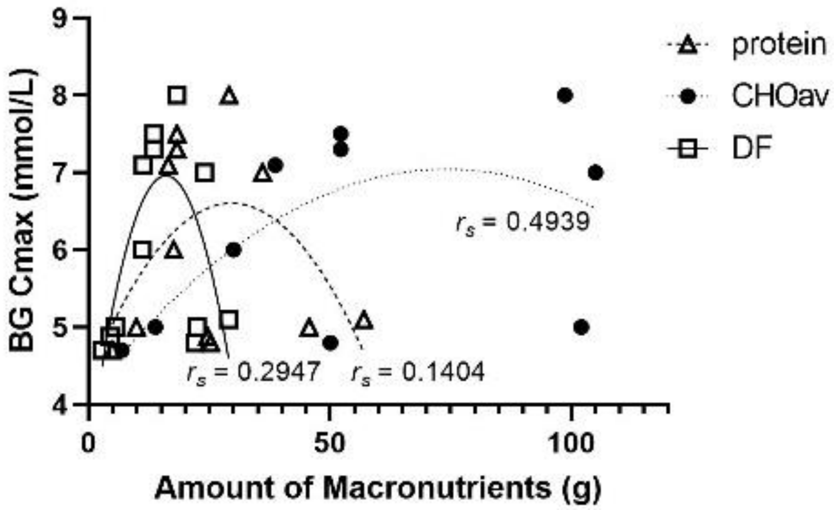

Figure 10. Maximum BG concentration (Cmax, mmol/L) according to the amount of macronutrients or dietary fibre (g) in the lentil treatments. Quadratic modeling best fit each component; protein ($r_s = 0.1404$; $n = 12$; *ns*), dietary fibre (DF; $r_s = 0.2947$; $n = 12$; *ns*) and available carbohydrates (CHOav; $r_s = 0.4939$; $n = 10$; *ns*).

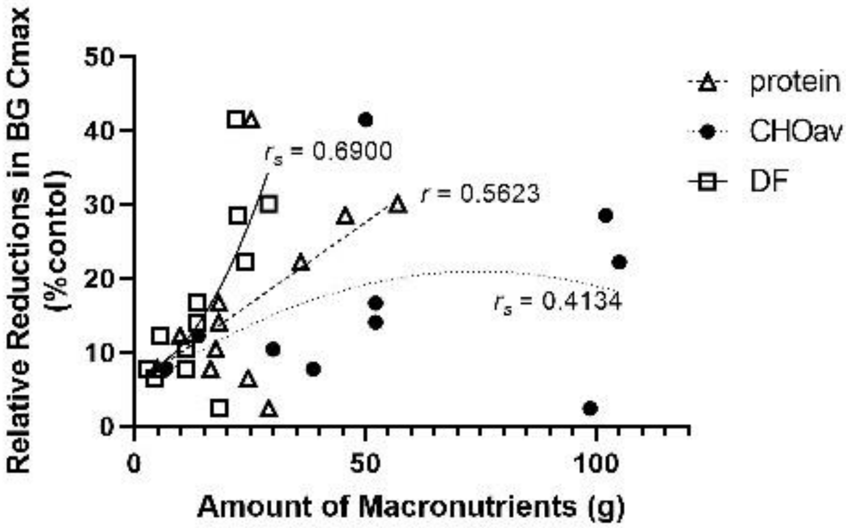

Figure 11. Relative reductions (%) of maximum BG concentration (Cmax, mmol/L) according to the amount of macronutrients or dietary fibre (g) in the lentil treatment group with respect to the control group. Available carbohydrates (CHOav; r_s = 0.4134; n = 10; *ns*) and dietary fibre (DF; r_s = 0.6900, n = 12; $p < 0.05$) were best described with quadratic modeling, and protein (r = 0.5623; n = 12; *ns*) was best fit with a linear model.

3.8. Insulin

In general, most studies did not report insulin data following lentil consumption; however, we identified six studies with insulin data: four studies included healthy participants and two with diabetic participants (Table 3). In healthy participants, the maximum concentration of insulin (Cmax) was 50 pmol/L after the consumption of a 100 g cooked green lentil treatment containing 9.9 g protein, 5.6 g fibre, and 26.3 g total carbohydrates. This represented a relative reduction in insulin Cmax of 37.5% at 15 min following consumption compared to control [11]. In another study with healthy participants, a considerably larger serving of cooked green lentils (715 g) led to a 56.5% relative reduction in insulin Cmax at 60 min compared to the control [10]. In diabetic participants, 225 g of cooked green lentils containing 20.5 g of protein was associated with an insulin Cmax of 216 ± 66 pmol/L at 100 min [18], and similarly a 297 g serving of cooked lentils with 22.4 g of protein led to an insulin Cmax of 174 ± 6 pmol/L at 120 min [19]. These two studies required T2D participants to consume 50 g of carbohydrates in control treatments, and the relative reductions of insulin Cmax were calculated to be 24% after a 225 g serving [18] and 31% after a 297 g serving of lentils [19]. The reduction of insulin Cmax appears to be independent of lentil serving, as reductions of similar magnitude were seen with both low and high lentil serving sizes.

Table 1. Summary of data obtained from studies involving healthy subjects.

		Lentil Treatment					Control Treatment					Outcomes						
Study	**Participants**	**Lentil Serving Size (g)**	**Protein (g)**	**DF (g)**	**CHOav (g)**	**TC (g) †**	**Control Serving (g)**	**Protein (g)**	**DF (g)**	**AC (g)**	**TC (g) †**	**BG Cmax Lentil Group**	**BG Cmax Control Group**	**Relative Difference in BG Cmax (%)**	**BG AUC Lentil Group (mmol × min/L)**	**BG AUC Control Group (mmol × min/L)**	**Relative Difference in BG AUC (%)**	**BG AUC Time Period**
Akhtar, Asim, and Wolever 1987 [16]	14 males aged 35.2 ± 1.54 years, BMI 23.6 ± 0.55 kg/m^2	89.3	24.6	4.5	-	25	110	15.1	1.5	-	50	4.88 @ 60 min	5.22 @ 120 min	6.51	35.5	79.4	55.3	3 h
Anderson, Liu, Smith, Liu, Nunez, Mollard and Luhovyy, 2014 [20]	males aged 18–30 years, normal BMI	405.5	16.5	11.3	38.7	50	405.5	10.5	7.9	38.7	46.6	7.1 @ 30 min	7.7 @ 30 min	7.79	97.1	125.5	22.6	2 h
Bennett, Chilibeck, Barss, Vatanparast, Vandenberg and Zello 2012 [21]	14 recreational soccer players, aged 22–27 years, BMI 22 kg/m^2	444	36	24	105	129	436	16	7	92	99	7.0 @ 15 min	9.0 @ 15 min	22.22	-	-	-	-
Jenkins, Ghafari, Wolever, Taylor, Jenkins, Barker, Fielden and Bowling, 1982 [22]	17 adults aged 28 ± 2 years	297.5 *	22	11	-	50	120	10.5	10.2	-	50	-	-	-	60	173	65.3	2 h
Jenkins, Wolever, Taylor, Griffiths, Krzeminska, Lawrie, Bennett, Goff, Sarson and Bloom, 1982 [10]	7 adults aged 26 ± 3 years	715 *	57	29	-	127	280	57	26	-	128	5.1 @ 30 min	7.3 @ 30 min	30.14	49	178	72.5	2 h
MacPherson 2018 [11]	adults aged 18–40 years, BMI 20–30 kg/m^2 male	100	9.88	5.55	13.8	26.3	54.6	2.23	1.07	15.5	13.6	5.0 @ 30 min	5.7 @ 30 min	12.28	30	65	53.9	2 h
	female	50	4.94	2.78	6.91	13.2	27.3	1.16	0.56	8.08	7.1	4.7 @ 15 min	5.1 @ 15 min	7.84	20	30	33.3	2 h
		Lentil Treatment Comparison					**Control Treatment Comparison**					**Outcomes**						
Study	**Participants**	**Lentil Serving Size (g)**	**Protein (g)**	**DF (g)**	**CHOav (g)**	**TC (g) †**	**Control Serving (g)**	**Protein (g)**	**DF (g)**	**AC (g)**	**TC (g) †**	**BG Cmax Lentil Group**	**BG Cmax Control Group**	**Relative Difference in BG Cmax (%)**	**BG AUC Lentil Group (mmol × min/L)**	**BG AUC Control Group (mmol × min/L)**	**Relative Difference in BG AUC (%)**	**BG AUC Time Period**
Mollard, Wong, Luhovyy and Anderson, 2011 [23]	25 males aged 20–30 years, BMI 20.0–24.9 kg/m^2	332.9	29.1	18.3	98.7	117	446.5	22.8	2.8	100.4	103.2	8.0 @ 40 min	8.2 @ 40 min	2.44	392.9	431.3	8.9	260 min
Mollard, Wong, Luhovyy, Cho and Anderson, 2014 [24]	15 males aged 18–35 years	332.9	18.3	13.5	52.2	65.7	116.6	9.9	2.8	64	66.8	7.5 @ 30 min	9.0 @ 30 min	16.67	133.8	239.7	44.2	135 min
Ramdath, Wolever, Siow, Ryland, Hawke, Taylor, Zahradka and Aliani, 2018 [15]	20 males and females, 18–75 years, BMI < 30 kg/m^2	321.8	25.3	22	50.1	72.1	68.1	5	4.6	50	54.6	4.8 @ 30 min	8.2 @ 30 min	41.46	65	144	54.9	2 h
Tovar, Granfeldt and Bjorck, 1992 [25]	10 adults aged 36 ± 2.5 years, BMI 22.4 ± 0.9 kg/m^2	221.52 *	17.6	11.1	30	41.1	70	19	1.4	30	31.4	6.0 @ 30 min	6.7 @ 30 min	10.45	-	-	-	2 h
Wolever, Jenkins, Ocana, Rao and Collier, 1988 [17]	5 adults aged 24 ± 0.3 years	3.2 g/kg, raw weight	45.7	22.5	102.1	124.6	1.7 g/kg	45.6	0	102	102	5.0 @ 45 min	7.0 @ 60 min	28.57	16	88	81.8	2 h
Wong, Mollard, Zafar, Luhovyy and Anderson, 2009 [26]	14 men aged 18–35 years, BMI 20–25 kg/m^2	451	18.3	13.5	52.2	65.7	235	9.9	2.8	64	66.8	7.3 @ 15 min	8.5 @ 15 min	14.14	96.3	175.4	45.1	2 h

DF, Dietary Fibre; CHOav, Available Carbohydrates; TC, Total Carbohydrates; BG, blood glucose; AUC, area under the curve. * Raw weights provided by these studies were converted to cooked weights using the average moisture content of green lentils (68.4%), as gathered from previous research (unpublished data). The cooked weight was calculated as follows: (dry weight/% solids) × 100, where % solid = 100–68.4. † Study did not include TC, AC and DF were summed to provide total carbohydrates value.

Table 2. Summary of data obtained from studies of subjects with T2D.

		Lentil Treatment					Control Treatment					Outcomes					
Study	Participants	Lentil Serving Size (g)	Protein (g)	DF (g)	CHOav (g)	TC (g) †	Control Serving (g)	Protein (g)	DF (g)	AC (g)	TC (g) †	BG Cmax Lentil Group	BG Cmax Control Group	BG AUC Lentil Group (mmol× min/L)	BG AUC Control group (mmol× min/L)	Relative Difference in BG AUC (%)	BG AUC Time Period
Akhtar 1987 [16]	14 adults aged 52.5 ± 2.46 years, BMI 24.3 ± 1.13 kg/m^2	89.3	24.6	4.5	-	25	110	15.1	1.5	-	50	11.2 @ 30 min	14.0 @ 30 min	95.5	215.5	55.7	3 h
Bornet, Costagliola, Rizkalla, Blayo, Fontvieille, Haardt, Letanoux, Tchobroutsky and Slama, 1987 [19]	18 adults aged 57 ± 2 years, BMI 27.9 ± 1.1 kg/m^2	225	20.5	3.25	50	53.25	-	-	-	50	50	2.1 @ 120 min †	6.1 @ 60 min †	-	-	-	-
Coulston, Hollenbeck, Liu, Williams, Starich, Mazzaferri and Reaven, 1984 [27]	8 adults aged 59 ± 2 years, BMI 27.3 ± 0.6 kg/m^2	49.9 **	12.3	5.8	30	35.8	-	3.7	4.1	38.2	34.1	13.7 @ 120 min †	17.5 @ 120 min †	2065 ‡	2731 ‡	24.4	3 h
Jenkins, Wolever, Jenkins, Thorne, Lee, Kalmusky, Reichert and Wong, 1983 [28]	12 adults aged 67 ± 2 years, 77.1 ± 4.4 kg	297.5 *	22.4	11	-	50	-	22.1	7.3	-	51.2	3.0 @ 120 min	6.2 @ 90 min	359	806	55.5	3 h
Jenkins, Wolever, Taylor, Ghafari, Jenkins, Barker and Jenkins, 1980 [29]	6 adults aged 43 ± 5 years	129.8 *	38.8	10	-	42.5	-	35.5	9.3	-	43.9	1.1 @ 30 min	4.7 @ 60 min	-	-	-	-
Krezowski, Nuttall, Gannon, Billington and Parker, 1987 [18]	8 male untreated diabetics aged 65 ± 2 years	297.5 *	22.4	11	-	50	-	-	-	-	50	1.9 @ 120 min †	7.4 @ 60 min †	380 ‡	1176 ‡	67.7	5 h

DF, Dietary Fibre; CHOav, Available Carbohydrates; TC, Total Carbohydrates; BG, blood glucose; AUC, area under the curve. * Raw weights provided by these studies were converted to cooked weights using the average moisture content of green lentils (68.4%), as gathered from previous research (unpublished data). The cooked weight was calculated as follows: (dry weight/% solids) × 100, where % solid = 100–68.4. ** Unspecified if wet or dry weight. † TC was calculated by adding AC and DF if the study did not state its own TC value. AC only included if value given in study. ‡ Values were converted from mg × h/dL to mmol × min/L using the conversion factors, 1 mg/dL glucose = 0.05551 mmol/L glucose and 1 h = 60 min. † Values were converted from mg/dL to mmol/L using the conversion factor, 1 mg/dL glucose = 0.05551 mmol/L glucose.

Table 3. Summary of studies that assessed blood insulin after lentil consumption in either healthy or diabetic subjects.

		Lentil Treatment				Control Treatment				Outcomes						
Study	Participants	Lentil Serving Size (g)	Protein (g)	DF (g)	TC (g)	Control Serving (g)	Protein (g)	DF (g)	TC (g)	Insulin Cmax Lentil Group	Insulin Cmax Control Group	Relative Difference Insulin Cmax (%)	Insulin AUC Lentil Group	Insulin AUC Control Group	Relative Reduction Insulin AUC (%)	Insulin AUC Time Period
Bennett, Chilibeck, Barss, Vatanparast, Vandenberg and Zello 2012 [21]	14 recreational soccer players aged 22–27 years, BMI 22 kg/m^2	444	36	24	129	436	16	7	99	135 pmol/L	125 pmol/L	8.0	-	-	-	-
Bornet, Costagliola, Rizkalla, Blayo, Fontvieille, Haardt, Letanoux, Tchobroutsky and Slama, 1987 [19]	18 type 2 diabetics	225	20.5	3.25	50		-	-	50	216 pmol/L †	283 pmol/L †	23.7	-	-	-	-
Jenkins, Wolever, Taylor, Griffiths, Krzeminska, Lawrie, Bennett, Goff, Sarson and Bloom, 1982 [10]	Healthy adults (5 men, 2 women)	715 *	57	29	156	280	57	26	154	100 pmol/L	230 pmol/L	56.5	-	-	-	-
Krezowski, Nuttall, Gannon, Billington and Parker, 1987 [18]	8 male untreated diabetics	297 *	22.4	11	50	120	10.6	10.2	50	174 pmol/L †	251 pmol/L †	29.7	44 μU×h/mL	91 μU × h/mL	51.7	5 h
MacPherson 2018 [11]	Healthy adult males and females aged 18–40 years, BMI 20–30 kg/m^2	100	9.88	5.55	26.3	54.6	2.23	1.07	13.6	50 pmol/L	80 pmol/L	37.5	1100 nmol × min/L	2000 nmol × min/L	45	2 h
Tovar, Granfeldt and Bjorck, 1992 [25]	10 healthy adults aged 36 ± 2.5 years, BMI 22.4 ± 0.9 kg/m^2	70	17.6	11.1	41.1	70	19	1.4	31.4	240 pmol/L	270 pmol/L	11.11	-	-	-	-

DF, Dietary Fibre; TC, Total Carbohydrates; AUC, area under the curve. * Raw weights provided by these studies were converted to cooked weights using the average moisture content of green lentils (68.4%), as gathered from previous research (unpublished data). The cooked weight was calculated as follows: (dry weight/% solids) × 100, where % solid = 100–68.4. † Insulin Cmax values were converted from μU/mL to pmol/L using the conversion factor 1 μU/mL = 6 pmol/L (Diabetes Care 1998). mU/mL was converted to pmol/L using the conversion factor of 1mU/L = 6 pmol/L (Vølund 1993). (Krezowski et al. provided an original value of 10.5 μU/mL and 23 μU/mL. for lentil and control treatments, respectively. Bornet et al. gave an original value of 25 mU/L and 42 mU/L for lentil and control treatments, respectively.

4. Discussion

This review provided several insights into the hypoglycemic effects of lentil consumption using a limited number of available studies involving both healthy and diabetic participants. Pooled data from these studies suggest that lentil serving sizes higher than 100 g cooked weight do not lead to further reductions in BG AUC in healthy participants. Relative reductions in BG AUC and BG Cmax were greater with increased levels of protein and dietary fibre content, as noted in cooked lentil servings of 715 g (57 g protein, 29 g dietary fibre) [10] and 3.2 g lentils/kg of participant body weight (average 45.7 g protein, 22.5 g dietary fibre/serving) [17]. These larger serving sizes had weaker correlations between CHOav and reductions in BG AUC or BG Cmax. The amount of CHOav proved to be a highly variable factor in relative reduction in BG AUC, as lentil servings with high CHOav (~100 g) displayed both high and low reductions. A lentil treatment with 102.1 g of CHOav that was associated with a greater relative reduction in BG AUC (82%) had higher protein content. Additionally, relative reductions in BG Cmax followed a similar pattern: increased protein (25.3–57 g) and dietary fibre (22–29 g) content led to greater reductions. Again, the impact of CHOav was difficult to interpret, as the relative reduction in BG Cmax associated with the amount of CHOav content was not consistent across the studies examined. Larger servings of lentils, leading to higher levels of protein and dietary fibre, may be optimal for achieving a maximum reduction in BG AUC and Cmax in healthy participants.

The hypoglycemic effect of lentils has been documented frequently in the literature, yet the effect size and lentil dosage vary greatly between studies and serving–response studies are scarce. Cumulative evidence from several studies has shown that BG AUC was lower in lentil groups when equivalent amounts of protein [10,17], dietary fibre [22], CHOav [15,17,20,25] and serving sizes [20] of control treatments were matched. This trend is in alignment with previous research in which lentils were found to have a low glycemic index compared to high-starch containing foods, thereby attenuating large fluctuations in BG [30,31]. The lack of a clear dose–response observed in this review indicates that both low and high serving sizes of lentils have similar effects on BG. At a relatively low serving size of 100 g of cooked green lentils, there was a 54% relative reduction in BG AUC compared to control [11]. Health Canada guidelines state that a minimum of 20% postprandial glucose reduction is significant [32]. Our analysis shows that consuming even a relatively small serving size of lentils (50–100 g) seems to confer this benefit. Consumers are more likely to eat smaller quantities of lentils [33], and the current trend suggests that they would continue to experience the BG attenuation effects of lentils at these lower serving sizes. In contrast to glucose, insulin Cmax differed between low and high lentil servings. We found that both healthy and diabetic participants had lower insulin Cmax with lentil treatment compared to control, as outlined in Table 3. As an example, healthy participants who consumed 715 g of cooked green lentils had an insulin Cmax of 100 pmol/L [10], compared to an insulin Cmax of 50 pmol/L with 100 g of cooked green lentils [11]. The higher serving size was associated with a 72% relative reduction in BG AUC, whereas the 100 g serving led to a 54% relative reduction compared to control. This data suggests that the hypoglycemic effect of lentils is not linear, and is not due to an increase in blood insulin levels [11,33]; this is an important finding since hyperinsulinemia is a hallmark of T2D [34].

Studies have used lentils in different forms and found that while processing can have an effect on the degree to which lentils lower BG, results from our analysis indicate that processed lentils also lowers BG AUC, compared to control treatments [15,20]. These studies suggest that consuming lentils in different forms (whole, powder, flour) maintains the BG AUC lowering property when compared to starchy controls. A study that examined the glycemic response of whole, puréed, and powdered green lentils, found that the pre and postprandial absolute glucose concentration in participants consuming these lentil preparations were lower than the control (whole wheat flour) overall [20]. In addition, all treatments in the Anderson et al. (2014) study had lower preprandial BG AUC compared to the control diet; whole and powdered lentils had a statistically lower preprandial BG

AUC ($p < 0.05$) compared to the control. Puréed lentils also had the lowest postprandial BG AUC compared to the control with a difference of 31.3 mmol × min/L, although none of the postprandial differences were reported to be significant [20]. Similar to lentil powder, another study that incorporated 20% lentil flour into baked muffins observed a relative reduction in BG AUC of 25% after 2 h [35]. This result falls within the range of relative reductions in BG AUC for the whole lentil studies (22.81% to 81.82%; Table 1), and despite the change in preparation, the reduction of BG AUC is still above the important threshold of 20% [32]. This finding suggests that the components responsible for the glucose-lowering action of lentils remain biologically active through both processing and baking. Unfortunately, a single lentil flour study does not provide enough evidence to conclude that lentils have the same effect regardless of how they are prepared and consumed. More human studies need to be carried out to determine if and how the form in which lentils are consumed changes the glycemic response in healthy and diabetic participants.

While lentils are known to reduce BG, the specific component responsible for this effect continues to be debated. Some studies have suggested that it is the protein content of a meal that lowers BG by increasing insulin secretion [36], referring to dietary protein as a "potent insulin secretagogue" [37]. However, the available studies show that those consuming the highest lentil serving sizes had the lowest insulin levels, therefore an increase in insulin is unlikely to be the primary factor in the glycemic effect of lentils. There is another potential mechanism by which proteins may reduce BG. Protein in lentils could lead to protein–starch interactions that block digestive enzymes from accessing starch, thereby reducing the amount of glucose available for absorption through the intestines [38]. Although unlikely, it was suggested that products of protein breakdown, such as small peptide chains, could lower BG through competitive inhibition of intestinal enzymes and prevent the breakdown of starch to glucose. These smaller peptide chains were shown to competitively inhibit enzymes responsible for breaking down insulin, thereby permitting insulin to persist longer and continue to lower the BG level while remaining at a lower concentration itself [39]. It has also been shown that lentil polyphenols are able to significantly inhibit α-glucosidase, a key enzyme in the digestion of dietary carbohydrates; this could partially account for the BG lowering effect of lentils [5]. Wolever et al. (1988) created a red lentil treatment that contained the same amount of protein content as the control diet (45 g), which resulted in significant BG responses, including reduced peak rise, BG AUC, and mean postprandial BG concentrations. The implications of the matched protein content study suggest that the BG lowering responses may be due to other differences in digestion and absorption rates, and are not contingent on protein content alone [17]. Based on the data analysed in this review, we determined that maximum relative reductions in BG AUC are observed at 45–57 g of protein content in the lentil treatments. Proteins certainly appear to have a role in the health benefits associated with consuming lentils; however, the mechanisms or combination of mechanisms that allow proteins to reduce BG is still unknown.

Studies analysing the impacts of dietary fibre on BG have produced varying results. A 2012 meta-analysis found that fibre supplementation of 4–42 g/d reduced fasting BG by 0.85 mmol/L (95% CI, 0.46–1.25) in participants with T2D when compared to placebo treatment [40]. A wide range of fibre servings was provided to participants during acute feeding trials, with 15 g/d being the most common serving [40]. Through our analyses, we determined that maximum relative reductions in BG AUC are observed at 22–30 g of dietary fibre content in the lentil treatments. Foods with high amounts of soluble viscous fibre, such as oat gum, significantly reduce BG and insulin relative to its viscosity [41]; however, less viscous soluble fibres such as pectin and psyllium were ineffective [42]. The largest relative reduction in BG AUC (81.8%) observed during our analysis was from a study in which only the amount of dietary fibre differed between the control (0 g) and lentil treatments (22.5 g), while protein, CHOav and energy content were matched [17]. However, the second-largest reduction in BG AUC (72.5%) had a control and lentil treatment that differed by only 3 g in dietary fibre content [10]. Taken together, the dietary fibre content in a meal likely has a role in reducing BG AUC, but the amount of dietary fibre needed for this effect and the associated mechanism(s) of action is yet to be determined.

Of the two macronutrients and dietary fibre examined, CHOav was expected to elicit a greater BG AUC as CHOav content increased, and this was observed from the available data. Like many studies, protein and dietary fibre showed U-shaped quadratic relationships with BG AUC, whereas CHOav displayed a linear relationship in our analyses. Similarly, a study involving untreated T2D participants reported that BG response increased linearly as the amount of ingested carbohydrates increased [43]. Results from the studies reviewed here show that the absolute BG AUC, BG Cmax, and the relative reductions of BG AUC and BG Cmax of healthy participants receiving lentil treatments are only weakly correlated with the amount of CHOav, and more moderate correlations in these measures were observed with dietary fibre. There were inconsistencies between how CHOav was reported in the collected literature, as some studies only mentioned total carbohydrates, while others were unclear as to whether the measurement was total carbohydrates or CHOav.

It was observed that dietary fibre content follows similar trends to protein in reducing BG AUC, and likely has an important role in its reduction. Evidence gathered in this review suggests that the amount of protein in a lentil treatment has a stronger influence on reducing BG AUC relative to control when compared to the amount of dietary fibre or CHOav; this relationship was previously examined through an assessment of glycemic index in combination with protein and total dietary fibre [44]. The GI of different foods was found to be associated with its protein and dietary fibre content [44,45], and our analysis indicates a moderate correlation with protein and relative reductions in BG AUC, as well as a strong correlation with dietary fibre with relative reductions in BG Cmax compared to controls. However, it was also suggested that the correlation between GI, protein, fibre, and fat is due to the fact that a large number of studies utilise legumes, which contain more of these macronutrients and dietary fibre when compared to other foods [45]. Furthermore, it was previously argued that while correlated, protein does not cause lower glycemic indices, and glycemic responses to foods cannot be predicted from their macronutrient composition since GI is a feature of the carbohydrates found in food [44].

5. Summary

The studies analysed in this review provide support for the ability of lentil consumption to lower BG in participants with or without T2D. This beneficial effect of consuming lentils is likely due to their complex macronutrient content [9,44]. Both protein and dietary fibre content were identified as potential factors in the glycemic response of lentils, however, the direct evidence for either remains inconclusive. Our analysis suggests a range of 45–57 g of protein and 22–30 g of dietary fibre content in lentil treatments are needed to obtain a maximum relative reduction in BG AUC, while the CHOav content was found to have only a weak relationship with relative reductions of BG AUC. Both high (>100 g) and low (<100 g) lentil serving sizes were assessed for BG AUC lowering; there were moderate correlations between serving and BG AUC and between serving and relative reductions in BG Cmax. Although increased lentil serving sizes moderately influenced these parameters, no clear relationship was found between serving and relative reductions in BG AUC, making it difficult to predict a minimal serving size for an optimal and consistent glycemic benefit. Another important aspect of this research is the potential that the beneficial effects of lentils may be due to an interaction with insulin. In studies that reported insulin levels, the insulin area under the curve was lower for lentil meals compared to controls, and this insinuates that lentil consumption has a role in mediating insulin levels. The relationship between lentil consumption and insulin response is a topic that requires more research in order to draw firm conclusions. Persons with T2D have the greatest potential to benefit from this research as BG and insulin control are central to the management of this condition. Overall, the studies examined for this review corroborate findings that lentil consumption provides beneficial effects on both BG and insulin levels, although further investigation is required to fully understand how lentils and other pulses are contributing to this lowering effect.

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Foxtail Millet Improves Blood Glucose Metabolism in Diabetic Rats through PI3K/AKT and NF-κB Signaling Pathways Mediated by Gut Microbiota

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Abstract: Foxtail millet (FM) is receiving ongoing increased attention due to its beneficial health effects, including the hypoglycemic effect. However, the underlying mechanisms of the hypoglycemic effect have been underexplored. In the present study, the hypoglycemic effect of FM supplementation was confirmed again in high-fat diet and streptozotocin-induced diabetic rats with significantly decreased fasting glucose (FG), glycated serum protein, and areas under the glucose tolerance test ($p < 0.05$). We employed 16S rRNA and liver RNA sequencing technologies to identify the target gut microbes and signaling pathways involved in the hypoglycemic effect of FM supplementation. The results showed that FM supplementation significantly increased the relative abundance of Lactobacillus and Ruminococcus_2, which were significantly negatively correlated with FG and 2-h glucose. FM supplementation significantly reversed the trends of gene expression in diabetic rats. Specifically, FM supplementation inhibited gluconeogenesis, stimulated glycolysis, and restored fatty acid synthesis through activation of the PI3K/AKT signaling pathway. FM also reduced inflammation through inhibition of the NF-κB signaling pathway. Spearman's correlation analysis indicated a complicated set of interdependencies among the gut microbiota, signaling pathways, and metabolic parameters. Collectively, the above results suggest that the hypoglycemic effect of FM was at least partially mediated by the increased relative abundance of Lactobacillus, activation of the PI3K/AKT signaling pathway, and inhibition of the NF-κB signaling pathway.

Keywords: foxtail millet; glucose metabolism; gut microbiota; PI3K/AKT signaling pathway; NF-κB signaling pathway

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1. Introduction

Diabetes and its associated disorders have reached an alarming level worldwide. In 2019, an estimated 463 million adults aged 20–79 years old worldwide had diabetes, and by 2045, 700 million adults will be living with diabetes [1]. Type 2 diabetes (T2D) accounts for the vast majority of diabetes. Recent decades have seen an exponential increase in the number of people suffering from T2D, despite the expanding number of anti-hyperglycemic medication options [2]. Fortunately, there is firm evidence that T2D can be prevented and effectively managed through the adoption of healthy lifestyles [1], including the increased consumption of whole grains [3].

Foxtail millet (*Setaria italica* L., FM) was arguably the first whole grain cultivated by humans [4]. Currently, it is the sixth-highest yielding grain in terms of worldwide production and is cultivated in 26 countries [5]. FM contains significant levels of protein, fiber, minerals, phenolic acids, and various phytochemicals. It has received ongoing increased attention, particularly due to its hypoglycemic, hypolipidemic, and antioxidant characteristics [4,6]. Many studies, including our previous work, have proven that FM has a lower glycemic index, which is conducive to the glycemic control of patients with abnormal blood glucose [7,8]. However, the mechanisms underlying the hypoglycemic effect of FM were still unclear.

Recent studies have provided a substantial body of evidence for the contribution of the gut microbiota to glucose metabolism [9,10]. It is generally believed that the occurrence and development of T2D is one result of gut microbial dysbiosis caused by an unbalanced diet [11]. Research suggested that changes in the diet could account for 57% of the variations in microbiota [12]. FM could indeed change the composition and relative abundance of gut microbiota. For instance, Li et al. found that FM supplementation decreased the population of Firmicutes and increased Actinobacteria in rats fed a high-fat diet [13].

However, the exact contribution of the gut microbiota to the hypoglycemic effect of foxtail millet is still not clear due to the complexity and diversity of gut microbes. A number of mechanisms by which gut microbiota may influence glucose metabolism have been investigated, such as the insulin signaling pathway and low-grade inflammation [14]. Specifically, the insulin-mediated PI3K/AKT signaling pathway and inflammatory factor-mediated NF-κB signaling pathway are two key processes in T2D. Many studies have proved that glucose metabolism, including glycolysis and gluconeogenesis, is mainly regulated by the PI3K/AKT signaling pathway [15]. The hypoglycemic function of bioactive substances and hypoglycemic drugs cannot be achieved without the participation of this pathway [16,17]. For example, the PI3K/AKT signaling pathway can inhibit the key enzymes of gluconeogenesis and thus play an important role in maintaining the homeostasis of glucose metabolism [18]. T2D is associated with low-grade inflammation [19], and the NF-κB signaling pathway is the primary method of the inflammatory response [20].

Thus, in the present study, 4 weeks of FM intervention was conducted in high-fat diet/streptozotocin (HFD/STZ)-induced diabetic rats. In addition to glycemic metabolism indicators, 16S rRNA and RNA sequencing technologies were employed to investigate the differences between the gut microbiota and liver transcriptome in diabetic rats. We evaluated the key gut microbe and liver signaling pathways affected by FM supplementation. The target genes and target biological processes of foxtail millet in improving glucose metabolism were identified. Finally, the mechanisms underlying the hypoglycemic effect of FM were partially clarified.

2. Materials and Methods

2.1. Animals and Diet

FM was provided by Shanxi Dongfangliang Life Sciences Co., Ltd. To maintain consistency with our previous clinical trial [8], the FM was processed into steamed bread according to the previous introduction [7]. After being freeze-dried and crushed, the powder of FM steamed bread was added to rat feed at a rate of 20%, which was similar to the intervention amount of subjects in a clinical trial [8]. The specific formulae for the different diets are listed in Supplementary Materials Table S1. The energy ratio between the 20% FM diet and the high-fat diet was equal.

Male SD rats (6 weeks old) were obtained from Vital River Laboratories Co., Ltd. (Beijing, China, SCXK (J) 2016-0006). They were kept in a climate-controlled room (22 ± 2 °C, 55% ± 5% relative humidity, and a 12 h light/dark cycle) with free access to food and water. All animal procedures were conducted according to the guidelines of the Laboratory Animal Ethics Association of China Agricultural University.

After one week of acclimatization, eight rats were randomly grouped into the normal control (NC) group and fed with the D12450J control diet (Research Diets, New Brunswick, NJ, USA). All the other rats were induced to diabetics by 4 weeks of a high-fat diet (D12492) and 35 mg/kg of STZ injection. Then, the diabetic rats were randomly divided into the diabetic control (DC) group and FM group with eight rats each for four weeks of intervention. The body weight and food intake of rats were recorded weekly. At the end of the intervention, rats were euthanized by decapitation under isoflurane anesthesia. Blood samples were collected and centrifuged at 3000 r/min for 10 min. The serum, liver tissues, and feces were collected and stored at −80 °C until analysis.

2.2. Biochemical Analysis

The serum concentrations of the fasting glucose (FG), total triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were measured using a COBAS INTEGRA 800 auto-analyzer (Roche, Basel, Switzerland) per the manufacturer's protocols. The fasting insulin (ml302840), glycated serum protein (GSP, ml037457), glucose kinase (GK, ml059525), glucose-6-phosphatase (G6P, ml196120), and phosphoenolpyruvate carboxy (PEPCK, ml059012) were determined using commercial kits (Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China). Then, via homeostasis model assessment, the insulin resistance index (HOMA-IR) was calculated [21].

In addition, i.p. glucose tolerance tests (GTTs) were performed three days before the end of the experiment. In brief, after a 12 h fast, all rats were administered a 50% glucose solution (2.0 g/kg body weight), and blood samples from the tail veins at 0, 30, 60, 120, and 180 min were collected successively to measure the blood glucose concentration.

2.3. Gut Microbiota Analysis

The gut microbiota of rats were investigated after 4 weeks of intervention, according to the method described before [22]. In brief, the total bacterial DNA was extracted from fecal samples using MoBio Power Soil HTP-96 extraction kits (MoBio Laboratories, Carlsbad, CA, USA). The 338F (5′-ACTCCTACGGGAGGCAGCAG-3′) and 806R (5′-GGACTACHVGGGTWTCTAAT-3′) primer pair targeting the V3–V4 region of the 16S rRNA gene was chosen for PCR amplification. The resulting PCR products were purified using a QIAquick PCR Purification Kit (QIAGEN, Valencia, CA, USA). Finally, qualified DNA samples were sequenced and analyzed on an Illumina MiSeq platform (Illumina, Inc., San Diego, CA, USA).

2.4. RNA Sequencing (RNA-Seq) Analysis

The total RNA was extracted from liver tissue using TRIzol reagent (Invitrogen, Thermo Scientific, MA, USA) following the manufacturer's instructions. The quantity and quality of RNA were determined using a NanoDrop 2000 ultramicro-spectrophotometer (ThermoFisher Scientific, Waltham, MA, USA). The RNA integrity was estimated using an RNA 6000 Nano Bioanalyzer 2100 Assay (Agilent, Palo Alto, CA, USA). Library construction and sequencing were performed with the Illumina HiSeq platform by Majorbio Biopharm Technology (Shanghai, China).

Expression profiles were obtained using the free online platform of Majorbio Cloud Platform (www.majorbio.com) (accessed on 20 January 2021). In brief, the fold changes were estimated according to the fragments per kilobases per million reads (FPKM) in each sample, and differential expression analysis was performed with the DESeq2 package. We considered differentially expressed genes (DEGs) with $p < 0.05$ and $|\log2\ FC| > 1$. Finally, enrichment analysis was performed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database.

2.5. Real-Time PCR (RT-PCR) Analysis

The total RNA was extracted from liver tissues with TRIzol reagent (Invitrogen, Carlsbad, CA, USA) according to the manufacturer's instructions. RNA was then reverse transcribed into cDNA using a RevertAid First cDNA Synthesis Kit (K1622, Thermo Scientific, CA, USA). RT-PCR was performed using SYBR Green dye for the relative quantification of DEG expression. The relative mRNA expression levels of the genes were calculated by the $2^{-\triangle\triangle CT}$ formula, and β-actin was used as the housekeeping gene. The primers are listed in Table S2.

2.6. Western Blot Analysis

Liver tissue was lysed in lysis buffer (100 mg:1 mL) supplemented with protease inhibitor. After determining the protein concentration, the lysates were separated on SDS-PAGE gels and transferred to 0.22 μm PVDF membranes. The membranes were blocked in PBS containing 1% Tween-20 and 5% milk for 1 h at 37 °C and incubated with primary antibodies (Beyotime Biotechnology, Shanghai, China) overnight at 4 °C. The specific primary antibodies used in the present study were AKT (60KD, AA326), p-AKT (Ser473, 60KD, AA329), NF-κB-p65 (65KD, AN365), p-NF-κB-p65 (Ser536, 65KD, AN371), p-IKBα (Ser32, 36KD, AF1870) and p-IKKα/β (Ser176/180, 86KD/87KD, AI139). After 1 h of incubation at 37 °C with goat anti-rabbit secondary antibodies (SA00001-2, Proteintech Group Inc., Chicago, IL, USA), Western blot images were captured using a Tanon-3500 gel imaging system (Tanon, Shanghai, China).

2.7. Immunofluorescence Staining

Immunofluorescence staining was performed on 5 μm thick paraffin sections of isolated liver tissues fixed in paraformaldehyde. Sections were deparaffinized in xylene and rehydrated in graded alcohols. Endogenous peroxidase was blocked, followed by antigen retrieval. After this, the tissues were incubated with the primary antibodies (p-NF-κB-p65, AN371, Beyotime Biotechnology, Shanghai, China) overnight at 4 °C, and then incubated with FITC modified second antibody (A0562, Beyotime Biotechnology, Shanghai, China) for 1 h at 37 °C. The nuclei were counterstained with DAPI. The images were captured using confocal scanning laser microscopes.

2.8. Statistical Analysis

Statistical analyses were conducted using SPSS software version 20.0 (IBM Corp., Armonk, NY, USA), and graphs were plotted using GraphPad Prism (GraphPad Software, San Diego, CA, USA). The data of biochemical, gut microbiota, RT-PCR, and Western blot were represented as the mean ± standard deviation (SD) and preanalyzed using Shapiro–Wilk test. The data of RNA-Seq were estimated according to FPKM. Differences between the two groups were compared using Student's *t*-test. Differences between the three groups were compared using one-way ANOVA with Tukey's multiple comparison post hoc test. All statistical tests were two-sided. Differences with $p < 0.05$ were considered statistically significant.

3. Results

3.1. FM Supplementation Improved the Blood Glucose Metabolism

Compared with DC rats, the FBG concentration, GSP concentration, and areas under the GTTs (AUC) of FM rats were significantly decreased, while the TC and HDL-C concentration were significantly increased after 4 weeks of FM supplementation. There were no significant differences in the concentrations of the FBG, TC, and HDL-C between the NC and FM groups (Figure 1A,D,F,J,K). FM supplementation improved glucose tolerance significantly. Although the blood glucose concentration of FM rats was still higher than that of NC rats throughout GTT, the concentration decreased significantly at 0, 60, and 120 min when compared with DC rats (Figure 1E). However, FM supplementation did not cause significant improvements in the fasting blood insulin secretion, insulin resistance (HOMA-IR), body weight, food intake, and blood triglyceride concentration (Figure 1B,C,G–I).

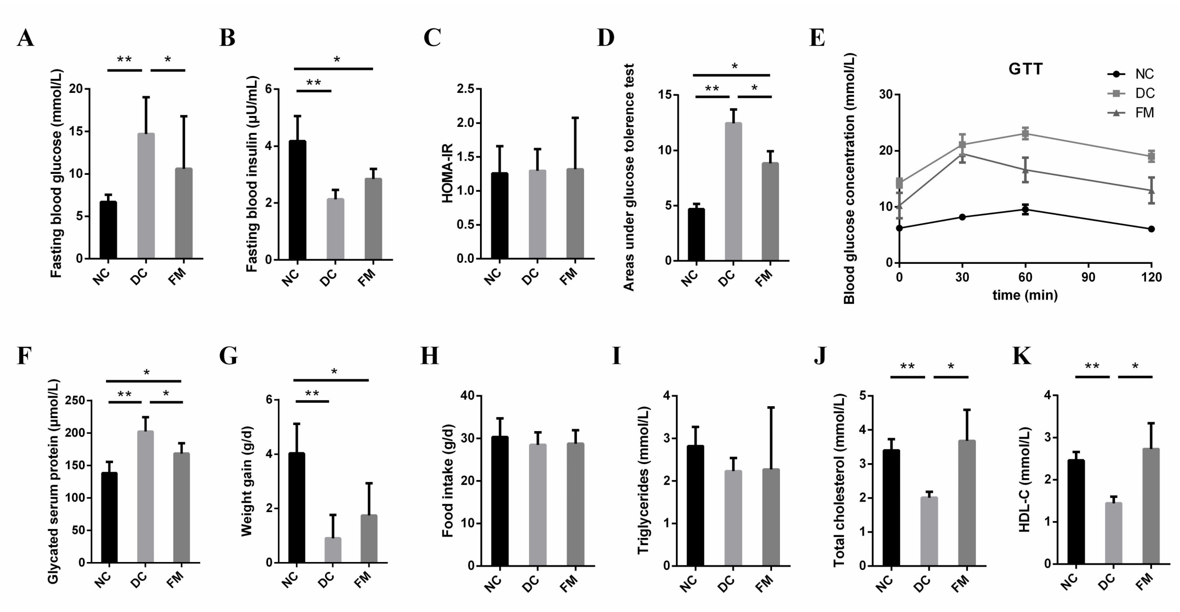

Figure 1. Effect of foxtail millet supplementation on glucose metabolism (**A**–**F**), weight gain (**G**), food intake (**H**), and lipid metabolism (**I**–**K**) in HFD/STZ-induced diabetic rats. Data were represented as mean ± SD. NC, normal control group (n = 8); DC, diabetic control group (n = 8); FM, foxtail millet supplementation group (n = 8); GTT, glucose tolerance tests; HDL-C, high-density lipoprotein cholesterol. Differences between groups were compared using one-way ANOVA with Tukey's multiple comparison post hoc test, * $p < 0.05$, ** $p < 0.01$.

3.2. FM Supplementation Changed the Gut Microbiota

To explore the role of the gut microbiota in the hypoglycemic effect of FM, we investigated the effects of FM supplementation on the composition and relative abundance of gut microbe using the 16S rRNA sequencing method. A total of 1,025,521 high-quality reads of 17 samples were generated, with an average of 56,973 ± 12,029 reads per sample. Based on 97% similarity, 787 OTUs were obtained, which could be divided into 12 phyla, 21 classes, 32 orders, 57 families, and 154 genera. The rarefaction and Shannon curves in Supplementary Materials Figure S1A,B indicated that the bacterial species were fully detected and evenly distributed. There were no significant differences in the richness (ACE) and α-diversity (Shannon and Simpson) of the gut microbiota among different groups (Supplementary Materials Figure S1C–E).

The Venn diagram illustrated that 586 out of 787 OTUs were shared among the three groups, while 35 OTUs were unique to the FM group (Figure 2A). To observe the effect of FM supplementation on the gut microbiota intuitively, we conducted both unsupervised principal component analysis (PCA) and supervised partial least squares discriminant analysis (PLS-DA). The PCA of three groups showed that the NC and DC groups were clearly clustered into two separate groups, while the FM group was clustered between them (Figure 2B). However, a completed separation of three groups in PLS-DA indicated significant differences among them (Figure 2C). These results suggested that FM supplementation significantly affected the gut microbial structure of diabetic rats. To a certain extent, this could alleviate the negative effects of diabetes on the gut microbiota.

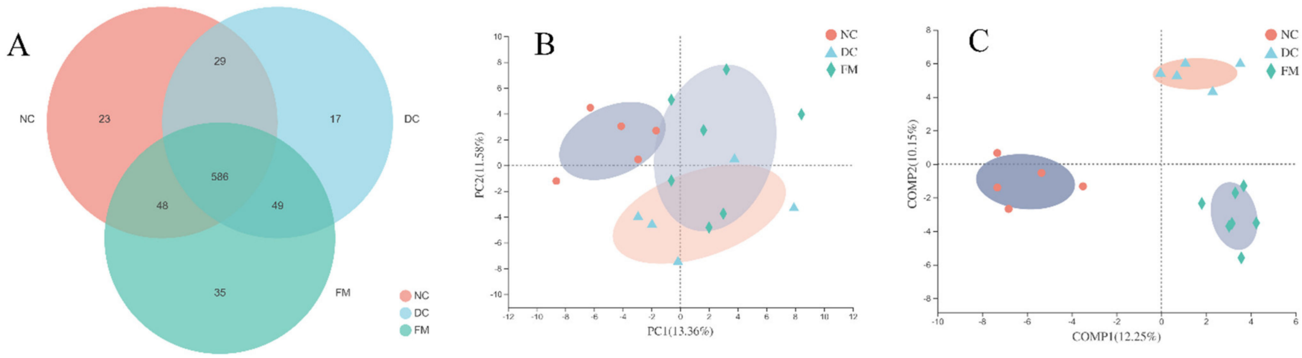

Figure 2. Effect of foxtail millet supplementation on the structure of gut microbiota: (**A**) Venn diagram on the OTU level; (**B**) unsupervised principal component analysis (PCA) on the OTU level; (**C**) supervised partial least squares discriminant analysis (PLS-DA) on the OTU level. NC, normal control group (*n* = 5); DC, diabetic control group (*n* = 5); FM, foxtail millet supplementation group (*n* = 7).

Next, we performed a taxonomy-based analysis at the phylum and genus levels to evaluate the specific alterations of the gut microbe. The phylum *Firmicutes* was dominant among the 12 phyla presented in the gut microbiota from the three groups of mice with an average relative abundance of 83 ± 12% (Figure 3A). The ratio of *Firmicutes/Bacteroidetes* was significantly increased in DC rats, compared with NC rats, but not significantly decreased in FM rats (Figure S1F). The average compositions of bacterial communities with relative abundance higher than 1% at the genus level are shown in the Circos diagram (Figure S1G).

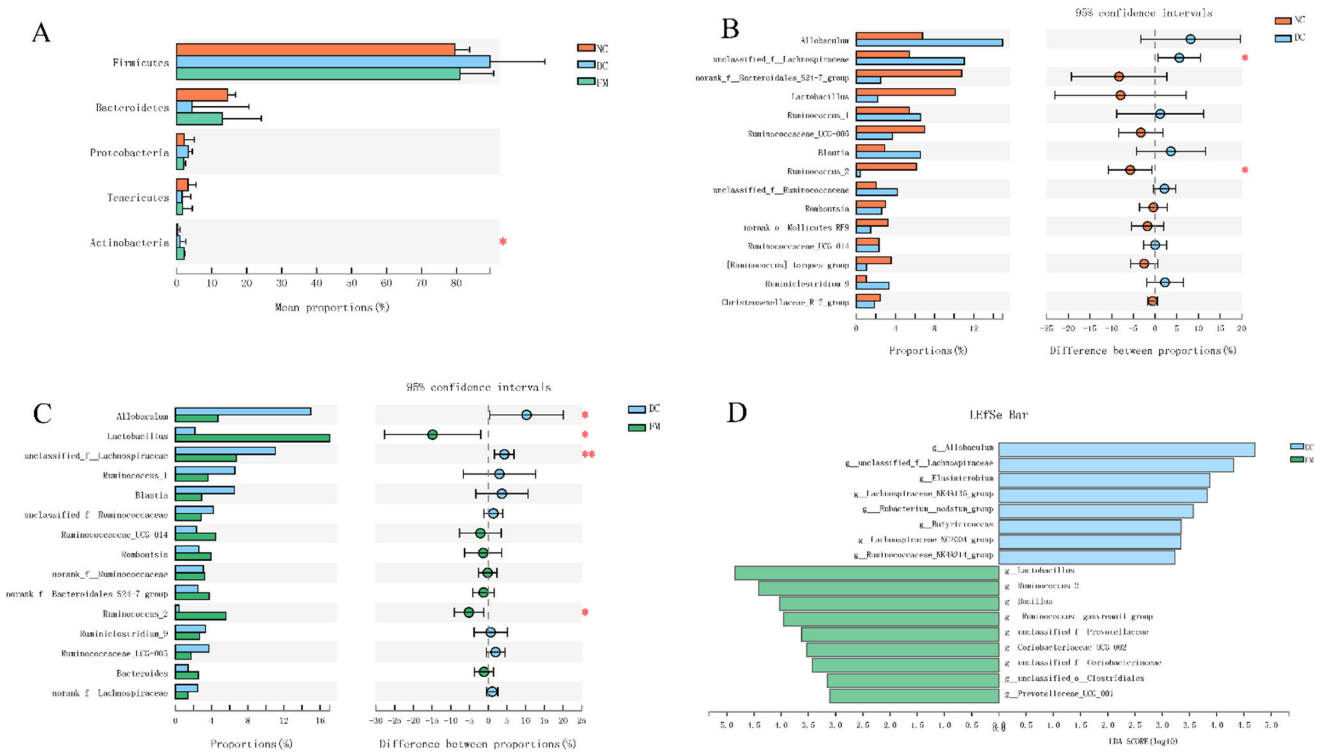

Figure 3. Effect of foxtail millet supplementation on the composition of gut microbiota: (**A**) phylum-level taxonomic distributions; (**B**,**C**) mean proportions of 15 key genera in different groups; (**D**) LDA scores derived from LefSe analysis, LDA > 3.0. Data were represented as mean ± SD. NC, normal control group (*n* = 5); DC, diabetic control group (*n* = 5); FM, foxtail millet supplementation group (*n* = 7). Differences between three groups were compared using one-way ANOVA with Tukey–Kramer post hoc test; differences between two groups were compared using Student's *T*-test, * $p < 0.05$, ** $p < 0.01$.

There were significant differences in the abundance of *Lactobacillus*, *Ruminococcus_2* etc. among the three groups. Specifically, HFD, combined with STZ injection, significantly increased the relative abundances of *unclassified_f__Lachnospiraceae* and decreased the relative abundances of *Ruminococcus_2* in the DC group, as compared with the NC group (Figure 3B). By contrast, FM supplementation significantly decreased the relative abundances of *Allobaculum* and *unclassified_f__Lachnospiraceae* and increased the relative abundances of *Ruminococcus_2* and *Lactobacillus* in the FM group, as compared with the DC group (Figure 3C). There was no significant difference in the relative abundances of the above gut microbe between the NC and FM groups (Figure S1H).

We then utilized the linear discriminant analysis (LDA) effect size (LEfSe) to identify further the specific bacterial taxa that significantly differed in response to FM supplementation. Compared with the DC rats, the FM rats had a higher abundance of *Lactobacillus* and *Ruminococcus_2* but a lower abundance of *Allobaculum* and *unclassified_f_Lachnospiraceae* (Figure 3D).

3.3. FM Supplementation Reversed the Liver Transcriptomic Profiles

To investigate the effect of FM supplementation on liver glucose metabolism, RNA-Seq was performed in the present study. The average alignment rate of the sequencing data was 95.48%, and more than 80% of the sequences were distributed in the coding region, indicating that the quality of the sequencing data met the requirements of the subsequent analysis.

The comparative analysis of the liver transcriptomic profiles indicated that there were 644 DEGs (Figure 4A–C). Among them, 230 DEGs were found between the DC and NC group (118 upregulated and 112 downregulated), and 487 DEGs were found between the FM and DC group (282 upregulated and 205 downregulated). There were only 32 DEGs found between the FM and NC rats (17 upregulated and 15 downregulated). We further screened and clustered the 86 shared DEGs between the NC-DC and DC-FM groups. As seen in the heatmap (Figure 4D), there were significant differences among the three groups. FM supplementation significantly reversed the trend of gene expression in diabetic rats.

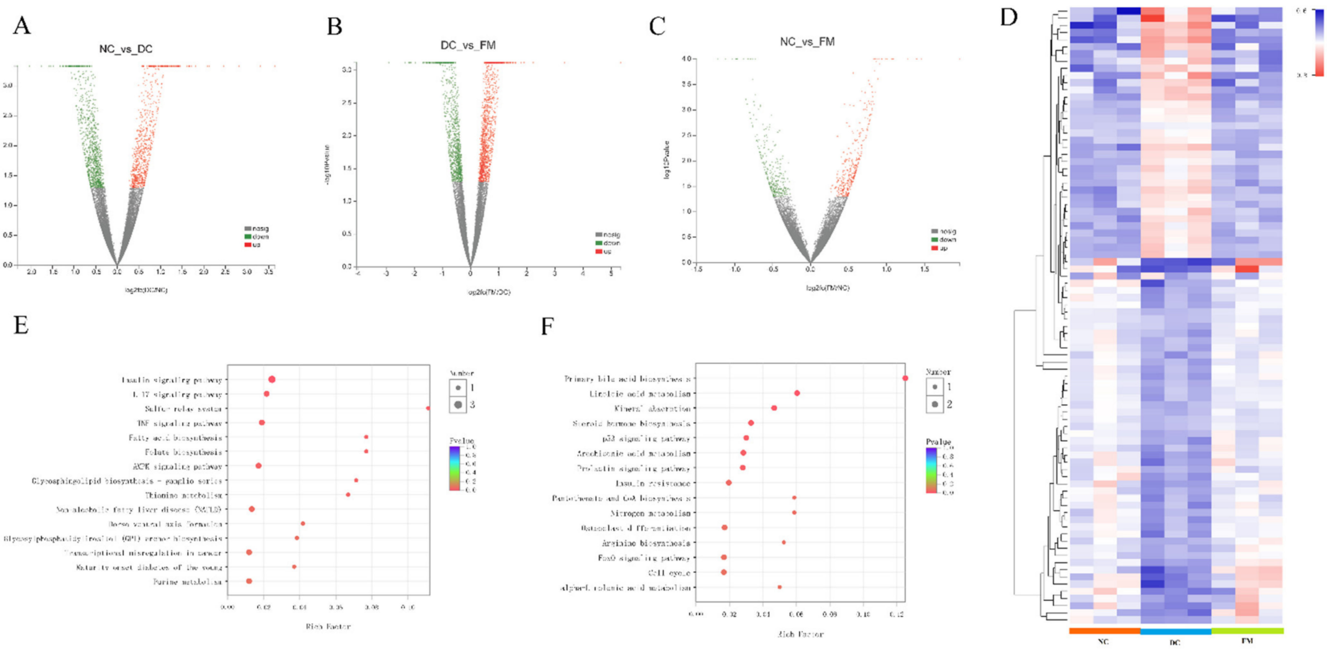

Figure 4. Effect of foxtail millet supplementation on liver transcriptomic profiles: (**A**–**C**) differentially expressed genes (DEGs) between different groups; (**D**) heatmap of 86 shared DEGs; (**E**) signaling pathways involved in upregulated DEGs; (**F**) signaling pathways involved in downregulated DEGs. NC, normal control group; DC, diabetic control group; FM, foxtail millet supplementation group.

To investigate the signaling pathways involved in DEGs further, we used the KEGG database to perform the enrichment analysis. There were 103 signaling pathways involved in the shared DEGs. Compared with the DC group, the upregulated DEGs in the FM group were mainly involved in the insulin signaling pathway, IL-17 signaling pathway, and sulfur relay system (Figure 4E), while the downregulated DEGs were mainly involved in the primary bile acid biosynthesis, linoleic acid metabolism, and mineral absorption (Figure 4F). Among them, the insulin signaling pathway was the most affected by FM supplementation, which mainly referred to the insulin-induced PI3K/AKT signaling pathway in the KEGG pathway database.

3.4. FM Supplementation Activated the PI3K/AKT Signaling Pathway

The PI3K/AKT signaling pathway is the primary method for insulin to mediate glucose metabolism in the liver. Compared with the DC group, the expression of IRS (*Irs3*), PI3K (*Pik3r1*), and AKT (*Akt1*) were significantly upregulated after 4 weeks of FM supplementation (Table 1). Further analysis showed that the mRNA levels of PI3K and AKT in the liver tissue of DC rats were significantly lower than those of NC and FM rats. At the protein level, there was no significant difference in the AKT expression among the three groups. However, the expression of phosphorylated AKT (p-AKT—activated AKT) in the FM group was significantly higher, compared with the DC group (Figure 5A–D). These results indicate that FM supplementation activated the PI3K/AKT signaling pathway.

Table 1. Expression levels of key genes in PI3K/AKT signaling pathway.

Name	Gene	Expression (FPKM)			Expression Fold		
		NC	DC	FM	DC/NC	FM/DC	FM/NC
PI3K/AKT signaling pathway							
Insulin receptor substrate (IRS)	*Irs3*	3.11	1.48	3.95	0.57 *	1.85 *	1.11
Phosphatidylinositol-3-kinase (PI3K)	*Pik3r1*	18.02	11.66	23.07	0.71 *	1.79 *	1.23
Protein kinase B (AKT)	*Akt1*	28.54	25.69	31.06	0.85	1.26 *	1.07
Glycolysis/Gluconeogenesis							
Glucose kinase (GK)	*Gck*	25.66	31.62	50.95	1.10	1.53 *	1.47 *
Pyruvate kinase (PK)	*Pklr*	54.18	47.68	113.96	0.90	2.27 *	1.54 *
Fructose bisphosphatase (FBP)	*Fbp1*	582.91	703.23	525.34	1.12	0.80 *	0.90
	Fbp2	0.45	0.77	0.22	1.26	0.29 *	0.83
Lipid synthesis							
Sterol regulatory element-binding protein-1c (SREBP1c)	*Srebf1*	58.18	36.01	138.23	0.67 *	2.66 *	1.71 *
Acetyl-CoA carboxylase (ACC)	*Acaca*	6.29	2.67	10.98	0.50 *	2.89 *	1.34
Fatty acid synthase (FAS)	*Fasn*	4.51	1.14	13.77	0.40 *	2.45 *	1.24

Note: NC, normal control group; DC, diabetic control group; FM, foxtail millet supplementation group. * $p < 0.05$.

Glycolysis and gluconeogenesis are the key steps to maintain blood glucose homeostasis in liver tissue. The RNA-Seq results showed that the key enzymes in glycolysis, GK, and pyruvate kinase (PK) in the FM group were significantly higher, compared with that of the DC group, which was consistent with the validation results of GK at both gene and protein levels (Table 1, Figure 4E,F). Compared with the DC group, the key enzymes in gluconeogenesis, G6P, and PEPCK were significantly decreased at the gene level (Figure 4G–I).

In addition, insulin also regulated the lipid metabolism in liver tissue. In the present study, the expression levels of the lipid-synthesis-related genes of the DC group were significantly lower than those of the NC group, such as sterol regulatory element-binding protein-1c (SREBP1c), acetyl-CoA carboxylase (ACC), and fatty acid synthase (FAS). However, these lipid-synthesis-related genes were significantly upregulated after 4 weeks of FM supplementation (Table 1); that is to say, FM supplementation could inhibit gluconeogenesis, stimulate glycolysis, and restore fatty acid synthesis through activating the PI3K/AKT signaling pathway.

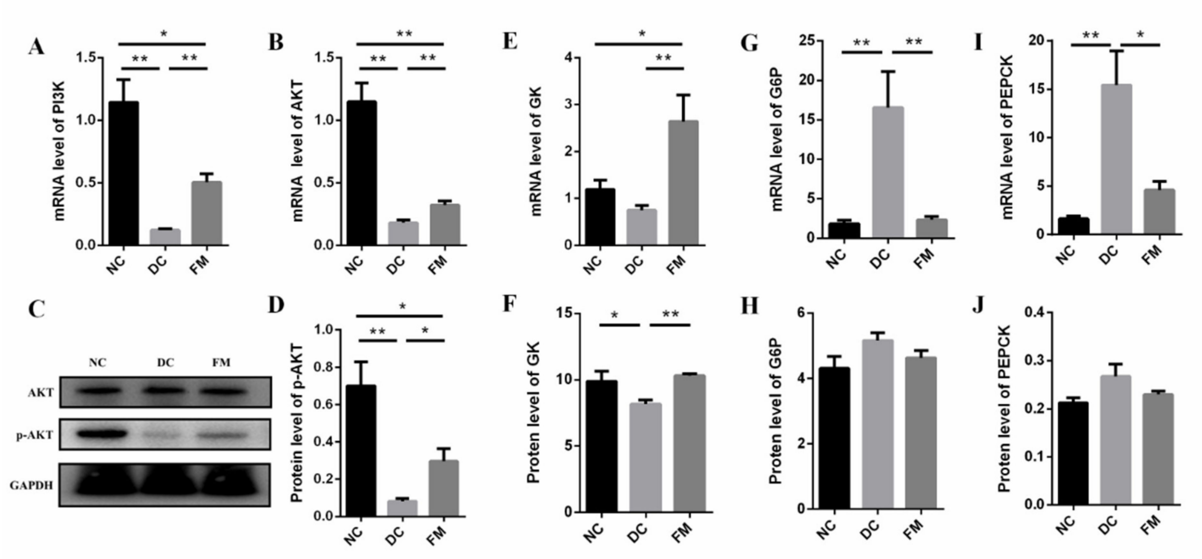

Figure 5. The expression of mRNA and protein of core factors in PI3K/AKT signaling pathway and its downstream effectors: (**A**–**D**) core factors in PI3K/AKT signaling pathway; (**E**,**F**) key enzymes in glycolysis; (**G**–**J**) key enzymes in gluconeogenesis. Data were represented as mean ± SEM. NC, normal control group; DC, diabetic control group; FM, foxtail millet supplementation group; PI3K, phosphatidylinositol-3-kinase; AKT, protein kinase B; G6P, glucose-6-phosphatase; GK, glucose kinase; PEPCK, phosphoenolpyruvate carboxy. Differences between groups were compared using Student's *T*-test, * $p < 0.05$, ** $p < 0.01$.

3.5. FM Supplementation Reduced Inflammation by Inhibiting NF-κB Signaling Pathway

T2D is associated with low-grade inflammation [19], which was confirmed again in our present study. The concentrations of IL-6 and TNF-α in the DC group were significantly higher than those in the NC group. After 4 weeks of FM supplementation, the concentrations of IL-6 and TNF-α were significantly decreased (Figure 6A,B).

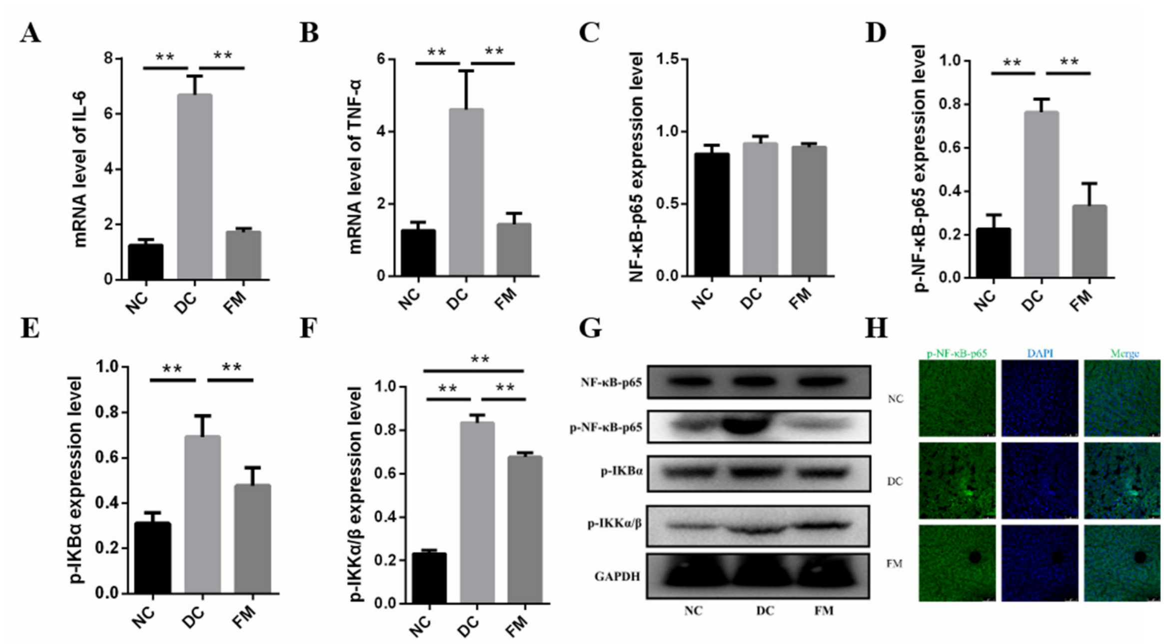

Figure 6. The expression of inflammatory cytokines (**A**,**B**), core factors in NF-κB signaling pathway (**C**–**G**), and nuclear translocation of p- NF-κB-p65 (**H**). Data were represented as mean ± SEM. NC, normal control group; DC, diabetic control group; FM, foxtail millet supplementation group; IKB, κB kinase; IKK, inhibitor of κB kinase. Differences between groups were compared using Student's *T*-test, * $p < 0.05$, ** $p < 0.01$.

The NF-κB signaling pathway is the primary method of the inflammatory response [20]. Thus, we further investigated the protein expression involved in the NF-κB signal pathway. Although there was no significant difference of the total NF-κB-p65 in the cytoplasm among the three groups, the expression of p-NF-κB-p65, the phosphorylated inhibitor of κB kinase (p-IKKα/β), and the phosphorylated κB kinase (p-IKBα) in the DC group were significantly higher than those in the NC group. The expression of these phosphorylated proteins was significantly decreased again after the FM supplementation (Figure 6C–G). In addition, the fluorescence of p-NF-κB-p65 in both the cytoplasm and nucleus of the DC group was significantly enhanced. However, no significant nuclear translocation was found in the FM and NC groups (Figure 6H). These results suggest that FM supplementation could reduce inflammation by inhibiting the NF-κB signaling pathway.

3.6. Correlations among the Bacteria, Signaling Pathways, and Metabolic Parameters

Spearman's correlation analysis was performed to explore further the correlation between the gut microbiota (the top 15 at the genus level) and metabolic parameters (Figure 7A). The results showed that the FM-supplementation-enriched *Ruminococcus_2* and *Lactobacillus* were significantly negatively correlated with the FG and 2-h G. The DC rats enriched *Allobaculum* and *unclassified_f__Lachnospiraceae* were significantly negatively correlated with the TC and HDL-C. Moreover, *Ruminococcus_2* also had a significant positive correlation with the WG, TC, and HDL-C.

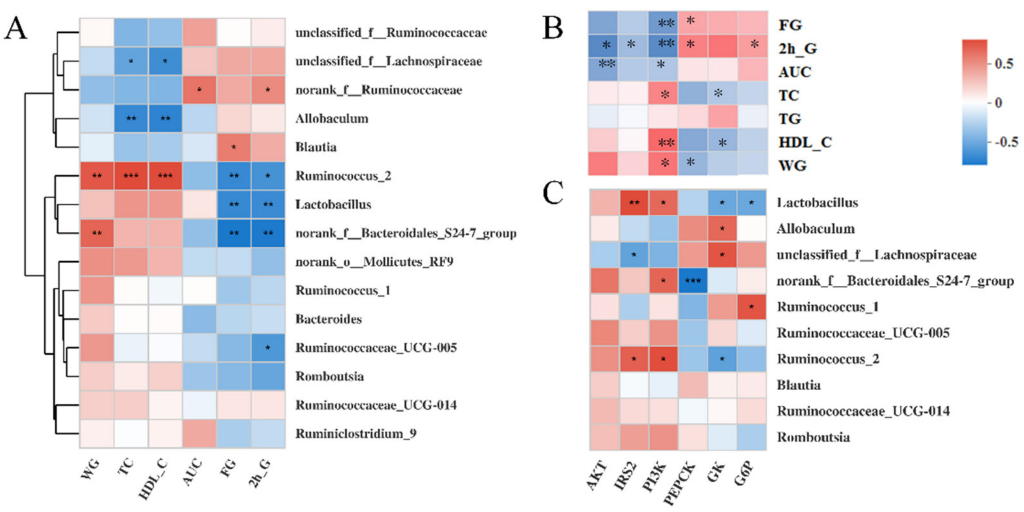

Figure 7. Heatmap of Spearman's correlation analysis between gut microbiota (top 15 at genus level) and metabolic parameters (**A**), liver gene expression and metabolic parameters (**B**), gut microbiota (top 10 at genus level), and liver gene expression (**C**). Significant correlations are marked by * $p < 0.05$; ** $p < 0.01$. IRS, insulin receptor substrate; PI3K, phosphatidylinositol-3-kinase; AKT, protein kinase B; GK, glucose kinase; G6P, glucose-6-phosphatase; PEPCK, phosphoenolpyruvate carboxy; WG, weight gain; TC, total triglycerides; FG, fasting glucose; HDL-C, high-density lipoprotein cholesterol; AUC, areas under the glucose tolerance test.

We also performed Spearman's correlation analyses between six key genes and seven physiological indices (Figure 7B). The results showed that these seven physiological indices were divided into two subgroups with opposing correlation results. Specifically, there was a significant negative correlation between the expression of PI3K and the concentration of FG, 2-h G, and the AUC. Similar correlation results were observed between AKT and the 2-h G, AKT, AUC, IRS2, and 2h-G. The expression of PI3K was significantly positively associated with the concentration of TC, HDL-C, and WG. Moreover, the expression of PEPCK was significantly positively associated with the concentration of FG and 2-h G but negatively associated with the concentration of WG.

To analyze further the association between the gut microbiota and the liver gene expression, we then performed correlation analyses between 6 key genes and the top 10 gut microbes at the genus level (Figure 7C). Similar to *Ruminococcus_2*, the relative abundance of *Lactobacillus* was significantly positively associated with the expression of PI3K and IRS2 and negatively associated with GK and G6P. Conversely, there was a significant negative correlation between the IRS2 expression and the *unclassified_f__Lachnospiraceae* abundance, which was positively correlated with the GK expression.

4. Discussion

Over the past few decades, numerous studies have demonstrated unambiguous evidence regarding the role of whole-grain consumption in improving blood glucose metabolism and preventing T2D [3]. However, the research on the health benefit effects of whole grains is far from sufficient particularly regarding the molecular mechanisms [4]. FM is one of the most important drought-resistant crops. It holds an immense assurance for food safety and nourishment in the arid and semiarid areas of Asia and Africa [5].

Our previous studies demonstrated that FM had a relatively low starch digestibility and moderate glycemic indices [7]. Habitual FM consumption could improve glycemic control in subjects with impaired glucose tolerance [8]. In the present study, the hypoglycemic effect of FM supplementation was confirmed again in HFD/STZ diabetic rats by the significantly decreased FG, GSP, and AUC. Tremendous attention has been given to understanding the underlying mechanism.

Dysfunctional gut microbiota have been considered one of the causes for a series of metabolic disorders, including T2D. Although the exact mechanism linking the gut microbiota to glucose homeostasis is far from being well understood, a substantial body of research has provided evidence for the important role of the gut microbiota in glucose metabolism [9,10]. The results in the present study showed that FM supplementation partially reversed the adverse changes of the gut microbiota in diabetic rats. Specifically, FM supplementation significantly increased the relative abundance of *Lactobacillus* and *Ruminococcus_2* and significantly decreased the relative abundance of *Allobaculum* and *unclassified_f_Lachnospiraceae*.

Lactobacillus is the most used probiotic in research and clinical settings. The beneficial effects on the gastrointestinal tract and immune system as well as the metabolic properties have been widely reported [23]. A substantial body of literature has provided evidence for the positive role of Lactobacillus in T2D. For example, *Lactobacillus casei* CCFM419 was shown to favorably regulate the blood glucose balance, increase glucose tolerance, and protect islets in diabetic mice through the underlying PI3K/AKT signaling pathway [20]. *Lactobacillus plantarum* Ln4 significantly stimulated glucose uptake in 3T3-L1 adipocytes, attenuated insulin resistance, and changed the hepatic mRNA levels (IRS and AKT) associated with glucose metabolism [24]. In addition, the hypoglycemic benefits of *Lactobacillus* were, at least in part, via changes in the microbiota composition and intestinal barrier. *Lactobacillus plantarum* X1 improved glucose tolerance by increasing the abundance of butyric-acid-producing bacteria [25]. *Lactobacillus reuteri* GMNL-263 supplementation decreased the pathogen abundances and improved the intestinal barrier [26].

Although *Ruminococcus* was reported in a positive association with T2D [9], it plays an important role in the biodegradation of resistant starch and other dietary fiber [27]. The FM used in this study was a whole grain food with a high content of resistant starch [7], which thus increased the relative abundance of *Ruminococcus*. *Allobaculum* demonstrated a high abundance in the gut of mice fed a high-fat diet [28], which was in accordance with our result of DC rats. A previous study reported that *unclassified_f_Lachnospiraceae* could significantly increase FG and reduce insulin sensitivity [29]. Interestingly, FM supplementation could reverse these adverse increases in diabetic rats. Collectively, the above results suggest that the hypoglycemic effect of FM was at least partially mediated by structural modulation of the gut microbiota.

The liver plays an important role in maintaining blood glucose homeostasis [30]. Liver glucose metabolism includes glucose transport, glycolysis, gluconeogenesis, hepatic glycogen synthesis, and decomposition [31], which were regulated by the insulin-mediated PI3K/AKT signaling pathway [15]. Therefore, to understand the underlying mechanism of the beneficial role of FM on glucose metabolism, we investigated the specific effect of FM supplementation on the PI3K/AKT signaling pathway and its downstream effectors.

Based on the accumulated evidence, the PI3K/AKT signaling pathway is the major effector of insulin in regulating metabolism [15]. Damage to the PI3K/AKT signaling pathway in liver tissues would thus lead to insulin resistance and, thereby, T2D. In turn, insulin resistance would exacerbate the PI3K/AKT signaling pathway, forming a vicious cycle [30]. IRS, PI3K, and AKT are the most critical factors in the PI3K/AKT signaling pathway. For example, AKT1 is ubiquitously expressed, with high levels in classical insulin target tissues, such as the liver. Studies have shown the positive role of AKT1 in the improvement of insulin sensitivity and decrease of blood glucose [32]. In the present study, the activation of the PI3K/AKT signaling pathway of FM supplementation was suggested by the significantly upregulated expression of IRS, PI3K, and AKT.

However, both the core factors in the PI3K/AKT signaling pathway and their downstream effectors perform distinct functions in the regulation of glucose homeostasis [15]. We then analyzed the expression profiles of the downstream effectors to clarify further the biological process and target genes of FM related to the hypoglycemic effect. Glycolysis and gluconeogenesis are two key steps involved in maintaining blood glucose homeostasis, which involves many key catalytic enzymes, such as G6P in glycolysis and GK in gluconeogenesis.

Insulin and phytochemicals could improve glucose metabolism by regulating the activity and expression of these enzymes [33,34]. For example, polysaccharide fromDendrobium officinale was shown to reduce the blood glucose concentration via the regulation of glucose metabolizing enzyme activity, including PK, hexokinase (HK), and PEPCK in the liver [34]. Our results showed that the expressions of GK and PK in the liver tissue of the FM group were 1.53-fold and 2.27-fold higher than those of the DC group, indicating that FM supplementation promoted glycolysis in the liver tissue of diabetic rats by upregulating the expression of the key enzymes GK and PK.

FoxO1 is the main inhibition target of AKT. FoxO1 induces the expression of PEPCK and G6P and subsequently increases gluconeogenesis in liver tissue [30]. A previous study showed that fructose administration enhanced the phosphorylation of FoxO1 and then suppressed the gluconeogenic gene expression, G6P activity, and glucose production from pyruvate [18]. Our results also indicated that FM supplementation suppressed gluconeogenesis by downregulating the expression of G6P, FBP, and PEPCK and then inhibiting the production and release of glucose from the liver.

As with the regulation of glucose metabolism, insulin can also stimulate fatty acid synthesis and inhibit the decomposition in normal hepatocytes via the PI3K/AKT signaling pathway [33]. However, in insulin-resistant hepatocytes, the regulation of the insulin signaling pathway is damaged [35]. SREBP1c is a major regulator of fatty acid synthesis. AKT could promote the production of FAS and ACC by upregulating the expression of SREBP1c [30,36]. Previous studies demonstrated the downregulation of the expression of SREBP1c in STZ-induced diabetic rats [37], which was consistent with our results. In the present study, 4 weeks of FM supplementation significantly upregulated the expression of SREBP1c, FAS, and ACC. FM supplementation repaired the impaired fatty acid synthesis function of diabetic rats and improved the balance of the energy metabolism.

In addition, inflammation is a common feature of T2D [19]. This was proven again by the increased inflammatory cytokines of the DC rats in the present study. However, FM supplementation significantly reduced the inflammation of diabetic rats. Considering the important role of the NF-κB signaling pathway in the inflammatory response [38], we detected the expression and translocation of key effectors in the NF-κB signaling pathway. The results showed that FM supplementation significantly reduced the phosphorylation levels of IKK, IκB, and NF-κB in the liver cells of diabetic rats. Immunofluorescence showed that there was no significant difference in the level of p-NF-κB-p65 between the NC group and FM group; however, the levels were significantly lower than for the DC group. The phosphorylation of IKK, IκB, and NF-κB and the entry of p-NF-κB-p65 from the cytoplasm into the nucleus are necessary for the activation of the NF-κB signaling pathway [38]. Therefore, FM supplementation could significantly reduce inflammation by suppressing the activation of the NF-κB signaling pathway.

Previous studies demonstrated that the activation of NF-κB was related to blood glucose control in diabetic patients. Inhibition of the NF-κB signaling pathway and the reduction of inflammation have been proven to be beneficial to blood glucose homeostasis [39]. Specifically, IKK decreased insulin sensitivity by catalyzing the serine phosphorylation of IRS and inhibiting its tyrosine phosphorylation [40]. The inhibition of IKK activity was shown to promote AKT phosphorylation and thereby improve blood glucose metabolism [41]. Inflammatory cytokines, such as TNF-α and IL-6, can also inhibit insulin signal transduction in hepatocytes [42].

In summary, we propose a molecular mechanism of the hypoglycemic effect of FM from the perspective of signaling pathways (Figure 8). On the one hand, FM supplementation might activate the PI3K/AKT signaling pathway by upregulating the expression of IRS, PI3K, and AKT and thereby promote glycolysis by upregulating the expression of GK and PK; inhibit gluconeogenesis by downregulating the expression of G6P, FBP, and PEPCK; and repair impaired fatty acid synthesis by upregulating the expression of FAS and ACC. On the other hand, FM supplementation might improve the blood glucose metabolism by inhibiting the NF-κB signaling pathway and reducing the expression of inflammatory cytokines, which can stimulate the activation of the insulin signaling pathway.

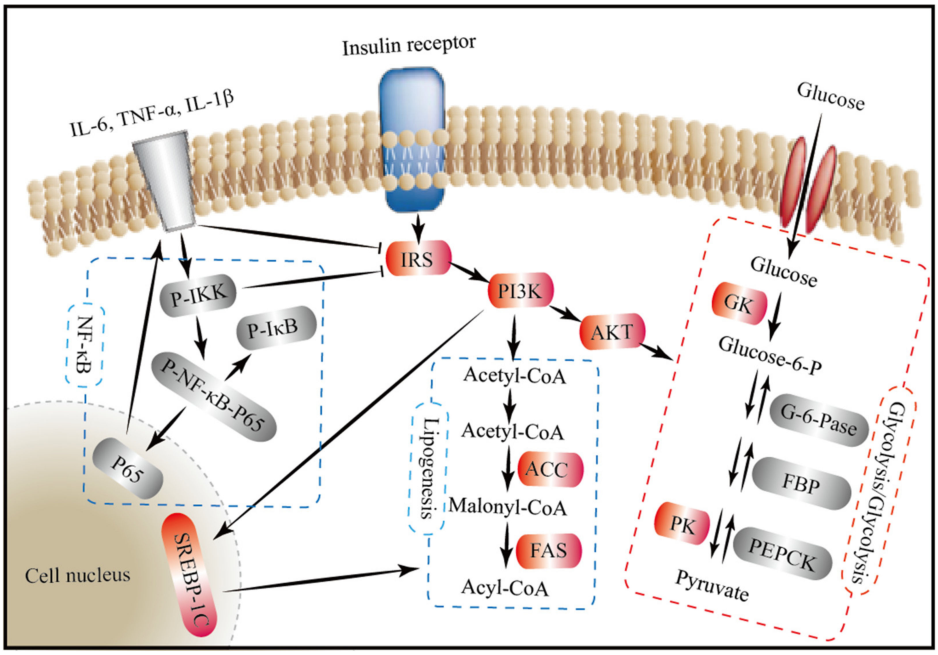

Figure 8. The mechanisms underlying the hypoglycemic effect of foxtail millet from the perspective of signaling pathways. Foxtail millet supplementation might improve the blood glucose metabolism by inhibiting gluconeogenesis, stimulating glycolysis, and repairing fatty acid synthesis through the insulin-mediated PI3K/AKT signaling pathway, as well as reducing inflammation through the NF-κB signaling pathway. Red background, significantly upregulated genes or proteins; grey background, significantly downregulated genes or proteins; arrow for promotion and —| for inhibition; IRS, insulin receptor substrate; PI3K, phosphatidylinositol-3-kinase; AKT, protein kinase B; GK, glucose kinase; PK, pyruvate kinase; G6P, glucose-6-phosphatase; FBP, fructose bisphosphatase; PEPCK, phosphoenolpyruvate carboxy; FAS, fatty acid synthase; ACC, acetyl-CoA carboxylase; SREBP1c, sterol regulatory element-binding protein-1c; IKB, κB kinase; IKK, inhibitor of κB kinase.

Human genes, microbial genes, and the diet share a complicated set of interdependencies [43]. Although dissecting the role of the gut–liver axis in glucose metabolism is a great challenge, the link between these is becoming clearer with increasing studies showing the involvement of the gut microbiota in insulin signaling and low-grade inflammation [10]. For example, *Lactobacillus casei* activated the PI3K/AKT signaling pathway by increasing the mRNA level of PI3K, IRS, and AKT in liver tissue [20]. *Lactobacillus paracasei* inhibited the NF-κB signaling pathway by suppressing the expression of IL-6 and TNF-α [9]. The relative abundance of *Lactobacillus* was also significantly positively associated with the expression of PI3K and IRS in the present study.

This study is a preliminary study on the hypoglycemic mechanism of foxtail millet (FM). Both the gut microbiota and the liver gene transcriptome are very complex systems. The FM is also a multicomponent complex. Although our study established a link between the hypoglycemic effect of FM, the relative abundance of Lactobacillus and PI3K/AKT signaling pathway, the specific association mechanisms among FM supplementation, glucose metabolism, the gut microbiota, and the signaling pathway still need to be further clarified. For example, what are the key components of FM for hypoglycemic effect, and how do these key components affect the PI3K/AKT signaling pathway?

5. Conclusions

Based on the confirmatory hypoglycemic effect of FM supplementation, tremendous attention has been given to understanding the underlying molecular mechanisms. Collectively, FM supplementation might improve the blood glucose metabolism by (a) modulating the structure of the gut microbiota, particularly by increasing the relative abundance of *Lactobacillus*; (b) inhibiting gluconeogenesis, stimulating glycolysis, and repairing fatty acid synthesis through the insulin-mediated PI3K/AKT signaling pathway; and (c) reducing inflammation through the NF-κB signaling pathway. However, the internal relationship among these different mechanisms requires further study.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nu13061837/s1, Table S1: Composition and energy ratio of experimental diets, Table S2: Primers for PCR, Figure S1: Changes in the structure and composition of gut microbiota.

Author Contributions: Conceptualization, X.R. and Q.S.; data curation, X.R. and Z.C.; formal analysis, X.R.; funding acquisition, Q.S.; methodology, X.R.; project administration, Q.S.; software, L.W.; validation, D.H., Y.X., and X.D.; writing—original draft preparation, X.R.; writing—review and editing, Z.C., D.H., and X.D. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Laboratory Animal Ethics Association of China Agricultural University. The ethical approval code is PONY-2020-FL-36.

Data Availability Statement: All data that support the findings of this study are available from the corresponding author on reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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nutrients

Article

Whole Grain Intakes Are Associated with Healthcare Cost Savings Following Reductions in Risk of Colorectal Cancer and Total Cancer Mortality in Australia: A Cost-of-Illness Model

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Abstract: Whole grain consumption has been associated with the reduced risk of several chronic diseases with significant healthcare monetary burden, including cancer. Colorectal cancer (CRC) is one of the most common cancers globally, with the highest rates reported in Australia. Three servings of whole grains provide a 15% reduction in total cancer and 17% reduction in CRC risk; however, 70% of Australians fall short of this level of intake. The aim of this study was to assess the potential savings in healthcare costs associated with reductions in the relative risk of CRC and total cancer mortality following the whole grain Daily Target Intake (DTI) of 48 g in Australia. A three-step cost-of-illness analysis was conducted using input parameters from: (1) estimates of current and targeted whole grain intakes among proportions (5%, 15%, 50%, and 100%) of the Australian adult (≥20 years) population; (2) estimates of reductions in relative risk (with 95% confidence intervals) of CRC and total cancer mortality associated with specific whole grain intake from meta-analysis studies; and (3) estimates of annual healthcare costs of CRC and all cancers from disease expenditure national databases. A very pessimistic (5% of population) through to universal (100% of population) adoption of the recommended DTI in Australia were shown to potentially yield savings in annual healthcare costs equal to AUD 1.9 (95% CI 1.2–2.4) to AUD 37.2 (95% CI 24.1–48.1) million for CRC and AUD 20.3 (95% CI 12.2–27.0) to AUD 405.1 (95% CI 243.1–540.1) million for total cancers. As treatment costs for CRC and other cancers are increasing, and dietary measures exchanging whole grains for refined grains are not cost preclusive nor does the approach increase energy intake, there is an opportunity to facilitate cost-savings along with reductions in disease for Australia. These results suggest specific benefits of encouraging Australians to swap refined grains for whole grains, with greater overall adherence to suggestions in dietary guidelines.

Keywords: colorectal; cancer; whole grain; healthcare cost; cost saving analysis; nutrition economics

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1. Introduction

Cancer care represents a leading burden of disease globally and accounts for 19% of the total disease burden in Australia [1]. Colorectal cancer (CRC) is the third most common in terms of new cases of cancers globally (1.93 million globally), after breast and lung cancers, and second most common in terms of causes of cancer death (935,000 deaths) in 2020, after lung cancer deaths [2]. Aligned with this, there is a significant healthcare monetary burden attributable to cancer including the direct and indirect healthcare costs and income losses. Furthermore, both Australia and New Zealand have CRC rates ahead of other countries [3]. Based on 2015/2016 data, cancer accounted for an estimated AUD 9.7 billion in diagnosing and treating cancer or just over 8.6% of all direct health expenditure, including AUD 876 million in costs for CRC including AUD 56 million on the National Bowel Screening program [4]. Although the mean age of diagnosis for CRC is 69 years, there is an increased risk after the age of 50 years, and more recent data suggests the incidence of an early-onset CRC under 40 years of age has emerged over the last two decades [5].

Nutrition, family history, body weight, alcohol intake, smoking, and sedentary lifestyles have all been implicated in the complex etiology of cancers, including CRC. Of all types of cancer though, there are a greater number of dietary factors influencing CRC. The World Cancer Research Fund and the American Institute for Cancer Research [6] noted in the Continuous Update Project, strong evidence that whole grain intake, and foods containing dietary fiber, dairy products, and calcium supplements (>200 mg/day), were protective against CRC and that red and processed meats, alcoholic drinks, excessive energy intake, and fast foods were associated with a higher risk of CRC. Lower-level evidence suggests that consuming foods containing vitamin C and consuming fish, multivitamins, and vitamin D supplements might decrease CRC risk, whereas low intake of non-starchy vegetables, low fruit, and foods containing heme iron might increase the risk. Physical activity was found to protect against colon cancer only [6].

A recent systematic review and meta-analyses of observational studies [7] identified 17 publications, involving 54 distinct meta-analyses for whole grains and five for refined grains, and reported significantly lower risk of total cancer and site-specific cancers in both "dose-response" and "highest vs. lowest" whole grain intake analyses [7]. Specifically, six studies examined CRC [8–13], four of which included dose-response data and suggested a 15–17% reduction in CRC risk for each 90 g/day intake of whole grains [7]. On the other hand, seven dose-response analyses indicated that 50–90 g/day intake of whole grains was associated with a 9–20% lower total cancer mortality risk. In these studies, the weight of the whole grain food was utilized, with 90 g (or three servings) providing approximately 48 g of whole grain. This difference in calculation of whole grain has been clarified by Ross et al. [14] and utilized in previous research of this nature [15].

Of concern is the greater increase in early-onset CRC in recent years. A re-analysis of the National Nutrition Physical Activity Survey (NNPAS) indicated that the median daily intake of whole grains was 21 g for adults (19–85 years) and 17 g for children/adolescents (2–18 years) [16]. Less than one third of children/adolescents (30%) did not consume whole grains on the day of the survey and consumption was lowest for the 14–18 years age group at 8.7 g/d [16], far short of the Daily Target Intake (DTI) of 48 g for Australians aged 9 years and older.

The suggested mechanism for the protection delivered by whole grains has been described previously [17]. Firstly, the intrinsic components of dietary fiber, resistant starch, oligosaccharides, and fermentable carbohydrates are thought to be protective through increasing fecal bulk and the production of short-chain fatty acids. Secondly, the micronutrient and antioxidant profile, with many of the vitamins and minerals having antioxidant effects. Thirdly, through mediation of the glucose response following consumption.

Over the past decade, numerous studies in the rapidly emerging field of nutrition economics have revealed substantial healthcare and related cost savings following healthy dietary behaviors among populations, accompanied by increasing scientific and public interests. Recently, a cost-of-illness analysis by our group [15] estimated an annual saving equal to AUD 1.4 billion in the combined type 2 diabetes (T2DM) and cardiovascular disease (CVD) related healthcare and lost productivity costs with higher whole grain intakes among Australian adults. Following a similar approach, the aim of the present study was to assess the potential savings in healthcare costs associated with reductions in the relative risk of CRC and total cancer mortality following the DTI 48 g for whole grains in Australia.

2. Materials and Methods

2.1. Study Design

In a conceptual framework model of input parameters derived from the relevant medical literature, a national nutrition survey, and a disease expenditure database in Australia, a three-step cost-of-illness analysis was developed based on: (1) current and targeted whole grain intake among estimates of proportions of the Australian adult population (≥20 years); (2) estimates of percent reductions in relative risk (with 95% confidence intervals) of CRC and total cancers mortality associated with whole grain intake; and (3) annual healthcare costs of CRC and all cancers in Australia. As previously modeled [15], a sensitivity analysis of four scenarios (very pessimistic, pessimistic, optimistic, and universal) was created to explore the impact of uncertainty, resulting in a range of assumptions withing each step.

The present analysis was conducted to reflect the reductions in cancer-related healthcare costs when the current intake of whole grains, as reported by the 2011-13 Australian Health Survey [16], were increased to the DTI level of 48 g/day for adults [18–20]. This is the cut-off value that policy makers, dietitians, and other healthcare providers typically use as guidelines in Australia. Table 1 summarizes the input parameters, and details around the analysis are discussed below.

Table 1. Summary of the cost-of-illness analysis input parameters and corresponding references.

Parameter	Men and Women	References
Current whole grain intake, g/day	21	Galea et al. [16]
Target whole grain intake, g/day	48	Griffiths et al., Chen et al., Zong et al. [18–20]
Difference, g/day	27	
Uptake rate (proportions of prospective consumers) [1]	Very pessimistic (5%), Pessimistic (15%) Optimistic (50%), Universal (100%)	Estimates
	Colorectal cancer risk	
Relative risk (95% CI) per 90 g/day increase in whole grain intake, no. of studies	0.83 (0.78–0.89), n = 6	Aune et al. [9]
% Risk reduction (95% CI) per 27 g/day [2]	−5.1% (3.3–6.6)	
	Total cancer mortality risk	
Relative risk (95% CI) per 90 g/day increase in whole grain intake, no. of studies	0.85 (0.80–0.91), n = 6	Aune et al. [21]
% Risk reduction (95% CI) per 27 g/day [2]	–4.5% (2.7–6.0)	

[1] Proportions of the Australian adult population (≥20 years) who would increase their whole grain consumption to the recommended (target) level of 48 g/day over the short term (very pessimistic), short-to-medium term (pessimistic), medium-to-long term (optimistic), and long term (universal). [2] Percent risk reduction (95% CI) per 27 g/day was calculated based on the summary relative risk (95% CI) values per 90 g/day by Aune et al. [9,21] assuming a linear relationship.

2.2. Step 1: Estimation of Current and Targeted Whole Grain Intakes among Proportions of Prospective Consumers

Insights around the consumer perception and dietary behavior are an integral part of any public health nutrition model. The first step of the present analysis made assumptions around the adult population that would adopt the targeted level of whole grains in Australia. Based on the dietary intake data from the 2011–2012 NNPAS (n = 12,153) [16], the current median whole grain intake of 21 g/day for adults (19–85 years) was compared to an established DTI of 48 g [18–20] and a calculation was built on estimates of proportions of Australian adults (20 y and over) who are likely to increase their intake of whole grains by the "gap" amount of 27 g daily.

As previously described [15], in applying the sensitivity analysis to this step, the very pessimistic and pessimistic scenarios were set to predict healthcare cost savings when 5% and 15% of Australian adults increase their whole grain intakes to the DTI of 48 g over the practical short term (0–4 years) and short-to-medium term (5–9 years), respectively. The optimistic scenario assumed that 50% of Australian adults would increase their intake of whole grains, denoting a medium-to-long term (10–14 years) pragmatic estimate of potential savings. Lastly, the universal scenario was used to assume a 100% uptake rate, i.e., all adult consumers would increase their whole grain intake from the current median to target levels, and to represent a best-case long term (15–19 years) estimate of potential savings. It is important to note that 73% of all Australians >9 years of age consumed less than the 48 g DTI, and 30% were considered non-consumers of whole grain [16].

2.3. Step 2: Evaluation of the Percent Reduction in Risk of Colorectal Cancer and Total Cancer Mortality

Numerous observational studies, and meta-analyses thereof, have associated whole grains with a reduced risk of total and site-specific cancers. Following a key word search and identification of the relevant English-language literature, the second step of this analysis estimated the percent reduction in relative risk of CRC and total cancer mortality, separately, corresponding to the mean gap between the current intake and DTI of whole grains in Australia, by employing data from two systematic reviews and dose–response meta-analyses of prospective studies.

The first of these meta-analyses included 25 studies (6 reporting on whole grain intake and CRC risk, with a total of 7941 cases among 774,806 participants) and suggested a summary relative risk (RR) per 3 servings (using 30 g of food as a serving size) per day, equal to 0.83 (95% CI 0.78–0.89; I^2 = 18%, $P_{heterogeneity}$ = 0.30) [9]. A relative risk of 0.83 indicates a 17% relative risk reduction for CRC. I^2 is the amount of total variation that is explained by variation between studies and $P_{heterogeneity}$ is used to determine whether significant heterogeneity exists. The second meta-analysis included 45 studies (six reporting on whole grain intake and risk of total cancer, including 34,346 deaths from cancer among 640,065 participants) and suggested a summary RR per 90 g/day (equivalent to 3 servings) of 0.85 (95% CI 0.80–0.91; I^2 = 37%, $P_{heterogeneity}$ = 0.16) [21]. A relative risk of 0.85 indicates a 15% relative risk reduction for total cancer. Building on the RRs for CRC and total cancer risk per 90 g of whole grain per day, while assuming a linear relationship, an RR reduction per 27 g whole grain intake was calculated (as shown in Table 1) for use in the final step of the analysis. In the present analysis, 30 g of whole grain "product" was assumed to be equivalent to 16 g of whole grain "content", with three servings being in line with the recommended DTI of 48 g. This conversion was recommended by the recent work of Ross et al. [14] and utilized in another analysis in the US by Murphy and Schmier [22].

2.4. Step 3: Calculation of the Potential Savings in Cancer-Related Direct Healthcare Costs

The third and final step of the present analysis imputed the annual savings in costs of healthcare-related services that could follow the estimated percent reductions in risk of CRC and total cancer mortality, separately, with the recommended increase in whole grain intake. Similar to our recent analysis [15], the 2015–2016 estimates of cancer-related direct health expenditure by the Australian Institute of Health and Welfare (AIHW) [23] were first inflated to their 2020 monetary equivalents based on the Australian Bureau of Statistics (ABS) Consumer Price Index (Health group) [24] (Table 2) and then employed within a set of arithmetic calculations involving the different proportions of the uptake rate and a 1% reduction in cost categories, individually, corresponding to each 1% decline in risk of disease.

Typically, the costs of disease are broken down into direct (i.e., healthcare-related) and indirect (i.e., productivity- and mortality-related) categories. As per the AIHW report [23], methodologies for measuring indirect costs are contentious and at an early stage of development. As such, the AIHW has decided to focus on the analysis of direct health system costs in the Disease Costs and Impact Study and to use, where appropriate, more direct measures of disease impact in health status terms, rather than estimates of indirect costs. Saving estimates of the cancer-related productivity losses and associated costs in Australia were thus not included in the present analysis.

Table 2. Summary of colorectal cancer and all cancers direct health expenditures (AUD million) in Australian adults (age 20 and up) [1].

	Colorectal Cancer		Total Cancers	
	2015–16	**2020** [2]	**2015–16**	**2020** [2]
Direct health expenditure				
Allied health and other services	0.3	0.3	5.0	5.7
General practitioner services	13.2	15.0	303.1	345.0
Medical imaging	2.9	3.3	93.6	106.5
Pathology	3.3	3.8	137.4	156.5
Pharmaceutical benefits scheme	113.8	129.6	1285.1	1462.8
Private hospital services	195.2	222.2	2318.0	2638.5
Public hospital admitted patient	168.6	191.9	2103.8	2394.7
Public hospital emergency department	0.5	0.6	28.9	32.9
Public hospital outpatient	102.6	116.8	949.0	1080.2
Specialist services	39.9	45.4	684.8	779.5
All direct health expenditure	640.3	728.9	7908.8	9002.3

Abbreviations: AUD, Australian dollar. [1] From the Australian Institute of Health and Welfare (AIHW) disease expenditure database (2015-16) [23]. [2] Current dollars based on adjustment of inflation rates according to the Australian Bureau of Statistics (ABS) Consumer Price Index (Health group) [24].

2.5. Discounted Rate

The discount rate refers to the interest rate used to determine the present value of future monetary figures [25]. Following the methodology that we have outlined recently [15], a real discount rate of 7% was applied to the sum of savings in CRC and total cancer costs, separately, to assess the discounted value of whole grain intake over the longer term, using the net present value equation:

$$\textit{Discounted cost savings} = \textit{savings at year } 0 \times \frac{1}{(1+r)^n}$$

where r = real discount rate (7%) and n = years into the future. The conservative discount rate of 7%, which has been used across Australian jurisdictions [26], was applied to present day savings in cancer-related healthcare costs at five-year increments for a 20-year period after 2020 (year 0), including 0–4 years (very pessimistic), 5–9 years (pessimistic), 10–14 years (optimistic), and 15–19 years (universal).

3. Results

Tables 3 and 4 summarize the potential savings in the annual direct healthcare costs associated with the reductions in relative risk of CRC and total cancer mortality, respectively, when whole grain intakes are increased from the current median level of 21 g/day to the DTI level of 48 g across proportions of the Australian adult population. Under the very pessimistic scenario, assuming a 5% uptake rate over the short term, our analysis predicted total healthcare savings equal to AUD 1.9 (95% CI 1.2–2.4) million in CRC cost and AUD 20.3 (95% CI 12.2–27.0) million in total cancer cost annually. With a 15% uptake rate over the short-to-medium-term, the pessimistic scenario showed savings of AUD 5.6 (95% CI 3.6–7.2) million for CRC and AUD 60.8 (95% CI 36.5–81.0) million for total cancer costs. The optimistic scenario, which assumed a 50% uptake rate and a medium-to-long-term effect, predicted savings of AUD 18.6 (95% CI 12.0–24.1) million for CRC and AUD 202.6 (95% CI 121.5–270.1) million for total cancer costs. Lastly, under the universal scenario, assuming a 100% uptake rate and a best-case, long-term estimate of potential savings with the targeted increase in whole grain intake, our analysis predicted total annual healthcare savings of AUD 37.2 (95% CI 24.1–48.1) million and AUD 405.1 (95% CI 243.1–540.1) million in avoided CRC and total cancer costs, respectively.

Table 3. Potential annual savings in direct health expenditures of colorectal cancer in Australian adults (≥20 years) from whole grain intakes (AUD million) [1].

	Scenario			
	Very Pessimistic	**Pessimistic**	**Optimistic**	**Universal**
Direct health expenditure savings				
Allied health and other services	<0.01 (<0.01 -< 0.01)	<0.01 (<0.01 -< 0.01)	0.01 (0.01–0.01)	0.02 (0.01–0.02)
General practitioner services	0.04 (0.02–0.05)	0.11 (0.07–0.15)	0.38 (0.25–0.50)	0.77 (0.50–0.99)
Medical imaging	0.01 (0.01–0.01)	0.02 (0.02–0.03)	0.08 (0.05–0.11)	0.17 (0.11–0.22)
Pathology	0.01 (0.01–0.01)	0.03 (0.02–0.04)	0.10 (0.06–0.13)	0.19 (0.13–0.25)
Pharmaceutical benefits scheme	0.33 (0.21–0.43)	0.99 (0.64–1.28)	3.30 (2.14–4.28)	6.61 (4.28–8.55)
Private hospital services	0.57 (0.37–0.73)	1.70 (1.10–2.20)	5.67 (3.67–7.33)	11.33 (7.33–14.66)
Public hospital admitted patient	0.49 (0.32–0.63)	1.47 (0.95–1.90)	4.89 (3.17–6.33)	9.79 (6.33–12.66)
Public hospital emergency department	<0.01 (<0.01 -< 0.01)	<0.01 (<0.01–0.01)	0.02 (0.01–0.02)	0.03 (0.02–0.04)
Public hospital outpatient	0.30 (0.19–0.39)	0.89 (0.58–1.16)	2.98 (1.93–3.86)	5.96 (3.86–7.71)
Specialist services	0.12 (0.07–0.15)	0.35 (0.22–0.45)	1.16 (0.75–1.50)	2.32 (1.50–3.00)
All direct health savings	1.86 (1.20–2.41)	5.58 (3.61–7.22)	18.59 (12.03–24.05)	37.17 (24.05–48.11)

Abbreviations: AUD, Australian dollar. [1] Data (95% CI) are monetary savings following colorectal cancer risk reduction with whole grain intake (Table 1). The very pessimistic and pessimistic scenarios are, respectively, practical short term and short-to-medium-term estimates of expenditure savings that could follow when 5% and 15% of Australian adults (≥20 years) consume the daily target intake of whole grain. The optimistic scenario is a medium-to-long-term pragmatic estimate of potential savings when 50% of adults in Australia adopt the recommended level of whole grain. The universal scenario is a best-case long-term estimate of potential savings when 100% of Australian adults increase their intakes of whole grains.

Table 4. Potential annual savings in direct health expenditure of total cancer in Australian adults (≥20 years) from whole grain intakes (AUD million) [1].

	Scenario			
	Very Pessimistic	**Pessimistic**	**Optimistic**	**Universal**
Direct health expenditure savings				
Allied health and other services	<0.1 (<0.1 -< 0.1)	<0.1 (<0.1–0.1)	0.1 (0.1–0.2)	0.3 (0.2–0.3)
General practitioner services	0.8 (0.5–1.0)	2.3 (1.4–3.1)	7.8 (4.7–10.4)	15.5 (9.3–20.7)
Medical imaging	0.2 (0.1–0.3)	0.7 (0.4–1.0)	2.4 (1.4–3.2)	4.8 (2.9–6.4)
Pathology	0.4 (0.2–0.5)	1.1 (0.6–1.4)	3.5 (2.1–4.7)	7.0 (4.2–9.4)
Pharmaceutical benefits scheme	3.3 (2.0–4.4)	9.9 (5.9–13.2)	32.9 (19.7–43.9)	65.8 (39.5–87.8)
Private hospital services	5.9 (3.6–7.9)	17.8 (10.7–23.7)	59.4 (35.6–79.2)	118.7 (71.2–158.3)
Public hospital admitted patient	5.4 (3.2–7.2)	16.2 (9.7–21.6)	53.9 (32.3–71.8)	107.8 (64.7–143.7)
Public hospital emergency department	0.1 (<0.1–0.1)	0.2 (0.1–0.3)	0.7 (0.4–1.0)	1.5 (0.9–2.0)
Public hospital outpatient	2.4 (1.5–3.2)	7.3 (4.4–9.7)	24.3 (14.6–32.4)	48.6 (29.2–64.8)
Specialist services	1.8 (1.1–2.3)	5.3 (3.2–7.0)	17.5 (10.5–23.4)	35.1 (21.0–46.8)
All direct health savings	20.3 (12.2–27.0)	60.8 (36.5–81.0)	202.6 (121.5–270.1)	405.1 (243.1–540.1)

Abbreviations: AUD, Australian dollar. [1] Data (95% CI) are monetary savings following total cancers mortality risk reduction with whole grain intake (Table 1). The very pessimistic and pessimistic scenarios are, respectively, practical short term and short-to-medium-term estimates of expenditure savings that could follow when 5% and 15% of Australian adults (≥20 years) consume the daily target intake of whole grain. The optimistic scenario is a medium-to-long-term pragmatic estimate of potential savings when 50% of adults in Australia adopt the recommended level of whole grain. The universal scenario is a best-case long-term estimate of potential savings when 100% of Australian adults increase their intakes of whole grains.

Using a 7% discount rate, as per the Australian government's recommendations [26], Table 5 summarizes the monetary figures associated with the percent reduction in cancer risk following the 48 g DTI of whole grains over a 20-year timeframe, where the total discounted savings over a 20 year period was shown to range between AUD 21.1 (95% CI 13.6–27.3) million and AUD 421.4 (95% CI 272.7–545.3) million for CRC and between AUD 229.6 (95% CI 137.8–306.1) million and AUD 4592.1 (95% CI 2755.2–6122.8) million for total cancer. On the other hand, the sum of total incremental healthcare cost savings with adoption of each of the 4 scenarios every 5 years was estimated at AUD 126.2 (95% CI 81.6–163.3) million for CRC and AUD 1374.8 (95% CI 824.9–1833.1) million for total cancer.

Table 5. Sum of potential total discounted savings on direct health expenditures of total cancers and colorectal cancer in Australian adults (≥20 years) from whole grain intakes over short term and long-term periods (AUD million) [1].

	Scenario			
	Very Pessimistic	**Pessimistic**	**Optimistic**	**Universal**
	Total savings of years 0 to 4			
Colorectal cancer	**8.2 (5.3–10.6)**	24.5 (15.8–31.7)	81.5 (52.8–105.5)	163.1 (105.5–211.1)
Total cancer	**88.9 (53.3–118.5)**	266.6 (160.0–355.5)	888.6 (533.2–1184.8)	1777.3 (1066.4–2369.7)
	Total savings of years 5 to 9			
Colorectal cancer	5.8 (3.8–7.5)	**17.4 (11.3–22.6)**	58.1 (37.6–75.2)	116.3 (75.2–150.5)
Total cancer	63.4 (38.0–84.5)	**190.1 (114.0–253.4)**	633.3 (380.1–844.8)	1267.2 (760.3–1689.6)
	Total savings of years 10 to 14			
Colorectal cancer	4.1 (2.7–5.4)	12.4 (8.0–16.1)	**41.5 (26.8–53.6)**	82.9 (53.6–107.3)
Total cancer	45.2 (27.1–60.2)	135.5 (81.3–180.7)	**451.7 (271.0–602.3)**	903.5 (542.1–1204.6)
	Total savings of years 15 to 19			
Colorectal cancer	3.0 (1.9–3.8)	8.9 (5.7–11.5)	29.6 (19.1–38.2)	**59.1 (38.2–76.5)**
Total cancer	32.2 (19.3–42.9)	96.6 (58.0–128.8)	322.1 (193.2–429.4)	**644.2 (386.5–858.9)**
	Total discounted savings for each scenario (2020–2039)			
Colorectal cancer	**21.1 (13.6–27.3)**	**63.2 (40.9–81.8)**	**210.7 (136.3–272.7)**	**421.4 (272.7–545.3)**
Total cancer	**229.6 (137.8–306.1)**	**688.8 (413.3–918.4)**	**2296.0 (1377.6–3061.4)**	**4592.1 (2755.2–6122.8)**
	Total incremental discounted savings: adoption of each scenario every 5 years (2020–2039)			
Colorectal cancer	-	-	-	**126.2 (81.6–163.3)**
Total cancer	-	-	-	**1374.8 (824.9–1833.1)**

Abbreviations: AUD, Australian dollar. [1] Data (95% CI) are monetary savings following total cancer and colorectal cancer risk reductions with whole grain intake. The very pessimistic and pessimistic scenarios are, respectively, practical short term and short-to-medium-term estimates of expenditure savings that could follow when 5% and 15% of Australian adults (≥20 years) consume the daily target level of whole grain. The optimistic scenario is a medium-to-long-term pragmatic estimate of potential savings when 50% of adults in Australia adopt the recommended level of whole grain. The universal scenario is a best-case long-term estimate of potential savings when 100% of Australian adults increase their intakes of whole grains.

4. Discussion

The resulting annual healthcare cost savings for total cancers of AUD 405 million, including AUD 37 million for CRC, equate to a possible 4.5% and 5% saving in annual healthcare cost, respectively. This research follows on from our recent analysis of T2DM and CVD [15] where AUD 1.4 billion in savings would be possible if more Australians met the 48 g whole grain DTI. Globally, by 2030, the direct medical and non-medical costs and income losses for cancer are projected to be USD 458 billion [27]. As a nation, Australia leads the world in CRC incidence, and the trends observed among younger adult diagnosis (<40 years) are concerning. Colon cancer has a long latency period, on average over 10 years, but can vary widely from 4 to 20 years [3]. This extended timeframe also provides an impetus to shift focus to slightly younger age groups for prevention messaging, improving dietary patterns, in addition to screening those over 50 years of age. For example, in 2019, AUD 10 million was reportedly spent just on the mass media campaign for CRC screening initiatives, equating to AUD 2500 per life saved, and a further prediction of 4330 lives to be saved over the following 40 years [28]. In comparison, over a 20-year timeframe, with increasing adoption of whole grain within diets (every five years), the expected saving due to prevention of total cancer is predicted to be AUD 1.4 billion with AUD 126 million attributable to CRC, a far greater saving in half the number of years.

Although Australians fall short of the 48 g whole grain daily target, total grain consumption on average has been stable between the NNPAS conducted in 1995 and then

2011–12, at 5.5 serves [29]. However, among adults over 19 years of age, there has been a decline in consumption of grain food serves from 5.6 to 5.5 per 10,000 kJ, the result of a 12% decrease in bread consumption (approximately 20 g less than 1995 [30]), with a 14% increase in consumption of other grains including rice, pasta and noodles, which would most probably be refined grain foods [31]. In the most recent survey, 66% of Australians consumed a median of 72 g of bread (approximately two average slices) on the day prior to the NNPAS interview [32]. For most (58%), this was white bread with mixed grain and wholemeal varieties accounting for 18% [32], noting that mixed grain breads rarely meet the definition of whole grain.

Whereas whole grain consumption sits below the target levels for adults (21 g) and children/adolescents (17 g), data for adolescents suggests their intake is lowest of all groups, at just 8.7 g/d, less than 20% of the 48 g DTI [16]. This is despite high energy needs, where core grain foods could be playing a role in providing energy, dietary fiber, and whole grains in addition to a range of other micronutrients. For example, wholemeal flour is naturally more nutrient dense than white flour with more calcium, chloride, fluoride, phosphorus, potassium, selenium, and zinc, twice as much magnesium and manganese, three times as much niacin, four times the folate, and eight times the amount of vitamin E [33]. As it is widely acknowledged that adolescent dietary patterns follow into adulthood, and poor habits may further predispose younger adults to earlier disease onset into the future, prevention strategies focused clearly on those food groups with the greatest modifiable effect need to be emphasized more clearly in dietary guidance at all stages of the lifecycle.

Although there are a number of meta-analyses examining CRC [9–12] this analysis utilized Aune et al. (2011) [9], as this represented a somewhat conservative view of risk reduction, 5.1% (95% CI 3.3–6.6) for the 27 g whole grain gap, compared to Reynolds et al. 2019 [12] with 5.4% (95% CI 1.8–9), indicating a potential larger saving at the higher end of the confidence interval from the latter. For a comparison of risk reduction results provided by the available meta-analyses, see Table A1 (Appendix A). As this study involved an etiological question, systematic reviews of level II evidence, such as case-control or prospective cohort studies, were identified as these provide more data than individual studies and the meta-analyses serves to increase the precision of the overall results and reduces the likelihood that results have occurred by chance.

Compared with biannual screening, expecting Australians to change their dietary pattern to adopt whole grain may be ambitious. In our earlier research, we acknowledged that a 100% adoption of the 48 g DTI across the entire population may not be possible due to specific dietary restrictions related to gluten containing grains and other special dietary requirements [15]. Unlike our earlier publication regarding CVD and T2DM, where we utilized healthcare costs and productivity loss savings [15], the data for productivity loss was not available from the AIHW for total cancer or CRC. For this reason, the results of the two publications cannot be directly compared or added together. Others have estimated the present value of lifetime income (PVLI) for men at AUD 2.9 billion and women at AUD 1 billion for total cancer, the most common and most costly cause of death for both genders based on 2003 data [34]. These figures indicate a likelihood of even higher cost savings for improving dietary related factors for both total cancer and CRC.

5. Conclusions

There is a compelling case for prevention strategies for cancer, but particularly where there are a range of modifiable dietary factors; such is the case for CRC. From this analysis, there are substantial healthcare cost-savings of AUD 37.2 million for CRC on its own and AUD 405.1 million, for total cancer with an increasing proportion of Australians meeting the 48 g whole grain DTI. CRC alone represents 9% of the overall possible healthcare cost savings for total cancers, an outcome that could be achieved by directing more Australians to consume the target amount of whole grain. Although there are a wide range of core whole grain options, wholemeal bread, whole grain breakfast cereals and crackers can be simply accommodated within diets and a regular inclusion of these provides sufficient whole grain to reach the DTI of 48 g. Yet, in Australia, where disease rates for CRC are the highest in the world, the focus is almost solely on screening those >50 years of age. While this is undoubtedly an effective strategy, a trend towards younger people being diagnosed may thwart screening efforts over time. Prevention through simple dietary modification could be playing a more prominent role through very specific guidance towards whole grain food choices and greater support of promotional campaigns aligned with food-based dietary guidelines.

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Appendix A

Table A1. Evidence from meta-analyses of cohorts or case-control studies associating different doses of whole grain intake with the relative risk or odds ratio of colorectal cancer and total cancer mortality [1].

Meta-Analysis	No. of Studies Included	Relative Risk or Odds Ratio (95% CI)	% Reduction in Relative Risk or Odds Ratio (95% CI) per 27 g/day [2]
Whole grain and risk of colorectal cancer			
Aune et al., 2011 [9]	6	0.83 (0.78–0.89) per 90 g/day	−5.1% (3.3–6.6)
Vieira et al., 2017 [10]	6	0.83 (0.79–0.89) per 90 g/day	−5.1% (3.3–6.3)
Schwingshackl et al., 2018 [11]	9	0.95 (0.93–0.97) per 30 g/day	−4.5% (2.7–6.3)
Reynolds et al., 2019 [12]	8	0.97 (0.95–0.99) per 15 g/day	−5.4% (1.8–9.0)
Whole grain and risk of total cancer mortality			
Aune et al., 2016 [21]	6	0.85 (0.80–0.91) per 90 g/day	−4.5% (2.7–6.0)
Benisi-Kohansel et al., 2016 [35]	3	0.90 (0.83–0.98) per 90 g/day	−3.0% (0.6–5.1)
Chen et al., 2016 [19]	6	0.82 (0.69–0.86) per 50 g/day	−9.7% (7.6–16.7)
Wei et al., 2016 [36]	7	0.91 (0.84–0.98) per 90 g/day	−2.7% (0.6–4.8)
Zong et al., 2016 [20]	10	0.80 (0.72–0.89) per 70 g/day	−7.7% (4.2–10.8)
		0.85 (0.76–0.94) per 50 g/day	−8.1% (3.2–13.0)
		0.89 (0.79–0.99) per 30 g/day	−9.9% (0.9–18.9)
		0.96 (0.91–1.01) per 10 g/day	−10.8% (0–24.3)
Zhang et al., 2018 [37]	14	0.97 (0.95–0.99) per 28 g/day	−2.9% (1.0–4.8)
Reynolds et al., 2019 [12]	7	0.95 (0.93–0.97) per 15 g/day	−9.0% (5.4–12.6)

[1] Adapted from Gaesser 2020 [7]. [2] Calculated based on relative risk or odds ratio values by each of the corresponding references assuming a linear relationship.

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Type 2 Diabetes-Related Health Economic Impact Associated with Increased Whole Grains Consumption among Adults in Finland

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Abstract: The prevalence of type 2 diabetes (T2D) is increasing rapidly worldwide. A healthy diet supporting the control of energy intake and body weight has major importance in the prevention of T2D. For example, a high intake of whole grain foods (WGF) has been shown to be inversely associated with risk for T2D. The objective of the study was to estimate the expected health economic impacts of increased WGF consumption to decrease the incidence of T2D in the Finnish adult population. A health economic model utilizing data from multiple national databases and published scientific literature was constructed to estimate these population-level health economic consequences. Among the adult Finnish population, increased WGF consumption could reduce T2D-related costs between 286€ and 989€ million during the next 10-year time horizon depending on the applied scenario (i.e., a 10%-unit increase in a proportion of daily WGF users, an increased number (i.e., two or more) of WGF servings a day, or alternatively a combination of these scenarios). Over the next 20–30 years, a population-wide increase in WGF consumption could lead to much higher benefits. Furthermore, depending on the applied scenario, between 1323 and 154,094 quality-adjusted life years (QALYs) could be gained at the population level due to decreased T2D-related morbidity and mortality during the next 10 to 30 years. The results indicate that even when the current level of daily WGF consumption is already at a relatively high-level in a global context, increased WGF consumption could lead to important health gains and savings in the Finnish adult population.

Keywords: whole grains; diabetes; healthcare costs; cost saving analysis; quality-adjusted life years; nutrition economics

1. Introduction

Type 2 diabetes (T2D) is one of the most common metabolic diseases and represents a leading cause of morbidity and mortality because of its related micro- and macrovascular complications. The number of people with T2D is expected to increase dramatically in the next decades [1]. Overweight and obesity associated with excess energy intake, Western dietary habits, and low physical activity are the major determinants of the rise in T2D prevalence [2,3]. As a result of this adverse development, global and regional diabetes-related health expenditures are expected to grow significantly [1].

Observational evidence has suggested that WGFs are beneficial in regard to T2D risk [4–10], and the finding has also been supported by an intervention study that has emphasized the consumption of WGFs as a way to increase dietary fiber intake [11,12].

In Finland, daily WGF consumption is relatively high compared with many other countries [13]. Currently around 76% and 67% of Finnish men and women, respectively, reach the daily goal of dietary fiber intake as recommended by the national nutritional guidelines [14]. In addition, fiber-rich WGFs contain other components, which may offer important beneficial effects including balanced glucose metabolism [15–17] and many other health conditions [18,19]. Thus, the formulation and promotion of WGFs may have significant health and economic consequences regarding the prevention of T2D at the population level, as indicated by previous modeling studies from Australia and Canada [20–22]. To highlight the potential of such policies in the Finnish setting, the aim of the present study was to evaluate the savings potential as well as health impacts in terms of quality-adjusted life years (QALYs) of increasing daily WGF consumption as a method to decrease the incidence of T2D and its consequences in the Finnish adult population.

2. Materials and Methods

2.1. Model Overview

To estimate the expected health and economic consequences of increased daily WGFs consumption among the Finnish adult population, a health economic model utilizing data from multiple national databases and published scientific literature was constructed. The developed Markov-type cohort model included four mutually exclusive health states (i.e., No T2D, T2D, T2D with complications, and death) to project the expected incidence of T2D and its complications based on the observed population risk factor levels of T2D in the national FinHealth 2017 study [23]. The year 2017 was applied as a baseline year in the present study. The developed model is schematically depicted in Figure 1. The graphical scheme of the study design is provided in Supplementary Figure S1.

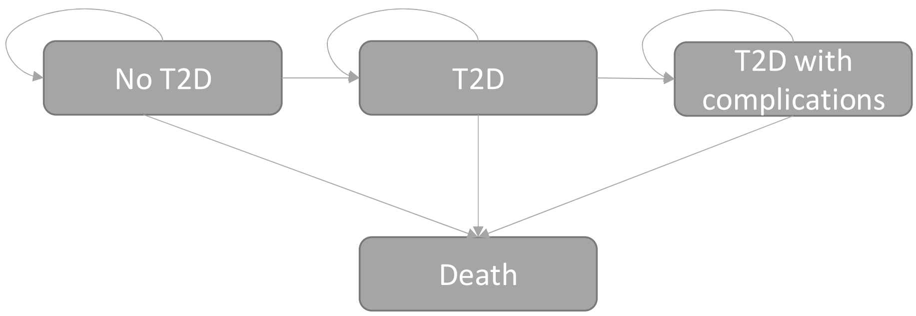


Figure 1. Schematic presentation of the applied Markov model showing the considered health states for the prevention of T2D. Arrows indicate possible transitions between health states in the model.

The model was populated with the characteristics of the Finnish adults aged 30–79 years without T2D at baseline (n = 2.97 million Finnish adults in 2017) as well as with the age- and sex-specific risk of T2D development during the next 10 years measured as the Finnish Diabetes Risk Score (FINDRISC) [24]. The FINDRISC is a validated questionnaire used to estimate the 10-year risk of developing T2D based on sex, age, body mass index (kg/m^2), use of blood pressure medication, history of high blood glucose, physical activity, daily consumption of vegetables, fruits, or berries, as well as family history of diabetes. In the present study, the FINDRISC score was divided in five age- and sex-specific categories (i.e., from low risk to very high risk) indicating the 10-year risk of T2D (see Supplementary Table S1 for details). Other baseline characteristics applied as the input parameters of the model are described in Table 1. In the developed model, this hypothetical cohort of Finnish adults without T2D at baseline were at risk of developing T2D or T2D-related complications (if already having T2D), or they might survive to the next year (i.e., 1-year cycle length was applied in the model) without any event. Finally, the developed model was used to estimate the expected number of new T2D cases and associated consequences (in terms of costs and QALYs) with and without expected increase in WGF consumption using 10-year, 20-year, and 30-year time horizons. All analyses were implemented in R using the HEEMOD package, which is an R toolset for health economic modeling [25].

Table 1. Baseline characteristics of the cohorts used to define the size of the target cohort and its underlying risk of T2D in the Markov model. See Supplementary Table S1 for further details.

	Men	Women	Both
Population (not excl. T2D) (30–79 years) * [26]	1,673,290	1,702,260	3,375,550
Prevalence of T2D in whole population (HbA1c $\geq$ 48 or fasting glucose $\geq$ 7) (%) **	14.6	9.4	12.0
Estimated population size without T2D (30–79 years)	1,428,990	1,542,248	2,971,238
Estimated average age of population at baseline	53.1	54.2	53.5

* Official Statistics of Finland (OSF): Population structure [e-publication], 2018; ** Koponen et al. [23].

2.1.1. Baseline Risk of T2D

In the health economic modeling, parametric survival regression models are commonly used to extrapolate event risks over the actual follow-up time [27]. In the present study, a parametric survival regression model was used to estimate the risk of T2D based on the national FINRISK data (n = 9512) linked with 10-year register-based follow-up data [28]. The Weibull survival regression model, which provided the most reliable fit (i.e., based on applied Akaike and Bayesian information criteria and visual inspections) to the available data, was used to estimate the relationship between baseline age, sex, and FINDRISC categories and the incidence of T2D (indicated as new reimbursement rights and/or the first purchases for T2D medicines observed from the national medicine reimbursement registry maintained by the Social Insurance Institution of Finland) over 10-year follow-up. Annual transition probabilities (conditional on age, sex, and FINDRISC categories) applied in the developed Markov model were estimated based on these estimated incidence rates. The coefficients of the Weibull regression for incidence of T2D are shown in Supplementary Table S2.

2.1.2. Risk of T2D with Complications

To estimate the risk of T2D-related complications in persons with newly diagnosed T2D, a real-world dataset based on electronic health record (EHR) data of patients with T2D and living in the county of North Karelia in Finland was applied [29]. For the purposes of the present study, the data of patients with a newly diagnosed T2D between 2011 and 2012 (n = 1151) were extracted from the dataset to estimate the development of T2D-related complications after the diagnosis of T2D. The data were available until December 2019 with the longest follow-up duration of 9.0 years. To estimate the risk of T2D-related complications, all T2D-related renal, eye, cardiovascular, cerebrovascular, neuropathic, and foot complications (see Supplementary Table S3 for details), as well as date of diagnoses were extracted from the data, and a Weibull survival regression model was fitted to estimate the annual rates of complications based on sex and baseline age. Annual age- and sex-specific transition probabilities applied in the developed Markov model were estimated based on these estimated complication rates. The coefficients of the Weibull regression for incidence of T2D with complications are shown in Supplementary Table S4.

2.1.3. Risk of Death

The national all-cause life tables for men and women were used to characterize the risk of death conditional on age and sex [30]. In addition, deaths in the modeled "T2D" and "T2D with complications" health states were adjusted to consider the increased risk of death in those health states by applying previously published HRs [31,32]. To avoid the risk of double counting, the increased WGF consumption was assumed to have no direct impact on all-cause mortality.

2.1.4. Estimating the Effects of Increased Whole Grain Intake in the Reduction of T2D

For the purposes of the present study, the developed model was calibrated to correspond with the observed 10-year incidence of T2D in the Finnish adults reporting no daily WGF consumption (i.e., no daily use of rye bread, porridge, or mixed bread) in the FINRISK study. Based on the FINRISK register-enriched follow-up dataset, the average observed 10-year incidence of T2D was 7.69% in this subpopulation. This approach enabled the use of the results of a recent meta-analysis studying the dose–response association between the daily WGF intake (measured as servings a day) and the long-term risk reduction of T2D (using no daily use of WGF as a reference) with a total of 4,618,796 person years of follow-up and with the average follow-up time of 24 years [10]. According to the multivariable-adjusted study results, one serving of WGF was expected to reduce the risk for T2D by 27% (Hazard Ratio (HR) 0.73, 95%CI 0.72–0.74), whereas two or more servings of WGFs were expected to reduce the risk of developing T2D by 35% (HR 0.65, 95%CI 0.61–0.68). Since the applied baseline risk of T2D was defined to represent the risk among those with no regular daily WGF consumption, the transition probabilities were adjusted by applying weighted HR estimates to correspond with a proportion (i.e., 69.5% according to the applied definition in the present study) of Finnish adults using at least one WGF serving a day as observed in the applied FINRISK dataset.

In the present study, three alternative scenarios were studied: (I) 10%-unit increase in the proportion of the Finnish adult population using at least one WGF serving a day, (II) one or more additional WGF servings a day [33] among those who already use at least one WGF serving a day, and (III) a scenario combining scenarios I and II. In addition, to simplify the analysis, the full effect of increasing daily WGF intake was assumed to be achieved immediately and to persist over time.

2.1.5. Cost Data

A limited societal perspective was applied in the present study, since direct non-medical costs, such as travel costs associated with the utilization of health care services, were not considered in the present study due to limited data availability. The estimates of additional health care and T2D-related productivity loss costs (i.e., costs associated with sick leaves, premature retirements, and premature deaths) were obtained from the national cost reports [34–36]. These estimates included both the additional secondary health care costs and T2D-related productivity losses estimated using the Finnish national registries and a case-control study design (with adjustments for age, sex, and living area). In the model, T2D-related productivity losses were applied to adults with T2D below the average age of retirement (i.e., 65 years of age).

In addition, the additional primary care costs due to T2D were estimated using the above-mentioned EHR dataset (n = 1151) from the county of North Karelia by applying a case-control study design with adjustments for age, sex, and living area. In addition, the annual average (per-person) T2D medication (ATC-code A10) costs were obtained from the national medicine statistics maintained by the Social Insurance Institution of Finland. Finally, all costs were adjusted to the 2019 price level using the official health care price index determined by Statistics Finland. All unit cost estimates are summarized in Table 2. In the base-case analysis, a 3% discount rate per year was applied for costs and QALYs in accordance with the national HTA guidelines [37].

2.1.6. Utility Weights

The published population-level EQ-5D-3L utility values (stratified by age and sex) were applied to represent the average health-related quality of life in the target population [38,39]. EQ-5D-3L-based disutility weights associated with T2D and its complications were also obtained from previously published studies [40–44]. Disutility associated with T2D with complications was estimated as a weighted average, where disutility values associated with a single complication were weighted by their observed incidences between years 2000 and 2017 in Finland [45]. The applied utility and clinical data are described in Table 3.

2.1.7. Sensitivity Analyses

To test the robustness of different assumptions related to modeling, different deterministic one-way sensitivity analyses were conducted. The results of these sensitivity analyses were presented in the form of a tornado diagram. In addition, parameter uncertainty associated with the model inputs was studied by using probabilistic sensitivity analysis (PSA) with 1000 random iteration rounds [27,46]. The correlation structure between the Weibull regression coefficients was also taken into consideration, and the regression coefficients were assumed to be normally distributed (Supplementary Table S5). Results of the PSA were presented on the X-Y plane demonstrating the joint distribution of cumulative savings and QALYs gained conditional on the selected time horizon. In addition, the probabilities of cumulative savings (with and without T2D-related productivity losses) given the available data were estimated based on the obtained PSA results [39].

Table 2. Costs applied in the Markov model, their distributions, and the values used to estimate the distributions. Costs before 2019 have been discounted to the latest values.

Parameter	Value (Variation) *	Distribution	Distribution Values Used in PSA Mean (SE)	Source
Additional health care costs of T2D excluding basic health care	3315 € (±25%)	Gamma	3315€ (423€)	[35]
Cost of T2D complications	4401€ (±25%)	Gamma	4401€ (561€)	[34]
Costs from productivity losses due to T2D	7632€ (±25%)	Gamma	7632€ (974€)	[36]
Additional T2D health care costs for primary health care	Men 562 € (SD 587€) Women 542 € (SD 649 €)	Gamma	Men 562€ (9.53€) Women 542€ (9.82€)	Based on own results
Additional medication costs of T2D	584 € (±25%)	Gamma	584€ (74€)	[47]

* For variables without available confidence interval, a variation of ± 25% has been used as an estimate. PSA; Probabilistic Sensitivity Analysis.

Table 3. Parameters applied in the Markov model, their distributions, and the values used to estimate the distributions.

Parameter	Value (Variation) *	Distribution Applied in PSA	Distribution Values Used in PSA Mean (SE)		Source
T2D-specific mortality risk, Hazard ratio (95% CI)	Women HR 2.47 (2.42–3.06) Men HR 1.93 (1.79–2.07)	Lognormal	2.47 (0.04) 1.93 (0.05)		[32]
Mortality risk associated with T2D with complications, Hazard ratio (95% CI)	HR 2.36 (1.70–3.29)	Lognormal	2.36 (0.41)		[31]
All-cause mortality	Based on age and sex	-	-		[30]
Utilities			Alpha (value)	Beta (value)	
Baseline utilities (EQ-5D-3L)	Women (Age, Utility, SE) 30–44 0.906 (0.003) 45–54 0.865 (0.005) 55–64 0.810 (0.006) 65+ 0.770 (0.008) Men (Age, Utility, SE) 30–44 0.917 (0.003) 45–54 0.876 (0.005) 55–64 0.821 (0.006) 65+ 0.781 (0.008)	Beta	8573 4040 3463 2130 Men 7755 3806 3351 2087	889 631 812 636 Men 702 539 731 585	[39]
Disutility of T2D (EQ-5D-3L) (SE)	0.041 (0.012)	Beta	Alpha 11.19	Beta 261.9	[38]
Weighted disutility of T2D complications (EQ-5D-3L)	0.119 (±25%)	Beta	0.119 (0.015)		Disutility values of individual complications [40–44] Proportion of complications [45]

* For variables without available confidence interval, a variation of ±25% has been used as an estimate. PSA; Probabilistic Sensitivity Analysis.

3. Results

3.1. Population Results

Based on the simulation results of the calibrated model when assuming no change in the current daily use of WGFs, the expected discounted total T2D-related costs among the Finnish adults aged 30–79 (*n* = 297 million) were 8032€, 25,867€, and 46,491€ million during the applied 10-year, 20-year, and 30-year time horizons, respectively. Assumed increased WGF consumption could reduce these total costs between 286€ and 989€ million during the next 10-year time horizon depending on the applied scenario. Over the next 20 to 30 years, a population-wide increase in WGF consumption could potentially lead to much higher cumulative savings in the health care sector and productivity gains in the society, as shown in Table 4. Furthermore, depending on the applied scenario, a total of 1323 to 154,094 QALYs could be gained at the population level due to decreased T2D-related morbidity and mortality at the population level during the next 10 to 30 years (Table 5).

Table 4. Projected cumulative economic changes compared with the baseline situation in the year 2017 with and without productivity costs.

Expected Savings Potential with Productivity Costs (M€) with 95% CIs; [Savings in %]									
Scenario #	**10-Year Time Horizon**			**20-Year Horizon**			**30-Year Horizon**		
	Women	**Men**	**Total**	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**
Scenario I	113.0 (41.8 to 236.7)	172.5 (74.1 to 316.0)	285.5 [3.3%] (115.9 to 552.7)	341.9 (132.7 to 663.2)	486.1 (224.3 to 842.0)	828.0 [3.0%] (357.0 to 1505.2)	565.0 (279.9 to 930.7)	656.9 (345.3 to 1015.7)	1221.9 [2.6%] (625.2 to 1946.4)
Scenario II	248.0 (79.0 to 517.0)	367.6 (138.0 to 745.5)	615.6 [7.2%] (217.0 to 1262.5)	707.8 (269.2 to 1368.8)	1043.1 (430.8 to 1925.5)	1750.9 [6.6%] (699.9 to 3294.3)	1200.3 (479.9 to 2156.3)	1402.3 (661.0 to 2316.9)	2602.6 [5.7%] (1140.9 to 4473.2)
Scenario III	402.1 (153.0 to 781.5)	587.0 (235.7 to 1111.9)	989.2 [12.2%] (388.7 to 1893.4)	1145.4 (441.5 to 2281.8)	1669.6 (770.2 to 2929.4)	2815.0 [11.2%] (1211.7 to 5211.2)	1871.7 (848.7 to 3164.0)	2365.7 (1235.1 to 3694.5)	4237.3 [9.6%] (2083.8 to 6858.5)
Expected Savings Potential without Productivity Costs (M€) with 95% CIs; [Savings in %]									
	10-Year Time Horizon			**20-Year Horizon**			**30-Year Horizon**		
Scenario #	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**
Scenario I	44.1 (15.2 to 91.8)	66.0 (26.2 to 125.5)	110.0 [3.4%] (41.4 to 217.2)	263.7 (102.5 to 516.7)	347.4 (174.9 to 599.3)	611.1 [3.0%] (277.4 to 1116.0)	488.5 (223.8 to 838.6)	531.2 (281.0 to 869.0)	1019.7 [2.5%] (504.8 to 1707.6)
Scenario II	91.9 (28.5 to 195.2)	136.9 (49.0 to 266.3)	228.8 [7.2%] (77.4 to 461.5)	565.7 (203.0 to 1074.8)	735.5 (310.0 to 1298.8)	1301.2 [6.4%] (512.9 to 2373.6)	1027.9 (439.0 to 1830.8)	1132.1 (533.1 to 1931.1)	2160.0 [5.4%] (972.1 to 3761.8)
Scenario III	146.1 (51.9 to 298.3)	222.1 (90.4 to 433.8)	368.2 [12.3%] (142.3 to 732.0)	909.7 (384.5 to 1665.7)	1219.2 (565.8 to 2091.2)	2128.9 [11.0%] (950.3 to 3756.9)	1678.1 (801.4 to 2871.1)	1824.0 (959.6 to 2805.2)	3502.2 [9.3%] (1760.9 to 5676.3)

Scenario I: a 10%-unit increase in the Finnish population using at least one whole grain serving a day, Scenario II: one or more additional whole grain servings a day among those who already use at least one whole grain serving a day, and Scenario III: the combination of Scenarios I and II. In all scenarios, the current situation was applied as a comparator.

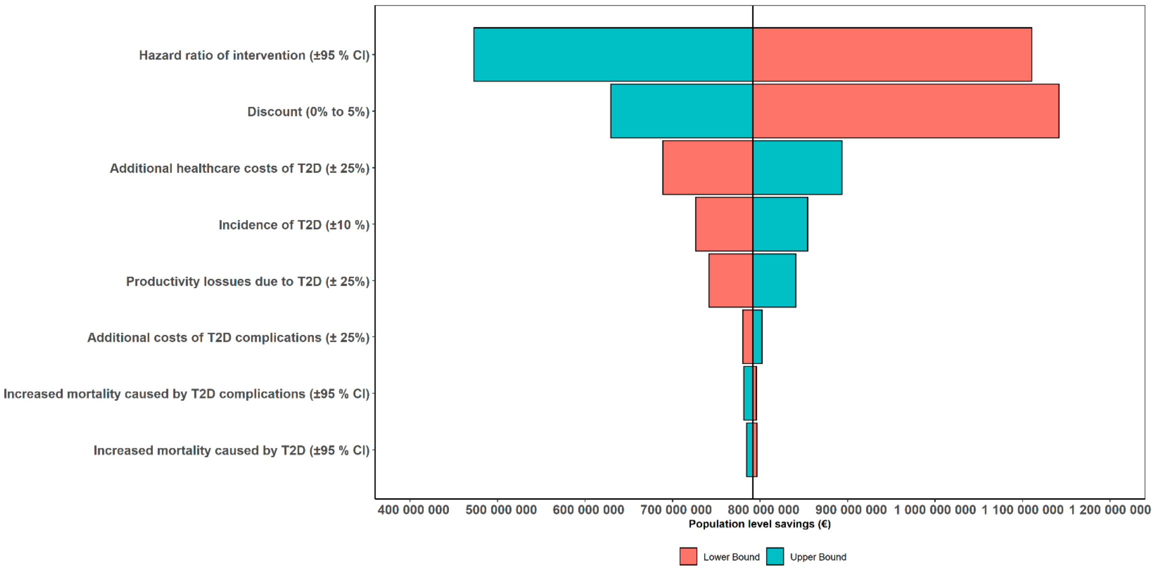
3.2. Results of One-Way Sensitivity Analyses

In one-way sensitivity analyses, when using the 20-year time horizon as an example, the largest effect on the results was the effectiveness of intervention and applied discount rate (Figure 2a,b). Savings variated from 473€ to 1110€ million and gained QALYs variated from 7583 to 17,812 when the effectiveness estimate was varied according to its 95%CIs. Changing the discount rate from 0% to 5%, the savings varied from 629€ to 1140€ million, and the gained QALYs variated from 9551 to 19,821. Other studied model parameters had a modest or small effect on the potential population level savings in all the studied scenarios.

Table 5. Projected cumulative mean QALY changes (95% CIs) compared with the baseline situation in the year 2017.

	10-Year Horizon			20-Year Horizon			30-Year Horizon		
Scenario #	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**	**Women**	**Men**	**Total**
Scenario I	501 (170 to 1041)	822 (310 to 1587)	1323 (480 to 2628)	5300 (2021 to 9990)	8314 (3224 to 15,691)	13,614 (5245 to 25,681)	20,310 (8407 to 36,205)	23,927 (9925 to 41,424)	44,237 (18,332 to 77,629)
Scenario II	1091 (331 to 2325)	1749 (570 to 3440)	2840 (901 to 5765)	11,012 (3673 to 21,294)	17,590 (6626 to 34,373)	28,602 (10,299 to 55,667)	41,850 (16,002 to 78,749)	50,842 (19,830 to 93,074)	92,692 (35,832 to 171,823)
Scenario III	1748 (593 to 3806)	2845 (1033 to 5603)	4593 (1626 to 9409)	17,620 (6882 to 34,991)	27,494 (10,632 to 52,799)	45,114 (17,514 to 87,790)	70,426 (31,723 to 124,935)	83,668 (36,171 to 148,325)	154,094 (67,894 to 273,260)

Scenario I: a 10%-unit increase in the Finnish population using at least one WGF serving a day, Scenario II: one or more additional whole grain servings a day among those who already use at least one whole grain serving a day, and Scenario III: the combination of Scenarios I and II. In all scenarios, the current situation was applied as a comparator.



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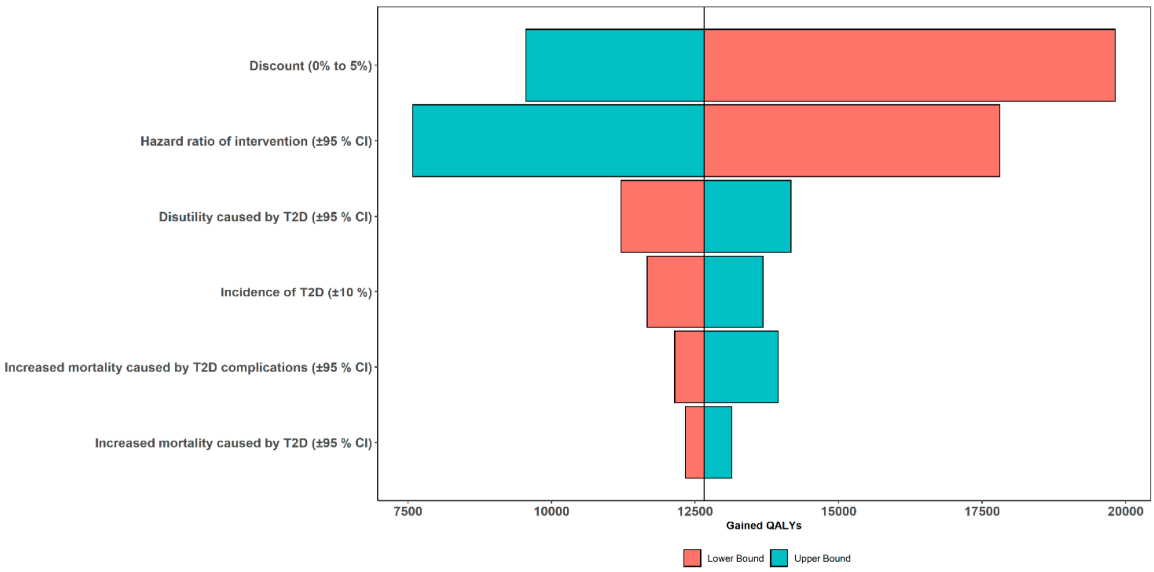

(**b**)

Figure 2. Tornado diagrams showing the results of one-way sensitivity analyses in terms of (**a**) cost savings and (**b**) additional QALYs in Scenario I (i.e., 10%-unit increase in the proportion of Finnish adults with the daily use of whole grain foods) with the 20-year timeframe as an example.

3.3. Results of Probabilistic Sensitivity Analysis

The results of the PSA are shown in Figure 3 in terms of population-level cost savings and QALYs gained using Scenario I as an example. The results of other scenarios are presented in Supplementary Figure S2A,B. As expected, the use of a longer time horizon increased the uncertainty related to the expected cost savings and QALY gains, leading to the wider joint distribution of cost savings and gained QALYs. However, regardless of this uncertainty, all plotted PSA iterations on an X–Y plane (Figure 3) constituted by cost savings and QALY gains remained in the southeast quadrant of the plane, where an intervention is expected to have greater effectiveness at lower costs. In addition, to take this parameter uncertainty into account, the probability of cost savings with and without T2D-related productivity loss costs conditional on the available data was estimated. Figure 4 illustrates the probabilities of cost savings in the modeled scenarios when applying the 20-year time horizon as an example. For example, as shown in Figure 4, there is around 97% probability at least for 1000 M€ savings in a case of Scenario III (when also considering the changes in productivity losses) conditional on the parameter uncertainty of the applied model. The results of other applied time horizons are presented in Supplementary Figure S3A,B.

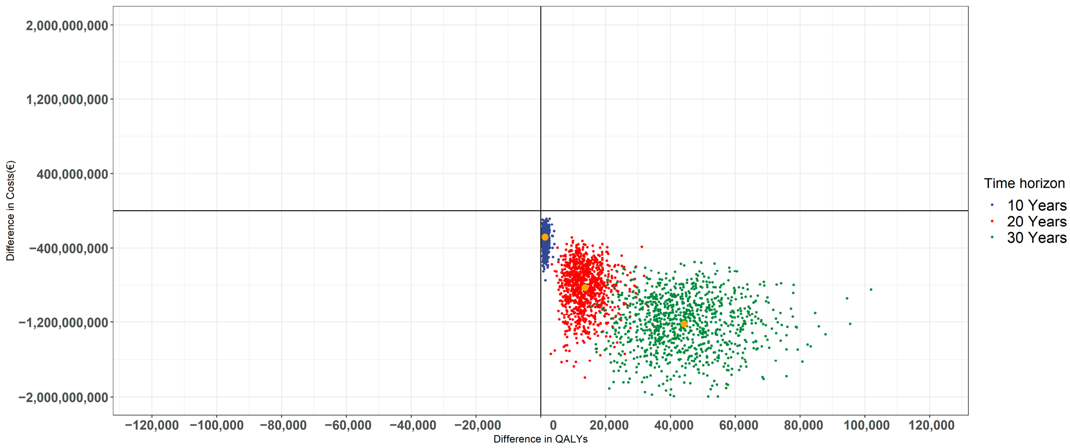

Figure 3. Results of the probabilistic sensitivity analysis showing the impact of applied time horizon on the distribution of expected population-level cost savings and gained QALYs on the X-Y-plane using Scenario I (current situation vs. a 10%-unit increase in the proportion of adult population using at least one whole grain servings a day) as an example. Blue, red, and green colors stand for 10-year, 20-year, and 30-year time horizons, respectively.

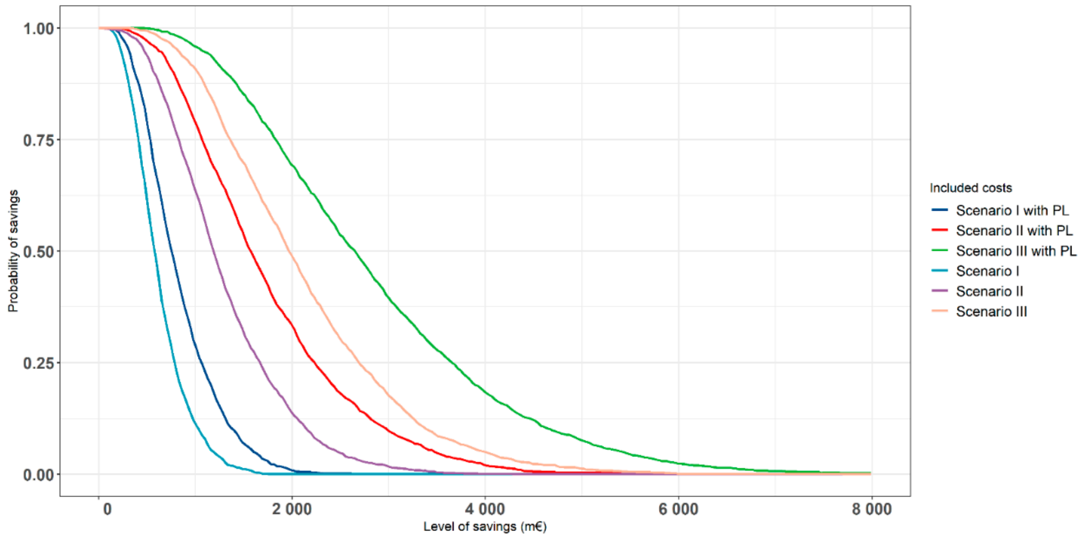

Figure 4. Probability of cumulative savings (with and without T2D-related productivity losses) in the modeled scenarios when applying the 20-year time horizon (2017 as a baseline year). Scenario I: a 10%-unit increase in the Finnish population using at least one whole grain food serving a day, Scenario II: one or more additional whole grain servings a day among those who already use at least one whole grain serving a day, and Scenario III: the combination of Scenarios I and II. In all scenarios, the current situation was applied as a comparator. PL = productivity losses due to T2D.

4. Discussion

The results of our study quantified the health economic significance of increased whole grain food consumption from the perspective of T2D prevention among the Finnish adult population. The inclusion of costs associated with T2D-related work absences and permanent work disabilities increased the savings potential, significantly highlighting the need for considering intervention consequences in a societal perspective in public health policy making. Our findings agree with the results of previous studies from Australia and Canada, showing a significant savings potential in the prevention of T2D among adult populations by increasing whole grain consumption [20–22]. However, our study demonstrated not only the significant savings potential but also significant gains in the number of QALYs (i.e., years lived in full health). This positive change in the number of years lived in full health is particularly important from the individual perspective, since the avoidance of T2D will provide life-years without T2D-related morbidity impacting negatively on an individual's health-related quality of life [40–44]. In addition, a previous Finnish study has shown the relationship between the future risk for T2D and current health-related quality of life [48]. Thus, the reduced future risk for T2D could also have an immediate positive impact on an individual's current quality of life mediated via changes in an individual's daily dietary habits and body weight. However, for simplicity, this positive immediate effect on health-related quality of life was not considered in the present study.

In the present study, we focused on assessing the expected population-level impacts of the hypothetical scenarios, where the proportion of Finnish adults using whole grain foods daily (i.e., at least one whole grain serving a day) is increased by a 10%-unit or alternatively where the number of daily whole grain servings is increased by one serving (i.e., two or more additional whole grain servings a day) among those who already use at least one whole grain serving a day. Based on our results, the increased whole grain consumption will lead to a higher number of health benefits and greater savings when focused on those who currently already use at least one whole grain serving a day due to the bigger size of the existing subpopulation among the Finnish adults (i.e., the majority of the Finnish adults already use at least one serving of WGF a day). However, as shown in the third scenario, the largest benefits could be expected to occur by combining these two approaches. The realization of these expected health benefits and cost savings will naturally require that public health policies supporting the increased consumption of whole grains, such as labeling, campaigns, and endorsement by manufacturers and catering services in schools, workplaces, health care, etc., can be implemented on a national level. Naturally, the implementation of such policies requires upfront investments, but these investments could be expected to be offset by the cost savings in the future with a potentially greater return on investment (ROI). However, the obtained level of ROI is conditional on an initial required investment as well as on the acceptable time horizon of that investment, since as in the case of all preventive policies, health benefits, and cost savings materialize beyond the present. Therefore, in the present study, we applied discounting to consider the fact that decisionmakers generally value future health benefits and cost savings less than current health effects and cost savings [49]. Thus, all results represent the present value of the future health and economic benefits of increased WGF consumption at the population level. Based on the conducted sensitivity analyses, the results of the study were sensitive among others to the applied annual discount rates, highlighting the need for the proper selection of discount rates to reflect societal preferences in public health policymaking.

A particular strength of the present modeling study is that we applied nationally representative data to estimate the long-term incidence of T2D in the target subpopulations [23,28]. Furthermore, we also applied the recent results by Hu et al. [10] providing the non-linear marginal effects of an increased number of whole grain servings a day, reducing the risk for T2D. In addition, we applied Finnish estimates for the incidence of complications in patients with newly diagnosed T2D and T2D-related additional health care costs as well as nationally representative estimates for productivity losses associated with T2D and its complications. As mentioned above, the inclusion of T2D-related productivity losses had a significant impact on the obtained results. This finding agrees with recent studies highlighting the significant role of productivity losses in T2D-related economic burden [50,51].

As in all modeling-based studies requiring assumptions, there are also several limitations that need to be considered when interpreting the results of the present study. First, in the present study, we defined the national level of daily whole grain consumption based on a self-reported daily use of rye bread, porridge, or mixed bread observed in FinHealth 2017 [23]. We did not have information on the consumption of other whole grain products e.g., whole grain cereals or brown rice, which may have led to the underestimation of WGF consumption in the Finnish adult population at the baseline of the study. Therefore, the obtained results may be too optimistic, assuming a lower baseline population-level whole grain consumption than there really is in practice. Second, we focused on the adult population aged 30–79 years without T2D at baseline, since the risk for T2D elevates gradually after the age of 30, ignoring the long-term health and economic benefits of increased whole grain consumption in the younger Finnish population (i.e., <30 years). Third, our present study considers only a partial savings and QALY gain potential produced by increasing daily whole grain consumption, since there is well-established evidence for the benefits of whole grains, for example, in the prevention of cardiovascular diseases and various types of cancers [52–54]. For example, a recent study from the US showed substantial cardiovascular health care savings potential associated with increased whole grains consumption among the US adults [55]. However, since cardiovascular complications are common in the patients with T2D, the benefits obtained by reducing cardiovascular morbidity are partly considered also in the present study. Fourth, in the present study, risk factor levels for T2D were assumed to stay at the same level as they were in year 2017. This may lead to an underestimation of expected benefits due to the current unfavorable increasing trends of obesity among the Finnish adult population [56]. Finally, in the present study, we did not consider the costs of different public policies promoting the daily use of whole grain products, thus not allowing the cost-effective considerations of different policy approaches. However, we believe that the results of the present study support the development of such policies, promoting whole grain consumption and providing possibilities to assess the cost-effectiveness of such policies in the future.

As a summary, the findings from this modeling study suggest that increased whole grain consumption could lead to significant health gains and societal savings by preventing the incidence of T2D in the Finnish adult population, even when its current daily whole grain consumption is already at relatively high level in a global context.

Supplementary Materials: The following are available online at https://www.mdpi.com/article/10.3390/nu13103583/s1, Figure S1: Graphical scheme of the study design, Figure S2: Results of the probabilistic sensitivity analysis using Scenario II and III. Figure S3: Probability of cumulative savings in 10 and 20-year time horizons, Table S1: The FINDRISC score distribution in the general population [23], Table S2: Coefficients of the Weibull regression for incidence of T2D, Table S3: The complications considered to be T2D-related in the Weibull regression model, Table S4: Weibull regression coefficients for the incidence of T2D-related complications, Table S5: The correlations between the Weibull regression coefficients.

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nutrients

Article

Pulse Intake Improves Nutrient Density among US Adult Consumers

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Abstract: The objective was to examine trends in pulse (dry beans, dry peas, chickpeas and lentils) intake over a 10-year period and to compare nutrient intakes of pulse consumers and non-consumers to better understand the impact of pulse consumption on diet quality in the US population. NHANES 2003–2014 data for respondents ($\geq$19 years) with 2 days of intake was used to evaluate trends in pulse intake. Pulse consumers were identified as those NHANES respondents who consumed pulses on one or both days. Differences in energy adjusted nutrient intakes between non-consumers and consumers were assessed. There were no significant trends in pulse intakes for the total population or for pulse consumers over the 10-year period. In 2013–2014, approximately 27% of adults consumed pulses with an intake of 70.9 $\pm$ 2.5 g/day over 2 days, just slightly <0.5 cup equivalents/day. At all levels of consumption, consumers had higher ($p < 0.01$) energy adjusted intakes of fiber, folate, magnesium. Higher energy adjusted intakes for potassium, zinc, iron and choline and lower intakes of fat were observed for consumers than for non-consumers at intakes $\geq$69.4 $\pm$ 1.01 g/day. These data suggest that pulse consumption in the US population may result in better diet quality with diets that are more nutrient dense than those without pulses.

Keywords: pulses; National Health and Examination Survey (NHANES); diet quality; nutrient density; legumes

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1. Introduction

Pulses, as defined by the Food and Agriculture Organization of the U.N., encompass a narrower class of legumes harvested as a dry grain that includes dry beans, peas, chickpeas and lentils [1]. Other legumes that are harvested while they are still green, contain significant levels of oil (e.g., soybeans and peanuts), or are garden vegetable varieties such as green peas and green beans are not considered pulses. There are hundreds of varieties of pulses grown around the world; however, the most commonly consumed pulses in the U.S. are dry beans (e.g., pinto, black and kidney beans), chickpeas, lentils and dry peas [2].

Legumes, including pulses, have been shown to have many health benefits. Higher intakes of legumes have been associated with satiety, weight management, improved gastrointestinal health, reduced risk of certain types of cancer, cardiovascular disease, hypertension and diabetes [3–10]. Pulses contain phytochemicals or non-nutritive bioactive components, which may have important health benefits [3]. They are a significant source of many nutrients, such as complex carbohydrate, protein, fiber, folate, iron, magnesium, and potassium and are a good source of many other nutrients (e.g., choline, zinc, selenium, phosphorus, and thiamin). For this reason, they are considered a nutrient dense food. Nutrient density is often used to qualify foods based on a given amount, standard serving, or calorie level and is calculated most often by expressing the amount of a specific nutrient per 100 g of food or per 1000 kcal of intake.

The 2020–2025 Dietary Guidelines [11] recommend consuming 1.5 cups of legumes defined as beans and peas per week as part of the vegetable group. However, given their high levels of protein, they can also count as a protein food. Therefore, as a replacement for meat, the relative contribution of pulses to the diet could exceed recommendations set for the vegetable group; however, most often they are consumed in place of other vegetables [2]. Pulses also contain 50–65% carbohydrate including resistance starch, soluble and insoluble fiber, and have a low glycemic index which may be beneficial for blood glucose management [12].

Despite dietary recommendations encouraging consumption of legumes, prevalence estimates from population studies of the National Health and Nutrition Examination Survey (NHANES) data from 1999–2002 showed that less than 8% of Americans were consuming pulses on any given day [2] and there is little evidence that this consumption level has changed since then.

To support dietary guidance that encourages healthy diet patterns with higher intakes of plant-based foods, an updated perspective on pulse consumption and their impact on diet quality is needed. Therefore, the purpose of this study is to update the literature on pulse consumption in U.S. adults by evaluating trends in intake over a 10-year period among pulse consumers and to examine the impact that pulses have on nutrient intakes. These data will contribute to our understanding of the role of pulses in the U.S. diet.

2. Materials and Methods

2.1. Data Source

Data from NHANES 2003–2014 gathered by the Center for Disease Control, National Center for Health Statistics (NCHS) was the source of data used in the analysis. NHANES is a cross-sectional survey conducted on a continual, annual basis to monitor the health and nutritional status of a nationally representative sample of the U.S. civilian, non-institutionalized population. Details on accessing the data, sampling designs and other methods used are available on the NCHS website [13]. The NCHS Ethics Review Board monitors and approves all survey procedures and written consent is obtained from all survey respondents. Publicly available data are released in 2-year increments as de-identified datasets and, therefore, are exempt from further institutional review board approval. Demographic characteristics and the "What We Eat in America" (WWEIA) or the dietary component of the survey was used to select adult respondents' age 19–65 years who reported 2 days of dietary intake.

2.2. Dietary Data Collection and Analysis

The dietary component of the NHANES survey consists of 2 days of intake collected using USDA's Automated Multiple Pass Method (AMPM) [14]. The first dietary intake data is collected in a Mobile Examination Center as an in-person interview. The second day of dietary data is collected by telephone within 2 weeks. The average of two-day dietary intakes was used to assess nutrient intakes and the quantity of pulses consumed. Pulse consumers were identified as those respondents who had reported consuming pulses at least once in the 2 days of reported intake. Non-consumers were identified as those who did not consume pulses an either of the 2 days of intake. Dietary intake files containing individual food level data and food codes were used in combination with the Food and Nutrient Database for Dietary Studies (FNDDS) recipe files to quantify the amount of pulses contained in 72 FNDDS food codes. Recipe files contain the amount of pulses in 100 g portions of all pulse containing foods and allows for the quantification of pulses consumed in a variety of mixed or combination foods. To examine nutrient intakes and amount of pulses consumed were derived using FNDDS versions 2003–2004 to 2013–2014 corresponding to each of the 6 cycles of survey used in this study.

2.3. Statistical Analysis

All data were analyzed in accordance to the NHANES analytical guidelines using the appropriate survey weights designed to account for unequal selection probabilities, clustered design and non-response. All analyses were conducted by Creme Global (Dublin, Ireland) using the Creme Nutrition® model. Creme Nutrition® is a scientific cloud-based software service used to assess and predict dietary intakes of foods and nutrients in populations of consumers [15]. In Creme Nutrition®, standard errors of statistics are calculated using bootstrapping, a resampling technique.

Six 2-year cycles of NHANES 2003 to 2014 were used to examine the trend of pulse consumption over a 10-year period. A linear regression model was applied over the weighted averages of the amount consumed to determine if there were statistically significant trends in pulse consumption in pulse consumers compared to the total population of adults ($\geq$19 years).

Significant differences in demographic characteristics between non-consumers of pulses compared to pulse-consumers were determined by a chi-square test. To test the hypothesis that the energy adjusted intake of nutrients is different between non-consumers and each quartile of pulse consumers, a paired Wilcoxon test was conducted with *p*-values at <0.01 considered to be statistically significant.

3. Results

There was no change ($p = 0.812$) over time in per capita consumption of pulses (i.e., average amount of pulses consumed on any given day based on 2-day average intakes) by adults' age 19 to 65 years across 6 cycles of NHANES from 2003-4 to 2013-14 (Figure 1).

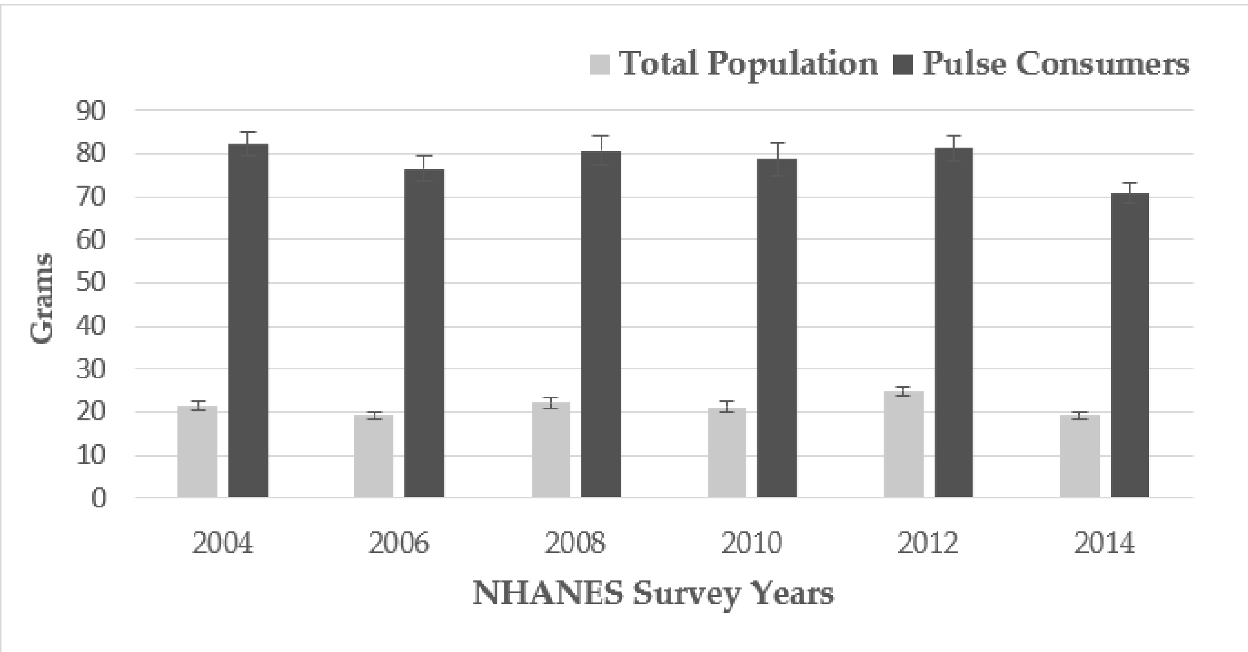

Figure 1. Pulse intake (grams) in the total population vs. pulse consumers, adults $\geq$ 19 years of age, National Health and Nutrition Examination Survey (NHANES) 2013–2014.

For the total population, per capita daily intakes were the highest in 2011-12 at 24.9 ($\pm$1.2) g/day and the lowest intakes were observed in 2006 (19.3 $\pm$ 0.9) and 2014 (19.3 $\pm$ 0.9) g/day consumed. Based on the average across 2 days, for pulse consumers, daily intakes of pulses were 82.2 ($\pm$2.7 g) in 2003-4 and 70.9 ($\pm$2.5 g/day) in 2013-14 and no significant difference was observed for levels of intake over time ($p = 0.247$). Furthermore, in 2013–2014, approximately 27% of adults consumed pulses at least once in the 2 days of intake reported. The amount of pulses consumed on pulse consuming days was higher at 117.8 ± 3.5 g/day (data not shown) than intakes based on the average of 2 days.

Demographic data showed that age, sex, ethnicity and education differed by consumer status (Table 1). Pulse consumers were more likely to be male and between the ages of 31 and 70. Both older adults (age >70 years) and younger adults (age 19–31 years) were less likely to be consumers. Mexican-Americans and other Hispanics were more likely to be pulse consumers than other ethnic groups. Those respondents with a greater than high school education were also more likely to be consumers than those with less education.

Table 1. Demographic characteristics of pulse [a] consumers and non-consumers based on 2-day intakes from NHANES, 2013–2014.

Characteristic	Consumers (n = 1325)	Non-Consumers (n = 3270)	p Value [b]
	——————-%——————		
Age (years)			0.0318
19–30	19.5	21.8	
31–50	38.4	33.8	
51–70	32.5	33.2	
>70	9.6	11.3	
Sex			0.0046
Male	50.7	45.7	
Female	49.2	54.3	
Ethnicity			<0.0001
Non-Hispanic White	59.7	70.1	
Non-Hispanic Black	8.8	11.7	
Non-Hispanic Asian	4.9	4.4	
Mexican American	15.2	6.3	
Other Hispanic	8.1	4.7	
Other (incl. multiracial)	3.1	2.8	
Education [c]			<0.0001
<High School	17.4	12.1	
High School	18.5	22.3	
>High School	63.0	63.9	

[a] Pulses include dry beans, peas, chickpeas and lentils; [b] χ^2 test for significance at $p < 0.05$ for the difference between consumers and non-consumers by demographic characteristic; [c] 1.1% of consumers and 1.7% of non-consumers did not report education.

At all levels (quartiles) of intake, pulse consumers had higher ($p < 0.01$) energy adjusted intakes of fiber, folate and magnesium (Table 2). Potassium was higher at intakes above 40 g/day (2nd quartile). For other nutrients such as choline, iron, zinc and phosphorus, significantly higher energy adjusted intakes were observed in the third and fourth quartiles (those consuming ≥69.4 ± 1.01 g/day). Fat intakes were lower in the third and fourth quartiles. Among pulse consumers, 26% of total folate and fiber intakes were from pulses (data not shown). Pulses also contributed >10% of total intakes of protein, thiamin, iron, magnesium, phosphorus, and zinc.

Table 2. Pulse amount, energy and nutrient intake for non-consumers and by quartile of pulse consumers based on 2-day dietary intakes from the National Health and Nutrition Examination Survey (NHANES), 2013–2014.

	Non-Consumers (*n* = 3270)	**Pulse Consumers (*n* = 1325)**			
		Quartile 1 (*n* = 294)	**Quartile 2** (*n* = 336)	**Quartile 3** (*n* = 322)	**Quartile 4** (*n* = 373)
		Mean ± SE			
Pulse intake (g/day)	——	17.1 ± 0.5	40.7 ± 0.4	69.4 ± 0.6	156.2 ± 4.2
Energy (kcal/day)	2029 ± 14	2014 ± 39	2101 ± 40	2333 ± 50 *	2486 ± 50 *
Macronutrients					
Protein (g/day)	81.0 ± 0.6	81.6 ± 1.8	84.5 ± 2.0	90.7 ± 2.4 *	100.1 ± 2.1 *
Protein (% kcal)	16.4 ± 0.1	16.5 ± 0.2	16.2 ± 0.3	15.9 ± 0.2	16.4 ± 0.2 *
Carbohydrates (g/day)	240.3 ± 1.8	229.2 ± 4.7	251.7 ± 5.0 *	284.1 ± 6.3 *	308.3 ± 6.2 *
Carbohydrates (% kcal)	47.6 ± 0.2	46.1 ± 0.5	48.5 ± 0.5	49.3 ± 0.5	50.2 ± 0.4 *
Total Fat (g/day)	78.8 ± 0.6	79.4 ± 2.0	80.6 ± 1.9	87.9 ± 2.6	89.7 ± 2.2 *
Total Fat (% kcal)	34.6 ± 0.1	35.1 ± 0.5	34.0 ± 0.3	33.3 ± 0.4 *	32.0 ± 0.3 *
Fiber, total dietary (g/day)	15.4 ± 0.1	18.1 ± 0.4 *	18.5 ± 0.4 *	23.6 ± 0.7 *	28.6 ± 0.6 *
Fiber, total dietary (g/1000 kcal)	7.8 ± 0.1	9.4 ± 0.2 *	9.3 ± 0.2 *	10.6 ± 0.2 *	12.2 ± 0.2 *
Micronutrients					
Calcium (mg/day)	940 ± 9	1050 ± 36	970 ± 26 *	1096 ± 28 *	1196 ± 31 *
Magnesium (mg/day)	285 ± 2	318 ± 6 *	310 ± 7 *	374 ± 12 *	383 ± 7 *
Iron (mg/day)	14.2 ± 0.1	14.5 ± 0.4	14.6 ± 0.3 *	17.4 ± 0.5 *	18.5 ± 0.4 *
Phosphorus (mg/day)	1341 ± 10	1409 ± 32	1405 ±31	1559 ± 39 *	1691 ± 34 *
Selenium (mcg/day)	116.0 ± 0.9	109.5 ± 2.4	116.1 ± 2.8	126.0 ± 4.2	131.3 ± 3.1 *
Zinc (mg/day)	10.9 ± 0.1	11.2 ± 0.3	11.5 ± 0.3 *	13.0 ± 0.4 *	13.1 ± 0.3 *
Potassium (mg/day)	2537 ± 18	2655 ± 49	2701 ± 54 *	3191 ± 69 *	3271 ± 58 *
Folate, food (mcg/day)	204 ± 2	239 ± 6 *	227 ± 5 *	282 ± 0.8 *	357 ± 10 *
Niacin (mg/day)	25.8 ± 0.2	26.0 ± 0.7	25.3 ± 0.9	28.0 ± 1.2	29.3 ± 0.7 *
Riboflavin (mg/day)	2.1 ± 0.0	2.3 ± 0.1	2.1 ± 0.1	2.3 ± 0.1 *	2.3 ± 0.1 *
Thiamin (mg/day)	1.6 ± 0.0	1.5 ± 0.0	1.6 ± 0.0	1.9 ± 0.1 *	2.0 ± 0.1 *
Choline, total (mg/day)	324 ± 3	328 ± 8	329 ± 8	375 ± 11 *	413 ± 10 *
Micronutrient Density					
Calcium (mg/1000 kcal)	475 ± 3	519 ± 12	467 ± 9	484 ± 10	448 ± 8
Magnesium (mg/1000 kcal)	146 ± 1	164 ± 3 *	152 ± 3 *	164 ± 3 *	161 ± 2 *
Iron (mg/1000 kcal)	7.1 ± 0.0	7.5 ± 0.2 *	7.2 ± 0.1	7.6 ± 0.1 *	7.7 ± 0.1 *
Phosphorus (mg/1000 kcal)	672 ± 3	704 ± 9	673 ± 8	681 ± 9 *	693 ± 7 *
Selenium (mcg/1000 kcal)	58.5 ± 0.3	55.8 ± 0.9	56.3 ± 1.1 *	54.2 ± 0.9 *	53.3 ± 0.8 *
Zinc (mg/1000 kcal)	5.4 ± 0.0	5.7 ± 0.1	5.5 ± 0.1	5.7 ± 0.1 *	5.4 ± 0.1 *
Potassium (mg/1000 kcal)	1296 ± 7	1370 ± 22	1330 ± 20 *	1357 ± 22 *	1345 ± 20 *
Folate, DFE ** (mcg/1000 kcal)	105 ± 1	124 ± 4 *	114 ± 3 *	127 ± 4.0 *	151 ± 4.0 *
Niacin (mg/1000 kcal)	13.0 ± 0.1	13.4 ± 0.3	12.1 ± 0.3 *	12.1 ± 0.2	11.9 ± 0.2 *
Riboflavin (mg/1000 kcal)	1.1 ± 0.0	1.2 ± 0.0	1.0 ± 0.0	1.1 ± 0.0	0.9 ± 0.0 *
Thiamin (mg/1000 kcal)	0.8 ± 0.0	0.8 ± 0.0	0.8 ± 0.0	0.8 ± 0.0	0.8 ± 0.0 *
Choline (mg/1000 kcal)	163 ± 1	166 ± 3	160 ± 3.0	165 ± 3.0 *	169 ± 3.0 *

* Significantly ($p < 0.01$) different from non-consumers; ** DFE = dietary folate equivalents

4. Discussion

Based on a nationally representative sample of adults' ≥19 years, pulse intakes for the total population and for pulse consumers have remained relatively stable from 2003 to 2014. With the exception of the present study, there is limited data evaluating consumption of pulses over time and few studies that examine pulses as a separate subgroup of legumes. Rehm et al. [16] examined trends from 1999–2010 in intake of nuts, seeds and legumes as a subcategory for scoring dietary quality according to the American Heart Association's 2020 Strategic Impact Goals. Results showed an increase for the subcategory, but was attributable to increases in nuts and seeds and not legumes. In a more recent study using NHANES 2011–2014, 2-day median intake of pulses were the same across the 4-year period [17]. The only other evidence that intakes of legumes or pulses have changed very little are general reports on WWEIA, and NHANES data that compared total vegetable intake, which includes legumes, in 2003–2004 and 2015–2016 [18].

There is also very little comparable data available on trends in global intakes specific to pulses. Data are country specific and inconsistent due to variability in economic factors (e.g., income, cost of pulses, production of animal sources of protein) that impact consumption of pulses [19]. The average level of global consumption as reported by the Food and Agriculture Organization is 21 g per capita per day and has not changed in three decades. These data, however, are based on per capita supply or the availability of pulses for use as food as an estimate of the average consumption. While not directly comparable, the data do offer some insight into overall consumption levels. The highest level of consumption based on per capita supply is Latin America and the Caribbean at 34 g per capita per day. South Asia and sub-Saharan Africa also have higher levels of consumption (33 g) than all other countries including North America with a level of consumption reported at 11 g [19]. Per capita daily pulse consumption based on our intake data was about 19 g. Depending on pulse type, 1/2 cup of cooked pulses weighs between 82 and 100 g and to meet the current 1.5 cup weekly recommendation according to the dietary guidelines [11], an individual would have to consume 246–300 g of cooked pulses per week and per capita daily pulse consumption would have to be 35–43 g per day which is considerably higher than the per capital daily consumption reported in 2013–2014.

The amount of pulses consumed by pulse consumers in this study (~71 g/day) is lower than previously reported data on pulses from NHANES 1999–2002 which was based on a single day of intake (~122 g/day) [2]. Similarly, in a Canadian study over a similar time period, pulse intake from a single day was 113 g/day [20]. The differences among these studies are also quite evident in the distribution of pulse intake across the quartiles and may be explained by differences in the analysis of 1 day of intake in the earlier study [2] vs. 2 days of intake in the current study. In this study, pulse intake was calculated as the average across 2 days with a pulse consumer defined as consuming pulses on at least 1 of 2 days. Unless pulses are consumed on both days, the average consumption across two days would be lower compared to when pulses are only consumed on 1 day.

There are also notable differences in the prevalence of pulse consumption reported among the previous survey published in 2009 [2], a Canadian study [20] and the current analysis. This current study found that 27% of U.S. adults reported consuming pulses on at least one day of their reported 2 days of intake and was considerably higher than the previous single day estimate of 7.9% [2] in the U.S. and 13% in Canada [20] These discrepancies were likely influenced by the number of days of intake examined and the frequency of pulse consumption in their respective populations. For episodically consumed foods (i.e., foods not consumed every day), more days of intake likely captured more respondents who were pulse consumers. For this reason, the use of both days may be more useful for describing population-based consumption patterns of episodically consumed foods [21]. Other factors such as sample size and ethnicity may also explain differences in prevalence and pulse intake estimates among these studies. For example, the Canadian study had twice the sample size than that of the U.S. study [2] with a high consumption of mung beans attributable to a high proportion of Asians in the sample [20]. Several studies have reported on the increases in nutrient density or diet quality in pulse or legume consumers [2,10,19,22] including some nutrients of concern, such as fiber, potassium, choline and magnesium as identified by the Dietary Guidelines Committee [23]. The data from this study support findings found in the earlier study on reported adult intakes from NHANES 1999–2002 for pulse consumers [2]. Nutrient intakes and energy adjusted nutrient intakes or nutrient density (amount of nutrient per 1000 kcal) of several key nutrients including fiber, iron, magnesium, zinc, selenium, phosphorus, potassium, folate, and choline were higher in consumers than non-consumers. The most pronounced improvements in nutrient intakes were seen at average intakes of greater than 69 g (<1/2 cup) of pulses across 2 days of intake. Fiber intakes were significantly higher in pulse consumers compared to non-consumers even at the lowest level of intake (~17 g/day). Increases in energy and percent of calories from carbohydrate were greatest at the highest levels of pulse consumption (i.e., 3rd and 4th quartile) and percent calories from fat was lower in pulse consumers than non-consumers.

This finding, in part, may be explained by the sources of pulse containing foods. Similar to what was previously reported by Mitchell et al. [2], food sources of pulses in the U.S. are largely from dry beans with a prevalence of 25% of the population consuming dry beans in the U.S. population over 2 days (data not shown). Dry beans were consumed by themselves, as the main ingredient in a side dish (e.g., baked beans and other canned dry beans), or as dry beans consumed in mixed dishes (e.g., burritos, beans and rice, chili, and soup). Hummus or chickpeas represented approximately 2% of all pulse consumers. The prevalence of other sources (lentils and dry peas) consumed were too low (<1% of all pulse consumers) to accurately estimate consumption.

Understanding the limitations of the dietary exposure literature relative to pulse consumption is important for the future direction of the research. Errors in self-reported dietary intake are inherent in all dietary exposure research and have been well documented in the literature including memory issues, under and over reporting of food intake and errors in portion size estimation [21]. NHANES and other populations-based dietary surveys capture cross-sectional dietary intakes and may not represent longer-term usual intake. These data are usually from a single day or 2 days of intake and are difficult to translate into consumption patterns over the course of week; which is the time frame used to provide dietary guidance in the U.S. This is particularly true for episodically consumed foods. Even with these efforts to characterize pulse consumers (pulse consumption on at least 1 day of intake) by disaggregating food sources that contain small quantities of pulses, there are likely sample respondents that consume pulses less frequently that were classified as non-consumers (no pulses consumed on either day of intake). Therefore, in this study and other cross-sectional surveys, the data may not be a true comparison of consumers and non-consumers, but rather an accounting of pulse intake and the impact on nutrient intakes on days when pulses were consumed.

The Dietary Guidelines recommend healthier dietary patterns by focusing on variety, nutrient density, and amounts of foods to stay within calorie limits. In the 2015–2020 Dietary Guidelines for Americans, the recommendations for the category of legumes (dry beans and peas) were updated so that they could be counted as both a vegetable and as a protein food [23]. Previous guidelines have often times confused consumers and health professionals by ambiguous terminology or by counting legumes in one of two groups (vegetable and meat or protein foods) but not both. Thus, the ability to count pulses as both a vegetable and protein, can better help consumers remain within caloric limits of the dietary patterns. In the most recent iteration of the Dietary Guidelines for Americans 2020–2025, the terminology for the vegetable subgroup legumes (dry beans and peas) has been replaced with beans, peas and lentils [11]. Further clarification has been added about the subcategory, beans, peas and lentils, including that they are also known as pulses. This change removes some of the ambiguity around the broader category of legumes that may have previously confused consumers.

There are many perceived barriers to consuming pulses including difficulty and time-consuming aspects of cooking dry forms, gastrointestinal discomfort, cultural and traditional influences, sensory issues and lack of diverse food choices containing pulses [24]. A strategy suggested by the Dietary Guidelines [20] is to use legumes or nuts and seeds in mixed dishes as a substitute for other foods that are often overconsumed and/or higher in saturated fat, sodium or refined carbohydrate. This shift to a more plant-based diet is sometimes referred to as a flexitarian approach to eating, is becoming increasingly popular because of its perceived health and sustainability benefit by encouraging plant-based protein sources such as pulses while allowing for some meat in moderation. In a recent study, food pattern or menu modeling by substituting less healthy dips and spreads with hummus showed that this simple substitution can reduce energy intake, increase protein intake, and more easily facilitate an increase in legume or vegetable recommendations [10]. Additionally, pulses contain complex carbohydrate and resistant starch and can easily replace foods that are a significant source of refined carbohydrates. With double the amount of protein found in wheat and about three times the amount of protein in rice, pulses may be a more nutrient dense alternative.

The unique composition of pulses makes them well suited for incorporation into a multitude of products. For example, flours made from pulses have been incorporated into snack foods, bread products, meat products, pastas, cereals, soups and beverages. More innovative food technologies could play a role in overcoming hurdles to increase pulse consumption making pulse-based food sources more palatable and nutritious. Future research from national food intake surveys that quantify the impact of pulse ingredients as additions and/or replacements in multi-component foods will be important to further capture the impact of pulses on nutrient intakes and to develop other strategies to increase intake.

As dietary guidance continues to evolve, it is also essential that future research aims to understand the effect of pulses on nutrient and food group intakes in a dynamic marketplace. In this study, trends in intakes over a 10-year period from 2003–2014 have remained stable. With the growing interest in a more sustainable food supply, and more knowledge about plant-based diets and healthier dietary patterns, increases in pulse intake could be on the horizon. Intakes of important nutrients were significantly higher in adults on days when pulses were consumed suggesting that diet quality could be improved by consuming pulses more frequently. Moving the U.S. diet towards a more sustainable and healthier dietary pattern that includes more pulses could have a significant public health impact.

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Institutional Review Board Statement: This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the National Center for Health Statistics, Center for Disease Control. Written informed consent was obtained from all survey respondents.

Informed Consent Statement: Written informed consent was obtained from all NHANES survey respondents.

Data Availability Statement: All data used for this study is from publicly available data sets available at the Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey. https://wwwn.cdc.gov/nchs/nhanes/ (accessed on 15 August 2019).

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nutrients

Article

The Changing Landscape of Legume Products Available in Australian Supermarkets

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Abstract: Evidence supports regular dietary inclusion of legumes due to their positive effects on both human and planetary health. Intake within Australia is suboptimal, with consumer data suggesting that an inability to integrate legumes into usual dietary patterns is a barrier to consumption. This places the food industry in a unique position to offer Australians the ability to incorporate legumes into usual dietary patterns via innovative new products. The aim of this study was to explore the legume category and compare nutrition product data and the use of nutrition and health claims between 2019 and 2021. An audit of legume products from four major metropolitan Sydney supermarkets (Aldi, Coles, IGA, Woolworths) collected ingredient lists, nutrition information and on-pack claims for baked beans, legume dips, legume flours, legume snacks (including subcategories of legume chips and whole legume snacks), canned legumes, dried legumes, frozen legumes, and pulse pasta. The total number of legume products available on the market nearly doubled from 2019 (n = 312) to 2021 (n = 610); this was driven by traditional plain canned and dried legumes and some new and convenient options, particularly snacks (legume chips) where the largest growth occurred. Of all legume products (n = 610), 82% met the Nutrient Profiling Scoring Criteria, 86.8% were at least a source of dietary fibre, and 55.9% were at least a source of protein. Nutrition content claims relating to dietary fibre, gluten free and protein more than doubled since 2019, with each featuring on over one third of the products identified in 2021. Vegan/vegetarian on-pack claims more than doubled since 2019, and claims related to the term plant-based/plant protein and environmental sustainability emerged on packs in 2021. By addressing barriers to consumption, such as lack of time and knowledge on how to prepare legumes, innovative legume products may help influence future consumption patterns.

Keywords: legumes; pulses; nutrition information; plant protein; sustainability

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1. Introduction

Legumes, such as chickpeas (*Cicer arietinum*), beans (*Phaseolus vulgaris*), peas (*Pisum sativum*), lentils (*Lens culinaris*) and dried pulses, are an excellent dietary source of plant protein, dietary fibre and minerals [1]. Regular consumption of legumes contributes to improved dietary quality and nutrient density [2], with regular intake associated with improved markers of metabolic health, weight management, reduced risk of coronary heart disease (CHD) and reduced risk of all-cause mortality [3–7]. Due to their nutritious and ecologically sustainable qualities, the Food and Agriculture Organisation of the United Nations (FAO) have recognised legumes as a key pillar in addressing the sustainability of agricultural and food systems as well as food security [1]. Recognised for their nitrogen-fixing properties, legume crops facilitate a regenerative effect, improving soil fertility and reducing greenhouse gas emissions via a reduction in the use of fertilisers [1,8]. Environmental sustainability and human health are both intricately linked to diet [9]. A substantial body of evidence indicates that dietary patterns rich in plant foods, including an emphasis on legumes, consumed in preference to animal-sourced foods hold the key to optimising human and planetary health [9]. Despite this, the integration of legumes into the dietary patterns of Western-based countries, such as Australia, presents a challenge [1,10].

National healthy eating guidelines globally recommend the consumption of legumes in variable quantities [11–15], with the Australian Dietary Guidelines (ADG) encouraging consumption as part of the 'vegetables' food group (1 serve = 75 g) and the 'lean meat and alternatives' food group (1 serve = 150 g) [13]. Variability exists within the evidence base, and a unified daily target is lacking [16]; however, the Eat-Lancet Planetary Health Diet suggests a scientific target of 50 g/day of legumes (dry beans, lentils and peas) (range 0–100 g/day) [9]. Irrespective of the discord surrounding an ideal daily target, legume consumption within Australia is inadequate. A secondary analysis of the 2011–2012 National Nutrition Physical Activity Survey (NNPAS), found that only 7.9% of the population sampled had consumed legumes the day prior to the survey, with an average serving size of 100 g [17]. The median intake is estimated to be 4 g/day, with 44% of a population of Australians sampled reportedly being non-consumers of legumes (unpublished data). On a global scale, the average per capita intake has remained largely unchanged in the previous three decades, at 21 g/day [8]. Global legume intake would need to increase by more than 100% to meet the reference intake as outlined in the Eat-Lancet Planetary Health Diet [9].

To influence population dietary consumption of legumes, consumer preferences, drivers and barriers to consumption must be understood [18]. While some consumers are increasingly making the conscious decision to select foods that are sustainably grown and produced [18], Australian consumer data suggests that there are several negating factors preventing increased legume consumption [19]. Barriers to consumption are reported to commonly arise from a lack of culinary knowledge and/or skills, the time (perceived and/or actual) required for preparation, the perception of legumes being inconvenient to prepare and an aversion to the taste and/or texture of legumes [19,20]. This has placed the food industry in a unique position, with the opportunity to enhance population consumption by offering innovative and convenient legume products. A greater understanding of the types of legume products that are available will assist in determining whether legume products can complement overall legume intake by offering additional opportunities for consumption. This study aimed to explore the legume category and compare product numbers and the use of nutrition and health claims between 2019 and 2021.

2. Materials and Methods

A comprehensive audit of commercially available legume products was conducted in February 2019 and 2021 across four major supermarkets within metropolitan Sydney, Australia. The data collection methodology replicated that previously published by Grafenauer et al. (2018) [21] and targeted four retail supermarket chains; Aldi, Coles, Independent Grocers of Australia (IGA) and Woolworths, which together represent 79.2% of the Australian grocery market share. This methodology is consistent with results reported by Figueira et al. (2019) [19], as 95% of surveyed respondents reported to purchase legumes for home use from supermarkets.

2.1. Eligibility and Exclusion Criteria

All legume products were assigned to one of eight categories, as outlined in Table 1 below, including baked beans, legume dips, legume flours, legume snacks, legumes canned, legumes dried, legumes frozen and pulse pasta.

Products excluded from the data collection process were those derived predominantly from peanuts (e.g., peanut butter), as despite botanical classification within the *Leguminosae* family, this oil-seed legume carries a distinctly different culinary classification to that of other legumes [22]. The exclusion of peanuts parallels the classification of peanuts within the 'seed and nut' category, rather than 'legumes and pulses', as per the 2011–2012 NNPAS [23]. Legume dips packaged with crackers were captured within the audit, however only the legume-containing component was included in the analysis (n = 13).

Combination legume products, for example, canned tuna and beans, mixed frozen peas and corn and ready-made meals containing legumes were deemed to be outside the scope of the current analysis and were therefore excluded from data collection. Legume-containing products marketed as meat alternatives (e.g., plant-based burgers), were also excluded from the data collection process as this category has been reviewed separately [24].

Table 1. Classification and description of legume product categories.

Category	Description of Categories
Baked beans	Navy/haricot beans canned in tomato sauce with the term 'baked beans' in the product name.
Legume dips	Commercial dips derived from cooked, blended legumes, with a type of legume captured in the product name or included as an ingredient, e.g., hummus or black beans.
Legume flours	Flour derived from dried, ground (uncooked) legumes, e.g., chickpeas, red lentils, or soybeans.
Legume snacks	Ready-to-eat packaged snack foods available in the snack food aisle or health food aisle, with a type of legume captured in the product name or included as the main ingredient. Sub-categories include legume chips, derived from legume flour, whole legumes, savoury and whole legumes, sweet.
Canned legumes	Legumes that have been boiled and canned in brine, as well as ready-to-eat legumes that have been boiled, drained, and packaged into pouches, e.g., chickpeas, lentils, kidney beans, peas. Excludes combination products, e.g., tuna and bean mixes.
Dried legumes	Dried and uncooked legumes, e.g., dried split peas, dried chickpeas, or soup mixes with legumes.
Frozen legumes	Commercial frozen legume products, e.g., frozen broad beans, edamame, or peas. Excludes combination products, e.g., corn and peas, ready meals, and meat alternatives.
Pulse pasta	Pasta made with flour derived from dried, ground legumes, e.g., chickpeas, red lentils, or peas.

2.2. Ethics Approval

This study was exempt from requiring ethics approval given the analysis focused solely on food products; however, permission for data collection in-store was obtained from supermarket store managers.

2.3. Data Collection and Analysis

Smartphones were used to photograph the following information for each product: Ingredient list, Nutrition Information Panel (NIP), health and nutrition-related claims and Health Star Rating (HSR). A data extraction form was created in Microsoft® Excel (Redmond, WA, USA), where the data (collected in both 2019 and 2021) was transcribed from photographs and collated for analysis according to the product category classifications outlined in Table 1. Data was confirmed by a second, independent reviewer to identify and amend inconsistencies or errors and cross-checked via the Mintel New Product Data Base. In addition to the in-store audit, a supplementary internet search was conducted via retailer websites and websites of manufacturers that were identified during in-store data collection. Although several products were available in numerous supermarket chains, each product was only recorded once, and data was screened to remove duplicates.

The Food Standards Australia New Zealand (FSANZ) Nutrient Profiling Scoring Criterion (NPSC) was calculated for all products identified in the 2021 data set. The NPSC is a nutrient profiling method used to determine whether a food is eligible to carry general-level and high-level health claims, based on its nutrient profile [25]. The NPSC algorithm considers both positive nutrients/food components (e.g., dietary fibre, protein, fruit, vegetable, nut and legume content) and risk nutrients (e.g., energy, sugar, sodium and saturated fat). For products outlined in Table 1, the final NPSC score must be less than four.

On-pack claims were classified as either nutrition content, general-level health claims or high-level health claims as per Standard 1.2.7 of the Australia New Zealand Food Standards Code (FSC) [26]. Other claims not covered by Standard 1.2.7 were also recorded (e.g., suitable for vegetarians/vegans, no artificial colours, flavours or preservatives). Data collected in 2021 was also assessed for eligibility to make nutrition content claims, in line with Standard 1.2.7 of the FSC. Australian labelling requirements do not require dietary fibre to be declared in the NIP unless a relevant on-pack nutrition content claim has been made [26]. Products that did not declare the dietary fibre content on the pack, were excluded from the dietary fibre claim eligibility calculation as to not skew the data and provide a misleading representation of the categories.

Descriptive analyses were conducted with the aid of Microsoft® Excel Version 16.50 (Redmond, WA, USA) to determine the number (*n*) and relative (%) change over time for each product category.

3. Results

As outlined in Table 2, a total of 610 products were identified in the 2021 audit, including legume snacks (*n* = 140) (comprised of legume chips (*n* = 96), whole roasted legumes, savoury (*n* = 37) and whole roasted legumes, sweet (*n* = 7)), canned legumes (*n* = 154), legume dips (*n* = 107), dried legumes (*n* = 92), baked beans (*n* = 47), frozen legumes (*n* = 32), pulse pasta (*n* = 32) and legume flours (*n* = 6). The 2021 audit revealed a 95.5% increase in the number of products as well as an increase among all defined product categories compared to 2019. The legume snacks category experienced the greatest growth in the number of products, specifically legume chips which increased by an additional 75 products, followed by canned legumes (*n* = 72), dried legumes (*n* = 63), and legumes dips (*n* = 31). Legume chips (357% increase), whole legumes, sweet (250% increase), and dried legumes (217% increase) experienced the greatest change over time.

Table 2. The number of legume products identified per category and sub-category in both 2019 and 2021 and the change over time.

Category	2019 *n* (% of Total)	2021 *n* (% of Total)	Change 2019–2021 *n* (%)
Canned legumes	82 (26.3)	154 (25.2)	72 (87.8)
Legume snacks	52 (16.7)	140 (23.0)	88 (169)
Legume chips	21 (6.73)	96 (15.7)	75 (357)
Whole legumes, savoury	29 (9.29)	37 (6.07)	8 (27.6)
Whole legumes, sweet	2 (0.64)	7 (1.15)	5 (250)
Legume dips	76 (24.4)	107 (17.5)	31 (40.8)
Dried legumes	29 (9.29)	92 (15.1)	63 (217)
Baked beans	35 (11.2)	47 (7.70)	12 (34.3)
Frozen legumes	25 (8.01)	32 (5.25)	7 (28.0)
Pulse pasta	11 (3.53)	32 (5.25)	21 (190)
Legume flours	2 (0.64)	6 (0.98)	4 (200)
Total	312	610	298 (95.5)

A total of 95 food manufacturers/importers were represented across products identified in 2021, with Woolworths (NSW, Australia), Coles (VIC, Australia) and H.J. Heinz Company Australia Ltd. (VIC, Australia) being the top three, which were responsible for a collective 16.1% of products. The total number of manufacturers/importers increased 72.7% compared to 2019 (*n* = 55).

3.1. Legume Varieties

As displayed in Table 3, a total of 22 different varieties of legumes were identified among products in 2021, a relative increase of 22.2% over time. The largest increase in the number of products over time occurred among beans (*n* = 100 additional products), followed by chickpeas (*n* = 76) and mixed variety products (a combination of beans, chickpeas, peas, lentils and/or lupin) (*n* = 50). Within the beans category, edamame/soybeans experienced the greatest increase in the number of products over time (*n* = 18 additional products), followed by black beans/black turtle beans (*n* = 17) and kidney beans (*n* = 15). Legume types with the greatest relative change over time included mung beans (an increase of 600%), edamame/soybeans (an increase of 300%) and adzuki beans (an increase of 300%).

Table 3. Legumes varieties used in legume products in 2019 and 2021 and the change in number of products over time.

Legume Type	2019 *n* (% of Total)	2021 *n* (% of Total)	Change 2019–2021 *n* (%)
Beans	117 (37.5)	217 (35.6)	100 (85.5)
Adzuki beans	1 (0.32)	4 (0.66)	3 (300)
Beans (unspecified)	1 (0.32)	5 (0.82)	4 (400)
Beans, mixed [a]	9 (2.88)	9 (1.47)	-
Black beans/Black turtle beans	12 (3.85)	29 (4.75)	17 (142)
Black-eyed beans	-	1 (0.16)	1
Borlotti beans	6 (1.92)	14 (2.27)	8 (133)
Broad beans/Faba (fava) beans	17 (5.45)	21 (3.44)	4 (23.5)
Butter beans/Lima beans	6 (1.92)	9 (1.47)	3 (50.0)
Cannellini beans	9 (2.88)	18 (2.95)	9 (100)
Edamame/Soybeans	6 (1.92)	24 (3.93)	18 (300)
Giant beans	-	1 (0.16)	1
Great northern beans	-	2 (0.33)	2
Haricot beans/Navy beans	28 (8.97)	37 (6.07)	9 (32.1)
Mung beans	1 (0.32)	7 (1.15)	6 (600)
Pinto beans	3 (0.49)	5 (0.82)	2 (66.7)
Kidney beans	14 (4.49)	29 (4.75)	15 (107)
White beans (unspecified)	4 (1.28)	2 (0.33)	−2 (−50.0)
Chickpeas	97 (31.1)	173 (28.4)	76 (78.3)
Peas	48 (15.4)	76 (12.5)	28 (58.3)
Lentils	30 (9.62)	73 (12.0)	43 (143)
Mixed [b]	20 (6.41)	70 (11.5)	50 (250)
Lupin	-	1 (0.16)	1
Total variety	18	22	4 (22.2)

[a] A combination of any bean variety listed. [b] A combination of any legume type listed.

3.2. On-Pack Claim Eligibility and NPSC

Product eligibility for nutrition content claims varied among product categories, as outlined in Table 4. Most canned legumes (63.6%), dried legumes (94.6%), baked beans (95.7%), frozen legumes (50%), pulse pasta products (100%) and legumes flours (100%) were at least a source of protein. Similar results were found for dietary fibre claim eligibility, with 86.8% (361/416) of all products that declared the dietary fibre content on the pack eligible to carry at least a source of fibre claim. Most legume flours, dried legumes, frozen legumes and pulse pasta products were considered low in sodium, however only 4.7% of legume dips, 6.4% of baked beans, and 7.1% of legume snacks, were eligible to carry a low sodium claim.

Table 4. The number and proportion of products meeting eligibility criteria for on-pack claims and NPSC in 2021; *n* (% of category).

Nutrition Content Claim	Canned Legumes (*n* = 154)	Legume Snacks (*n* = 140)	Legume Dips (*n* = 107)	Dried Legumes (*n* = 92)	Baked Beans (*n* = 47)	Frozen Legumes (*n* = 32)	Pulse Pasta (*n* = 32)	Legume Flours (*n* = 6)
Low fat (≤3 g per 100 g)	143 (92.6)	2 (1.43)	3 (2.80)	67 (72.8)	46 (97.9)	29 (90.6)	17 (53.1)	1 (16.7)
Low saturated fat (≤1.5 g per 100 g)	145 (94.2)	39 (27.9)	26 (24.3)	90 (97.8)	47 (100)	32 (100)	32 (100)	5 (83.3)
Source of protein (≥5 g per serve)	77 (50.0)	27 (19.3)	8 (7.48)	22 (23.9)	26 (55.3)	15 (46.9)	9 (28.1)	1 (16.7)
Good source of protein (≥10 g per serve)	21 (13.6)	18 (12.9)	2 (1.87)	65 (70.7)	19 (40.4)	1 (3.13)	23 (71.9)	5 (83.3)
Low sodium (≤120 mg per 100 g)	52 (33.8)	10 (7.14)	5 (4.67)	87 (94.6)	3 (6.38)	30 (93.8)	31 (96.9)	6 (100)
Eligible for fibre claim (≥2 g per serve)	136 (100) [a]	65 (63.1) [b]	8 (32.0) [c]	48 (100) [d]	47 (100)	22 (100) [e]	30 (100) [f]	5 (100) [g]
Source of fibre (≥2–<4 g per serve)	38 (27.9) [a]	2 (1.94) [b]	4 (16.0) [c]	1 (2.08) [d]	1 (2.13)	6 (27.3) [e]	4 (13.3) [f]	0 (0.00) [g]
Good source of fibre (≥4–<7 g per serve)	66 (48.5) [a]	20 (19.4) [b]	2 (8.00) [c]	22 (45.8) [d]	16 (34.0)	16 (72.7) [e]	6 (20.0) [f]	2 (40.0) [g]
Excellent source of fibre (≥7 g per serve)	32 (23.5) [a]	5 (4.85) [b]	2 (8.00) [c]	25 (52.1) [d]	30 (63.8)	0 (0.00) [e]	20 (66.7) [f]	3 (60.0) [g]
Meets NPSC [h]	154 (100)	73 (52.1)	63 (58.9)	92 (100)	47 (100)	32 (100)	32 (100)	6 (100)

[a] 136 products reported dietary fibre. [b] 103 products reported dietary fibre. [c] 25 products reported dietary fibre. [d] 48 products reported dietary fibre. [e] 22 products reported dietary fibre. [f] 30 products reported dietary fibre. [g] 5 products reported dietary fibre. [h] Nutrient Profiling Scoring Criterion (NPSC). To pass the NPSC, the final score must be <4.

As presented in Table 4, all canned legumes (*n* = 154), dried legumes (*n* = 32), baked beans (*n* = 47), pulse pasta (*n* = 32) and legume flours (*n* = 6) categories passed the NPSC and were considered a healthier choice. Of the legume dips, 58.9% passed the NPSC with a median legume content (per 100 g) of 60 g (range 10–86 g). More than half of legume snacks passed the NPSC with an overall median legume content (per 100 g) of 43 g (5–98 g), 87 g (15–100 g) and 43 g (43–50 g) for legume chips, whole legumes, savoury and whole legumes, sweet, respectively.

3.3. On-Pack Claims

Table 5 outlines the number and proportion of legume products that displayed nutrition content claims, general-level health claims, high-level health claims, and other claims. Nutrition content claims related to dietary fibre, gluten free and protein more than doubled since 2019, with each featuring on over one third of the products identified in 2021. A total of 14 different products displayed general-level health claims in 2021, increasing from just six products in 2019. Protein-related general-level health claims increased four-fold, while the number of products displaying claims related to dietary fibre, iron, and micronutrients (unspecified) doubled in 2021. Claims that emerged in 2021 included protein for longevity (*n* = 3) and optimal health (*n* = 1), and dietary fibre for improved satiety (*n* = 2), while claims in relation to dietary fibre for improved digestive health and bowel function doubled in the last two years (*n* = 3 additional products). The presence of high-level health claims experienced no change over time. Other claims such as 'vegetarian/vegan' more than doubled over time, representing the greatest increase since 2019 with an additional 151 products identified, followed by 'no artificial colours/flavours/preservatives' (*n* = 140 additional products). 'Plant-based' (*n* = 27) and 'sustainability' (*n* = 27) claims only emerged in 2021.

Table 5. Frequency of legume products displaying nutrition content and health claims in 2019 and 2021.

	2019 *n* (% of Total)	2021 *n* (% of Total)	Change 2019–2021 *n* (%)
Nutrition Content Claim			
Dietary Fibre	118 (37.8)	246 (40.3)	128 (108)
Gluten Free	100 (32.1)	216 (35.4)	116 (116)
Protein	94 (30.1)	208 (34.1)	114 (121)
Fat	68 (21.8)	90 (14.8)	22 (32.4)
Salt	32 (10.3)	56 (9.18)	24 (75.0)
Sugar	8 (2.56)	34 (5.57)	26 (325)
Energy	10 (3.21)	28 (4.59)	18 (180)
Vitamins/Minerals	5 (1.60)	24 (3.93)	19 (380)
Glycemic Index	10 (3.21)	19 (3.11)	9 (90.0)
Carbohydrate	1 (0.32)	15 (2.46)	14 (1400)
General-Level Health Claim			
Protein	3 (0.96)	13 (2.13)	10 (333)
Dietary Fibre	6 (1.92)	12 (1.97)	6 (100)
Iron	1 (0.32)	3 (0.49)	2 (200)
Vitamin C	3 (0.96)	3 (0.49)	-
Micronutrients (unspecified)	1 (0.32)	2 (0.33)	1 (100)
Thiamin (B1)	-	2 (0.33)	2
High-Level Health Claim			
F&V; CHD	1 (0.32)	1 (0.16)	-
Saturated fat; CHD	1 (0.32)	1 (0.16)	-
Other Claims [a]			
No Artificial C/F/P [b]	112 (35.9)	252 (41.3)	140 (125)
Vegetarian/Vegan	81 (26.0)	232 (38.0)	151 (186)
Organic	34 (10.9)	115 (18.8)	81 (238)
Plant-based [c]	-	27 (4.43)	27
Sustainability	-	27 (4.43)	27

[a] Claims that are not outlined in Standard 1.2.7 of the Food Standards Code. [b] Colours/Flavours/Preservatives (C/F/P). [c] Includes specific terms 'plant-based', 'plant protein' and 'plant power'. Fruit and Vegetables (F&V); coronary heart disease (CHD).

4. Discussion

This study aimed to provide an insight into the legume food category and compare nutrition product data and nutrition and health claims obtained in 2019 and 2021. The results demonstrated an increase of 298 legume products over the two years preceding 2021 ($n = 610$), including an increase among all product categories and a relative increase in the variety of legume types available (22.2%), with black-eyed beans, giant beans, great northern beans and lupin making a debut into the market according to our analysis. An increase in product manufacturers (72.7%) suggests a substantial interest within the food industry. The increase in the number of legume products identified by this study is consistent with the trajectory reported by Gilham et al. (2018) [27], who observed an increase of 208 new products with at least half a serve of legumes between 2012 and 2017.

The legume snack category increased 169% compared to 2019, the largest increase among all legume categories, especially legume chips, which increased four-fold. This notable increase demonstrates the innovation within the category, providing consumers the opportunity to obtain dietary legumes via convenient, ready-to-eat snack foods, rather than the more traditional methods such as in soups [27]. While some of these products may not be nutritionally equivalent to their whole food counterparts, several products do show promise as a convenient way to increase legume intake. The legume content of the snack products ranged from 5% to 100% indicating that these products are a means of complimenting overall legume intake.

Legumes are increasingly being recognised as an ecologically sustainable food [9], and the notable emergence of 'sustainability' claims featuring on legume products in the two years following 2019 parallels this; however, both the positive health and environmental effects may be offset by the heavy processing required to transform some of these products [28]. In addition to the emergence of on-pack 'sustainability' claims, the prevalence of on-pack labeling to identify products as suitable for vegans/vegetarians also increased considerably, demonstrating the largest increase (n = 151) compared to all other on-pack claims. In line with the theme of vegan/vegetarianism, food marketing has evolved to appeal to consumer trends. This has seen the emergence of the term 'plant-based' used on-pack among legume products in a bid to appeal to consumers. A total of 4.43% of products displayed the term 'plant-based' in 2021, with a comparator of zero in 2019. This trend is widespread among the food industry with use of the term among all Australian food product launches increasing by 26.7% over the two years preceding 2021 [29].

As the evidence base for diet-induced modulation of the gut microbiome to improve overall health has grown [30], so too has consumer interest in eating to improve gut health, and this was demonstrated among on-pack claims identified among legume products. Both general-level health claims related to digestive health and nutrition content claims related to dietary fibre doubled over the last two years. As the body of evidence suggesting an association between legume consumption and modulation of the gut microbiota continues to emerge [31,32], it may be expected that on-pack claims of this nature will continue to increase in prominence among legume products.

This study is the first of its kind, to our knowledge, to comprehensively review legume products available in Australian supermarkets. There are several limitations within the study design that must be acknowledged. While all efforts were made to identify legume products in their entirety, differences in product availability may exist within different geographic locations of supermarkets. Furthermore, the 2021 data collection took place after the global COVID-19 pandemic had commenced, which may have impacted some product availability.

The findings of the research provide insight into the changing landscape of legume products available to Australian consumers. The data obtained by this research may be used as an aid to inform government bodies involved in the reform of national healthy eating guidelines, as it indicates that the scope of dietary legume consumption may no longer fall within traditional culinary classifications of 'vegetables' and 'lean meat and alternatives', but instead as a distinct food group on its own. Future development of legume consumption surveys should also consider the findings of this research, as variability in nutritional quality among categories of legume foods may present as a complexity when aiming to quantify legume intake, particularly in consumption studies. While this research points to an increase in the legume products available, it is unknown whether this has translated to an increase in legume consumption. To progress research within this area, future studies could include a focus on the consumption patterns of such products.

5. Conclusions

The main findings of this research demonstrate that the legume product market within Australia has expanded by 95.5%, including an expansion across all categories, with new and innovative opportunities to increase legume intake. Among these legume products, variability does exist with respect to legume content and nutritional composition. While consumption of whole, minimally processed foods is preferable for both human and planetary health, this research suggests that emerging legume products do have the capacity to offer a means of complementing legume intake and may assist with increasing overall consumption.

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nutrients

Article

Nutritional Quality of Wholegrain Cereal-Based Products Sold on the Italian Market: Data from the FLIP Study

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Abstract: The consumption of wholegrains (WG) is encouraged worldwide, but the lack of a common legal definition of such products leads to an unclear classification and identification on the grocery store shelf. In Italy, several products are generally sold as WG, but it cannot be determined if they are made entirely with all WG cereal(s) or if they are partially produced with WG ingredients (PWG). The aims of this study were to (a) survey the number of cereal-based food items formulated with WG, PWG, or refined (RG) present on the Italian market; and (b) analyse the nutritional quality, intended as nutrition facts, of WG products in comparison to PWG and RG. Nutritional information and declarations were retrieved from packs of 3040 products belonging to five different categories: breakfast cereals, biscuits, sweet snacks, bread, and bread substitutes. A descriptive analysis of the products and comparison of energy, macronutrients, fibre and salt among RG, PWG and WG products within each category was performed. In all categories, a major portion of the products did not contain WG ingredients. Results showed that the nutritional quality of RG, PWG, and WG products varied in relation to the product category and that WG inclusion cannot be always considered a marker of the overall nutritional quality of foods. Instead, it is necessary to evaluate the global product characteristics, and it is important to pay attention to differences between WG and PWG products that can be perceived by consumers as equivalent.

Keywords: cereals; fibre; nutrition claim; health claim; nutrition declaration; food labelling

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1. Introduction

Several cereals are key ingredients of many of the foods consumed worldwide on a daily basis. These cereals have a common kernel structure and are composed of a starchy endosperm surrounding the germ and external hard outer layers called bran, which particularly rich in micronutrients and bioactive compounds other than fibre [1]. In agreement with many dietary guidelines, cereal-based products are staple foods that should provide the major part of the daily calorie intake [2]. This energy is mainly due to the high content of complex carbohydrates and to a discrete amount of proteins. As mentioned, there is a notable presence of fibre and other micronutrients and bioactives concentrated in the bran layer which is almost totally removed during the milling process, thus resulting in much higher amounts in wholegrain (WG) cereal-based products than in the refined ones [3,4].

As a result of this different nutritional composition, dietary patterns rich in WG and WG-based products have different effects on nutritional status and health outcomes compared to the ones including refined cereal [5]. For instance, consumption of WG in adults was associated with significantly higher daily intakes of dietary fibre and several vitamins (thiamine, riboflavin, vitamin B6) and minerals (iron, calcium, potassium, phosphorus, zinc, magnesium) that are abundant in these products, compared to those who did not consume them [6]. Moreover, it is well-established that a high consumption of WG products is associated with a lower risk of non-communicable diseases, such as cardiovascular diseases [7–9], colorectal cancer [10], type-2 diabetes [11], symptoms of metabolic syndrome [12], and to a lower mortality rate for several causes [13,14]. Moreover, WG cereals represent one of the key foods at the base of the Mediterranean Diet pyramid, which therefore should be included daily and preferred to their refined counterparts [15]. For all these reasons, dietary guidelines worldwide suggest an increase in the consumption of WG, even though quantitative recommendations of WG are not clearly defined and/or consistent among the countries [16]. This last aspect may be also attributable to a lack of a legally binding definition of WG and, in turn, of WG flour and products [16]. According to the European Union's agricultural legislation, WGs are "grains from which only the part of the end has been removed, irrespective of characteristics produced at each stage of milling [17]". The European Food Safety Authority supports the definition of the American Association of Cereal Chemists, which states that WGs "consist of the intact, ground, cracked or flaked caryopsis, whose principal anatomical components—the starchy endosperm, germ and bran—are present in the same relative proportions as they exist in the intact caryopsis", while EU-sponsored HEALTHGRAIN forum agreed that "whole grains shall consist of the intact, ground, cracked or flaked kernel after the removal of inedible parts such as the hull and husk [3]". The definition of WG products is even more complex and not consistent across countries. For instance, wholegrain products in the UK and USA must include ≥51% of WG ingredients (on a wet matter basis). In European countries, such as Sweden and Denmark, WG ingredients must be ≥50% (on a dry matter basis) in WG products, while in Germany, WG bread must contain 90% WG [18]. The one recommended by the HEALTHGRAIN forum is that a WG food should contain "at least 30% whole-grain ingredients in the overall product and more whole grain than refined grain, both on a dry weight basis [16,19]". Because of this uncertain and arbitrary definition for WG products, only a few countries and health-promoting organizations around the world defined and approved food labeling criteria and health claims on WG and WG products, but this was not done unanimously [20]. This leads to the presence on the market of products labelled as WG but meeting different requirements that vary from country to country. As a result, in Italy and Europe, a wide range of foods are sold as WG products or as products containing at least one WG cereal within the ingredients, which can therefore differ for the number and the amount of WG cereal constituting the product. Moreover, just the presence of WG may allow the consumer to perceive that these foods healthier than the ones without WG, independent of their content of WG. Besides that, previous investigations have shown that a large amount of the population is still not aware of the health benefits of WG [21,22]. Moreover, it is well-known that the overall nutritional quality of a food product is the result of many different aspects, including but not limited to the energy, macro and micronutrient content, as reported in the mandatory nutrition declaration in agreement with the European Union Regulation n.1169/2011 [23].

In this regard, even if WG products are supposed to be healthier than refined ones, the overall nutritional quality of commercially prepacked WG products sold on the Italian market have been barely investigated, and the hypothesis of the presence of the WG claim as a proxy of the total nutritional quality of the product has not been verified. Therefore, the aims of the present work were (a) to provide a descriptive analysis of WG products present on the Italian market, and (b) to investigate the overall nutritional quality of such products in comparison with products either only partially formulated with WG cereals or completely refined in nature.

2. Materials and Methods

2.1. Data Collection

Data were collected from the online surveys conducted in previous studies of the same project [24–26] and updated in June 2021. Prepacked cereal-based products considered in the present study were selected from the major Italian retailers on a home-shopping website (Bennet, Carrefour, Conad, Coop Italia, Crai, Despar, Esselunga, Il Gigante, Iper, Pam Panorama, Selex, Sidis). Products were considered eligible for the study if belonging to the following food categories: breakfast cereals, cereal-based sweet snacks, biscuits, bread, and bread substitutes. All the prepacked foods for which mandatory product information must be included directly on the package or on a label attached, as stated in the European Union Regulation n.1169/2011 were included as eligible products. Conversely, foods excluded after the online search were: (i) not prepackaged foods; (ii) items with incomplete images on all of the sides of the packaging; (iii) unclear images of information required; (iv) and products that were marked as 'product currently unavailable' on all the online stores selected during the whole data collection period.

2.2. Data Extraction

The complete images of all the sides of the pack were analysed and all information was extracted for each eligible product. For each item, the quali-quantitative and specifically regulated [23] information was collected: company name, brand name, descriptive name, energy (kcal/100 g), total fat (g/100 g), saturates (g/100 g), carbohydrate (g/100 g), sugars (g/100 g), protein (g/100 g), salt (g/100 g), and fibre (g/100 g). For the samples without indication of fibre content (since it is not mandatory according to Regulation n.1169/2011 [23]), this was calculated by subtracting the energy provided by each macronutrient (carbohydrates, protein and fats) from the total energy and dividing the resulting value by 2 kcal/g, which is the conversion factor for the calculation of energy as stated in the Regulation (EU) n. 1169/2011 [23]. All the ingredients reported in the "list of the ingredients" were extracted. Moreover, voluntary regulated declarations such as nutrition or health claims (NHC) as listed in the Regulation (EC) n.1924/2006 [27], gluten-free (GF) declarations (either 'specifically formulated for celiacs' or 'containing gluten') [28], and products declared as organic [29], were collected. The accuracy of the extracted data was double-checked by two researchers (MDA and DA), and inaccuracies were resolved through secondary extractions made by a third researcher (DM). A dataset was created with all the collected data, and items were sub-grouped for specific comparisons. By considering the descriptive name and the list of ingredients reported on the pack, items were labelled in detail as: (i) WG products when the product was defined as WG and all cereal-based ingredients in the list were defined as WG (e.g., "WG bread"); (ii) products partially formulated with WG ingredients (PWG), when one or more (but not all) cereal-based ingredients were WG (e.g., "breakfast cereals with WG wheat flakes") and (iii) refined products (RG), when none of the ingredients was wholegrain.

2.3. Statistical Analysis

Data distribution was assessed using the Kolmogorov-Smirnov test. Data are expressed as a percentage or reported as median (interquartile range) for nutritional values. Differences in terms of energy, macronutrients, fibre and salt contents per 100 g of products for each item among WG, PWG and RG were analysed with Kruskal–Wallis non-parametric one-way ANOVA for independent samples with multiple pairwise comparisons. A Principal Component analysis (PCA) with varimax rotation was performed in order to evaluate the inter-product nutritional variability of products in terms of energy, macronutrients, salt and fibre contents per 100 g. In particular, score plots were organized to highlight product characteristics, i.e., category and presence/absence of wholegrains. Statistical analyses were carried out using IBM SPSS Statistics® (Version 25.0, IBM corp., Chicago, IL, USA) and performed at $p < 0.05$ of significance level.

3. Results

3.1. Food Items Analysed

From a total of 3284 products initially retrieved, 244 products were excluded based on the exclusion criteria. In detail, among categories, "biscuits" was the one with the highest number of excluded products (18%), while in all other categories the % of exclusion ranged from 1 to 8%. As a result, a total of 3040 products were included in the analysis and grouped into the five different categories considered ("breakfast cereals", "biscuits", "sweet snacks", "bread", and "bread substitutes"). In Table 1, the number of items considered for each category of products, divided on the basis of the inclusion of WG (RG, PWG, WG), is reported. In all the categories, RG products prevailed on WG and PWG. WG products were more abundant than PWG in all categories, excepted for "breakfast cereals".

Table 1. Descriptive analysis of RG, PWG and WG products for each category.

WG Inclusion	Breakfast Cereals	Biscuits	Sweet Snacks	Bread	Bread Substitutes
RG (%)	289 (76%)	708 (89%)	478 (94%)	281 (83%)	843 (83%)
PWG (%)	62 (16%)	33 (4%)	11 (2%)	4 (1%)	51 (5%)
WG (%)	31 (8%)	57 (7%)	21 (4%)	52 (16%)	119 (12%)
Total	382	798	510	337	1013

RG: refined grain; PWG: partially produced with wholegrain; WG: wholegrain. Total is the sum of all the products in each category.

Both WG products and products formulated with PWG ingredients represent a limited part of the total considered products: 24% for "breakfast cereals", 17% "bread substitutes", 17% for "bread", 11% for "biscuits", and 6% for "sweet snacks". The categories with the highest % of WG products were "bread" (n = 52 out of 337), representing the 16% of products in this category, followed by "bread substitutes" (n = 120 out of 1016), representing the 12% of total samples. Conversely, the categories with the lowest number of WG items were "Sweet snacks" (n = 21 out of 510), corresponding to the 4% of the total category, "breakfast cereals", and "biscuits", with 31 and 57 items (8% and 7%), respectively.

For each category, the number of RG, PWG and WG products carrying at least one NHC, or boasting GF declarations, organic certification other than being brand or private label was calculated (Table 2). Among them, we found that few WG or PWG products carried specific declarations. In particular, a low number of products carried health claims in all categories, except the "breakfast cereals" category (14% and 34% of WG and PWG products, respectively). Moreover, few WG products displayed GF declarations in all categories and no one product belonged to the "sweet snacks" category; concerning this latter category, no organic PWG products were found. On the contrary, many WG or PWG products boasted a nutrition claim, with the highest percentage in the "breakfast cereals" category (87% WG products and 84% PWG products).

The number of products carrying nutrition claims concerning fibre ("source of fibre" corresponding to $\geq$3 g/100 g or "rich in fibre" corresponding to $\geq$6g/100 g), which can be related to WG inclusion, was analysed. Interestingly, the majority (i.e., >50% for all categories except for PWG "sweet snacks") but not all WG and PWG items carried these claims on the packaging. A further analysis was conducted to quantify the number of products without a claim concerning fibre that were potentially eligible for this declaration. About 62% of products in total showing a content of fibre higher than 3 g/100 g were found to be potentially eligible to make a fibre-related claim, without presenting this nutrition claim on the packaging.

Table 2. Number of products in each category in relation to regulated declarations reported on the packaging and brand of products.

		Breakfast Cereals			Biscuits			Sweet Snacks			Bread			Bread Substitutes		
WG Inclusion		**RG**	**PWG**	**WG**	**RG**	**PWG**	**WG**	**RG**	**PWG**	**WG**	**RG**	**PWG**	**WG**	**RG**	**PWG**	**WG**
Nutrition claim	No	101	10	4	549	14	21	415	7	6	219	1	24	607	19	39
	Yes	197	52	27	159	19	36	63	4	15	62	3	28	238	32	81
	%	66	84	87	22	58	63	13	36	71	22	75	54	28	63	68
Nutrition claim on fiber	No	167	20	12	627	15	25	460	7	7	225	1	25	730	24	43
	Yes	122	42	19	81	18	32	18	4	14	56	3	27	113	27	76
	%	42	68	61	11	55	56	4	36	67	20	75	52	13	53	64
Health claim	No	257	41	20	704	32	54	475	11	20	281	4	50	804	51	113
	Yes	41	21	11	4	1	3	3	0	1	0	0	2	41	0	7
	%	14	34	35	1	3	5	1	0	5	0	0	4	5	0	6
Organic	No	210	59	21	646	22	41	450	11	15	246	3	45	622	33	89
	Yes	88	3	10	62	11	16	28	0	6	35	1	7	223	18	31
	%	30	5	32	9	33	28	6	0	29	12	25	13	26	35	26
Gluten free	No	269	62	30	661	32	56	446	9	21	251	3	50	684	35	115
	Yes	29	0	1	47	1	1	32	2	0	30	1	2	161	16	5
	%	10	0	3	7	3	2	7	18	0	11	25	4	19	31	4
Branded	No	139	35	13	276	10	20	220	5	9	117	1	23	316	21	50
	Yes	159	27	18	432	23	37	258	6	12	164	3	29	529	30	70
	%	53	44	58	61	70	65	54	55	57	58	75	56	63	59	58

RG: refined grain; PWG: partially produced with wholegrain; WG: wholegrain. %: percentage of product with the declaration (yes) or branded.

3.2. Nutritional Composition of WG, PWG, RG Products for Each Category

Considering the nutrition facts reported on the pack, differences among RG, PWG and WG products within each category were analysed (Table 3). PWG and WG products had a similar ($p > 0.05$) energy content for "Biscuits", "Bread", "Bread substitutes", and "Sweet snacks". Particularly, the latter was the only category in which WG and PWG products did not differ either from each other or from RG products. On the contrary, WG "Breakfast cereals" presented lower energy compared to RG and PWG products, which resulted in them being not significantly different each other. For total and saturated fats, differences among RG, WG and PWG were not consistent among categories. "Biscuits" and "Bread substitutes" were the only categories showing a lower fat content for WG products than RG, despite that for "bread substitutes" a similar fat content was found for WG and PWG items. Total carbohydrate content was similar for WG and PWG products in the "biscuits", "sweet snacks" and "bread" categories, while WG "bread substitutes" presented a lower carbohydrate content compared to both PWG and RG products. The protein content was higher in WG products for "breakfast cereals" and "bread substitutes" than in PWG and RG products, while for "biscuits", "bread" and "Sweet snacks" categories a similar content of protein for WG and PWG was found ($p > 0.05$). The salt content was lower for RG "breakfast cereals", "biscuits" and "sweet snacks" compared to the respective WG-containing products. Instead, the salt content was similar for RG, PWG, WG "bread", and among "bread substitutes" was the highest in RG items and the lowest in the PWG ones ($p < 0.05$). The fibre content was similar among PWG and WG products, and higher with respect to the RG ones ($p < 0.05$) in most categories. The only exceptions were registered for "breakfast cereals" in which PWG products presented a similar fibre content to RG, and for "bread substitutes" in which PWG was lower in fibre than WG but higher than RG products.

Table 3. Comparison of nutritional composition within each category of product analysed in relation to WG inclusion.

Category		Energy kcal/100 g	Fats: Total g/100 g	Fats: Saturated g/100 g	Carbohydrates: Total g/100 g	Carbohydrates: Sugars g/100 g	Fibre g/100 g	Protein g/100 g	Salt g/100 g
Breakfast cereals	RG	385 (371–425) a	5.1 (2.5–14.0)	1.3 (0.5–3.4)	69.0 (61.0–80.0)	20.0 (7.0–26.6)	5.6 (3.6–8.2) b	8.0 (7.0–10.0) b	0.4 (0.1–0.8) b
	PWG	388 (379–406) a	5.8 (1.8–10.1)	2.2 (0.5–3.8)	74.5 (64.0–79.0)	19.0 (15.0–24.1)	5.5 (4.2–8.0) b	8.6 (7.0–9.5) b	0.6 (0.3–0.9) a
	WG	374 (367–385) b	2.9 (2.1–7.4)	0.8 (0.5–1.8)	68.0 (62.1–74.8)	16.0 (2.5–22.3)	7.4 (5.8–10.0) a	9.4 (8.4–13.0) a	0.7 (0.2–0.8) ab
Biscuits	RG	473 (451–493) a	19.0 (15.7–22.4) a	5.8 (2.4–11.0) a	67.0 (62.7–71.) a	24.0 (21.0–29.0) a	2.7 (2–3.5) b	7.2 (6.3–7.9) b	0.5 (0.3–0.7) b
	PWG	463 (445–473) b	18.0 (16.0–19.5) a	4.3 (2.2–6.7) ab	63.0 (61.4–67.) b	23.3 (19.0–26.0) b	6.0 (4.3–6.7) a	7.6 (7.5–8.8) a	0.6 (0.5–0.7) a
	WG	453 (445–467) b	17.0 (16.0–19.5) b	2.4 (1.9–4.4) b	64.0 (61.4–66.0) b	19.2 (18.0–24.0) c	6.7 (5.7–8.2) a	8.3 (7.7–9.0) a	0.6 (0.5–0.7) a
Sweet snacks	RG	408 (388–427)	18.7 (15.0–21.4)	6.8 (3.8–9.9)	53.3 (50.5–57.0) a	28.3 (22.0–34.0) a	1.8 (1.4–2.5) b	6.2 (5.5–7.1) b	0.5 (0.4–0.7) b
	PWG	410 (395–414)	19.0 (18.0–20.2)	3.5 (2.8–8.2)	49.0 (45.0–50.3) b	27.0 (24.0–29.0) a	3.4 (2.6–3.6) a	8.0 (5.2–10.4) a	0.7 (0.3–0.9) a
	WG	405 (378–429)	17.7 (15.0–21.0)	6.1 (2.9–8.9)	47.0 (46.0–50.0) b	19.7 (14.8–25.8) b	4.1 (3.5–6.0) a	8.3 (6.8–8.6) a	0.7 (0.5–0.7) a
Bread	RG	276 (259–290) a	4.5 (3.5–5.7) a	0.7 (0.5–1.0) a	48.6 (45.2–51.0) a	4.6 (3.2–6.2) a	3.0 (2.6–4.10) b	8.5 (7.9–9.5)	1.3 (1.1–1.4)
	PWG	228 (208–289) b	1.9 (1.5–2.7) b	0.5 (0.3–0.9) ab	40.5 (38.5–53.5) ab	1.6 (1.2–1.8) b	5.5 (4.8–6.6) a	7.6 (6.4–10.2)	1.2 (1.0–1.7)
	WG	259 (243–268) b	4.3 (2.0–5.2) a	0.6 (0.4–0.8) b	42.0 (40.3–44.3) b	4.0 (3.0–5.3) a	6.3 (5.0–7.9) a	8.8 (8.1–9.6)	1.3 (1.1–1.4)
Bread substitutes	RG	417 (380–443) a	10.3 (6.6–14.5) a	1.7 (1.0–3.0) a	68.0 (62.5–73.0) a	1.9 (1.1–3.0) b	3.1 (2.3–4.0) c	10.0 (8.0–11.7) b	1.8 (1.0–2.2) a
	PWG	393 (383–424) b	7.0 (3.3–10.1) b	1.0 (0.6–1.7) b	70.0 (66.0–74.5) a	2.0 (0.7–6.5) ab	6.0 (3.8–6.9) b	11.0 (8.2–12.0) b	1.4 (0.5–1.7) c
	WG	393 (376–413) b	8.0 (5.8–10.3) b	1.1 (0.8–1.6) b	64.2 (61.0–68.0) b	2.0 (1.5–4.0) a	7.5 (6–10.0) a	11.4 (10.0–13.0) a	1.5 (1.2–2.0) b

Values are expressed as median (25th–75th percentile). For each category, different letters in the same column indicate significant differences among RG, PWG, and WG (Kruskal–Wallis non-parametric one-way ANOVA for independent samples with multiple pairwise comparisons), $p < 0.05$. RG: refined grain; PWG: partially produced with wholegrain; WG: wholegrain.

3.3. Inter-Product Variability of the Nutritional Composition of Products in Analysed Categories

The variability in the nutritional composition of the considered products was deepened by means of a PCA, as shown in Figure 1. On the whole, the PCA explained 72.7% of the total variability, but with the need for three main PCs. PC1, describing the 31.8% of the total variability, was positively loaded by energy, total and saturated fats and sugars, while PC2—24.3% of the variability, was positively loaded by protein, fibre and salt. Lastly, PC3—16.6% of the variability—was positively loaded by total carbohydrates, energy and sugars, while negatively loaded by total fats and saturates (Figure 1A,D,G). Concerning the product variability (Figure 1B,E,H) some categories may be defined on the basis of their nutritional content: bread substitutes were mainly described by high energy, total carbohydrate and salt contents, while sweet snacks were high in total fat, saturates, and sugars. When the presence of wholegrains in the product was taken into account, it was not possible to cluster RG products from those presenting wholegrains in terms of nutritional profile. Again, no grouping was demonstrated between the PWG and WG types of products in terms of energy, nutrients, fibre or salt (Figure 1C,F,I).

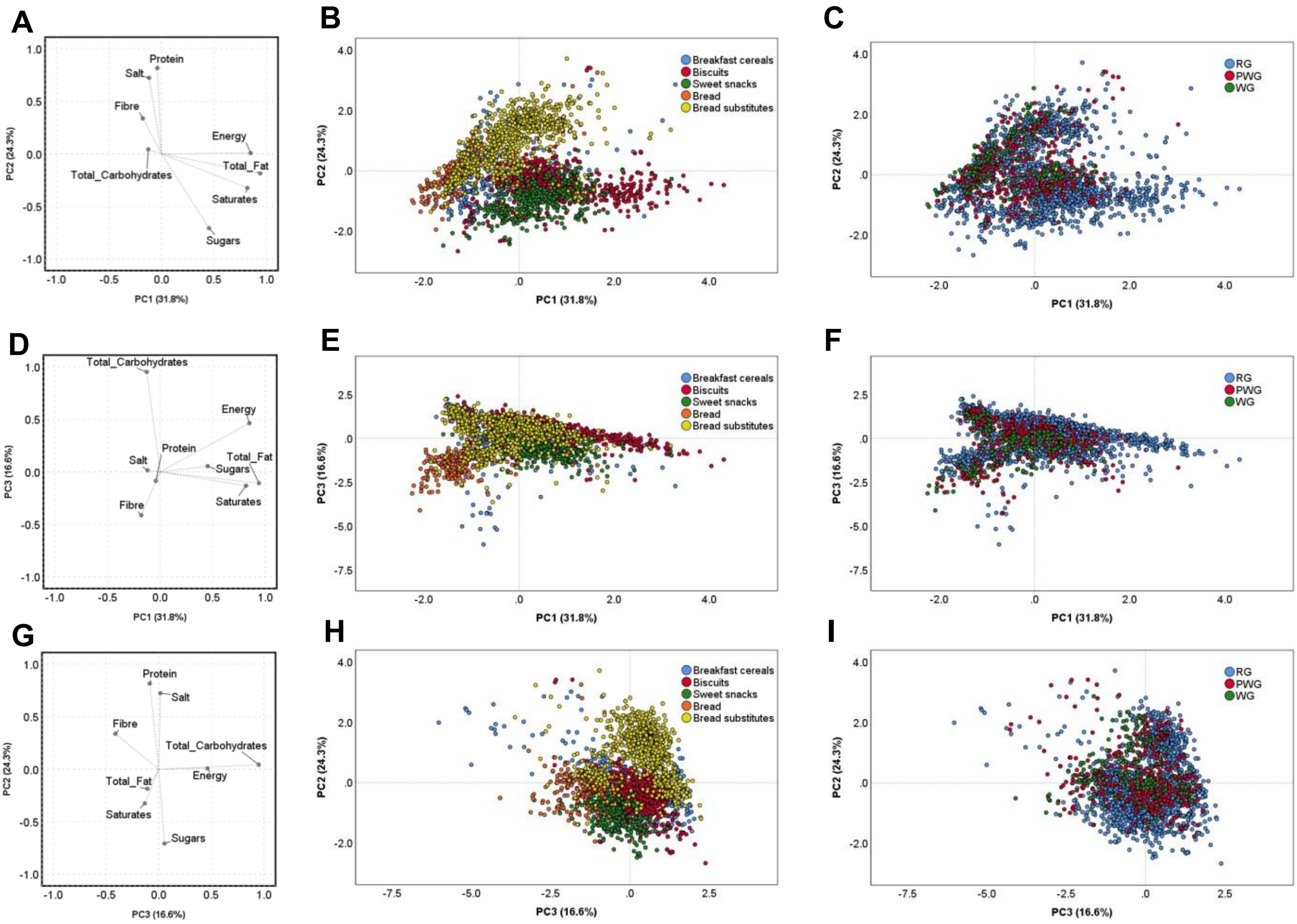

Figure 1. Principal component analysis (PCA) describing the inter-product variability based on the nutritional composition. Loading plots of PC1 versus PC2 (**A**), PC 1 vs. PC3 (**D**), PC3 vs. PC2 (**G**) are showed by considering energy (kcal/100 g), total fat (g/100 g), saturates (g/100 g), carbohydrate (g/100 g), sugars (g/100 g), protein (g/100 g), salt (g/100 g), and fibre (/100 g). Score plots of the nutrient composition of items are shown by considering the categories of products (**B**,**E**,**H**) and the classification by WG presence (RG, PWG, WG) (**C**,**F**,**I**). RG: refined grain; PWG: partially produced with wholegrain; WG: wholegrain.

4. Discussion

To the best of our knowledge, this is the first survey focusing on prepacked wholegrain cereal-based products sold on the Italian market by dividing items into wholegrains, with at least one wholegrain ingredient (partially produced with wholegrains), and refined products. In particular, this study gives an overview of the characteristics and nutritional composition of more than three thousand products from several food categories, such as “breakfast cereals”, “biscuits”, “sweet snacks”, “bread”, and “bread substitutes”, as well as to the mandatory and voluntary information reported on the packaging of products.

Overall, and as expected, the main load of prepacked products considered in this survey was prepared with refined cereals (in the range 76–94% corresponding to “breakfast cereals” and “sweet snacks”, respectively). These data reflect the scarce demand and in turn the low consumption of WG-formulated products by Italian consumers, as previously reported [30]. In fact, data from the Italian Nutrition and Health Survey carried out between 2010 and 2013 described a regular consumption of WG products (more than once per week) in only 26.7% of adults, with bread representing one of the main sources of WG for the Italian population [30]. In the present survey, the “Bread” category presented the highest number of products prepared with 100% WG cereals (16%), even though this percentage described well the low presence of WG products on the shelf, which should be increased to promote the consumption of wholegrain products. Many strategies for promoting WG intake have been proposed, such as to increase the availability of WG products on the market, to ameliorate sensory properties, to reduce product costs, to gradually increase the “exposure” of consumers to these products, and finally to improve labelling for a clear identification of WG products [31]. As already mentioned, it is noteworthy that, despite the ascertained health benefits [5,19], the consumption of WG products is still lower than recommended. In 2010, the Global Dietary Database examined the wholegrain intake in 28 EU countries [32]. Considering the adult populations, the mean wholegrain intake in Italy was 11 g/day for both males and females, in Germany it was ~120 g/day and in France it was 36 g/day for both males and females. In Italy, in particular, the percentage of WG consumers from 2010–2013 appears to be quite low and still below that recorded in other countries of Europe, where consumption is frequently over 50% [30]. Interestingly, one of the main causes could be the scarce knowledge of WG products’ healthy benefits. Among adults, a greater consumption of WG was associated with a higher educational level and healthier lifestyle, including physical activity and the avoidance of smoking, while eating-related behaviours such as eating out of the home were inversely associated with wholegrain intake [30].

In this study, we compared the nutritional declaration of RG, PWG, and WG products for a better understanding of whether the WG presence in product formulation, as an exclusive source of cereals or as one of the product ingredients, can be a marker of product quality. In fact, it is important to reiterate that the lack of a shared legal definition of the WG product leads to a heterogeneous scenario in which WG products can strongly differ in their product formulation and nutritional characteristics. Therefore, in Italy and in Europe, due to a lack of regulation on the percentage of WG cereal that has to be included for the “claimed” WG product, it is interesting to comprehend whether nutritional characteristics of products only partially formulated with WG ingredients may have a nutritional profile similar to that of 100% WG products. By comparing the nutritional characteristics, WG-formulated products (both WG and PWG) presented differences and similarities that were not consistent among categories. In general, as expected the fibre content was the lowest in RG products but did not differ between PWG and WG, except for “breakfast cereals” and “bread substitutes”, in which PWG products contain less fibre than their WG counterpart. Interestingly, not all WG and PWG products presented a fibre content sufficient for bearing a fibre claim on the package. Energy, macronutrients and salt varied across WG, PWG and RG products depending on the category. For instance, WG and PWG “sweet snacks” and “biscuits” presented a similar nutritional profile, except for simple sugars, which were lower only in WG products. Interestingly, the salt content, whose consumption represents an urgent nutritional issue in Italy [33] and worldwide [34], proved to be higher in both PWG and WG sweet products (i.e., breakfast cereals", "sweet snacks" and "biscuits") than their RG counterparts. Bitterness is one of the key sensory attributes known to restrict the use of products containing WG. Several approaches have been proposed to mask the bitter taste in WG products, and one of them is the addition of salt [35]. Bakke et al. [36] successfully demonstrated that the bitterness of three green vegetables was reduced by adding salt without changing other attributes such as aroma or texture. This finding highlights even more the need to pay attention to the whole nutrition characteristics of products.

The present study showed that, likely due to the lack of a non-binding definition, WG products cannot be considered a marker of product quality a priori, but it is necessary to take into account the overall nutritional quality of products, especially for some product categories. Similar results have been recently underlined within the same project (FLIP project) in which the authors also stated that fibre-related nutrition claims, which can in some cases also be related to WG products, should not be considered as a marker of a better nutritional profile for breakfast cereals [37]. Other studies from the same project already highlighted the need to consider the global quality of the products instead of declarations about the general characteristics of products which may be misleading [24,26,38].

To help consumers in clearly identifying WG products, it would be desirable to reach a clear definition of WG products that is shared by the scientific community worldwide. In our opinion, cereal-based WG products should be produced only with WG ingredients, as is done in the WG category considered in this survey, and they should contain a relevant amount of WG ingredients in the products as recently proposed [39]. This would avoid providing misleading information to consumers and will likely promote WG consumption and in turn increase fiber intake.

This study clearly demonstrated that the nutritional profile of PWG and WG is strictly dependent on the category of product. In fact, PWG products generally showed similar characteristics to their 100% WG counterparts, but there are some cases where PWG were more similar to refined products. Certainly, due to a lack of a clear WG product definition at the national level, it is difficult to investigate the best criterion for classifying and fixing the standard of quality of WG products. As a consequence, it is challenging to promote WG product consumption through correct and regulated declarations on the packaging and therefore to correctly help consumers during a purchase. Previously, other authors underlined the need to find the best criteria for WG product classification and for supporting consumers in identifying the WG products with the best nutritional characteristics during purchase [40]. This issue is even more pronounced for products formulated with one or more, but not all, WG cereals, which can be perceived by consumers as being as healthy as 100% WG cereal-based products even if presenting a nutritional characteristic more similar to refined products. This phenomenon is well described as the "halo effect" [41], which induces consumers to "assign" to foods a healthy value in relation to their characteristics reported on the packaging. Certainly, labelling foods as "wholegrain" may be the right way to promote the consumption of WG products among consumers and to increase the overall quality of the diet. In this regard, Marinangeli et al. highlighted that labelling WG is one of the multiple opportunities to use labelling to promote the consumption of quality carbohydrate-rich foods, together with focusing on the low glycaemic index and glycaemic response claims or boasting dietary fibre nutrient content claims and associated dietary fibre-based health claims [42]. Thus, initiatives aimed at helping consumers in reading and understanding information reported on the food labeling would be useful to help them in making conscious food choices, which is also related to the selection of WG products.

An additional tool to promote WG consumption is through international and national dietary guidelines. As already pointed out, dietary guidelines include a variety of starchy foods in wholegrain form [2] and only a few countries in the European Union have adopted a quantitative recommendation on wholegrain intake. The Italian Dietary Guidelines for Healthy Eating suggests a preference for foods naturally rich in dietary fibre, such as whole cereals, pulses, fruit and vegetables, without establishing a specific quantitative indication for the consumption of WG products [43], which could help in reaching the daily reference intake for fibre of 12.6–16.7 g/1000 kcal for adults and 8.4 g/1000 kcal in childhood, and the suggested dietary target for pathology prevention fixed at 25 g/day of fibre [44].

The present study has several strengths and limitations worthy of mention. Among the former, this is the first study investigating the characteristics and the nutrition facts of a wide large of WG and not WG products currently on the market, including almost all categories of cereal-based products. Secondly, by collecting information on the food labelling, we were able to simultaneously focus on the nutrition declaration but also on other aspects (i.e., brand, NHC, organic and gluten-free declaration) which may be of interest for the consumers. Among limitations, it is noteworthy that the information reported on the pack does not allow, for instance, for the inclusion of some nutrients not mandatory in the nutrition declaration, such as micronutrients, which may be higher in WG compared to not WG products. Moreover, it was not possible to take into account other characteristics of products, such as the quality of the starting ingredients, which may be rich, for instance, in other components not accounted for in the nutritional declaration, but potentially abundant in WG products (e.g., bioactive compounds). Lastly, although a large part of the products have been collected through the home shopping websites of the major retailers, not all food items present on the market have likely been evaluated. Finally, since a barrier to WG product purchase can be the price, it would be interesting to investigate, in the future, differences among the cost of WG, PWG and RG products.

5. Conclusions

The results of the present study suggest that wholegrain products included in this survey have only limited beneficial nutritional characteristics than refined products, mainly in terms of fibre content and, only in some cases, to products partially formulated with wholegrain ingredients.

These data certainly support the lack of a need to consider a WG "declaration" on the pack as a synonym of a healthy product without taking into account the general quality of the products. Moreover, data highlight the need of introducing a legal definition of "wholegrain" that will avoid the current heterogeneity of products on the market, which also causes misunderstanding among consumers. This would promote a clear and regulated WG product formulation and labelling.

Reaching this goal would be useful to the food industry for reformulating food products with the purpose of improving the nutrition profile. Likewise, this will also be beneficial for consumers, who would be able to more easily identify WG products on the shelf. In turn, this will likely lead to increased consumption of these products and the reaching of dietary guideline goals that may positively influence dietary intake and human health.

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Consumer Choices in the Pasta Market: The Importance of Fiber in Consumer Decisions

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Abstract: The aim of the current study was two-fold: (1) to identify consumer segments based on pasta selection motives and (2) to examine the differences between the identified segments in terms of perception of pasta and pasta with added fiber and information on the food label. The data were collected using a CAPI (computer-assisted personal interview) survey on a sample of 1013 consumers. The k-means clustering method was used to identify four clusters of consumers, namely, quality-oriented, sensory-oriented, convenience-oriented, and neutral consumers. The quality-oriented group was the group that expressed the most positive opinions about the pasta and about the addition of fiber to pasta. Moreover, they appreciated the information placed on the pasta label the most. Consumers in the sensory-oriented segment were the least likely to agree that the addition of fiber to pasta deteriorated its taste and to agree that it looked worse compared to pasta without fiber. These findings are of significance for those involved in the public nutrition sector as well as for those responsible for preparing well-targeted marketing messages. The conclusions may constitute invaluable insights for those devising educational initiatives and campaigns.

Keywords: consumer choices; fiber; pasta; pasta with added fiber

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1. Introduction

Today's customers have limited time to prepare meals and, thus, convenience food is sought after [1]. At the same time, a growing interest in a healthy diet has been observed [2,3]. Consequently, consumers' perceptions and purchasing behaviors are influenced by their health awareness [4].

Dietary fiber is a promising food ingredient with health benefits [5]. Moreover, dietary fiber is involved in disease prevention and enhances the health of consumers [6]. Epidemiological and short-term interventional studies emphasize the association between a higher fiber intake and improvements in the lipid profile as well as fasting and postprandial glycemic control. Some fractions of fiber are more effective, e.g., for the management of diabetes, obesity, dyslipidemia, and hypertension [7]. However, the current intake of fiber is still far below the recommended level in most nations worldwide [8]. Although the consumption of wholegrain foods has been encouraged due to the association between whole grains and health benefits, changes in the technological parameters and sensory attributes may limit the consumption of these products [9].

Consumers' preferred staple foods, such as bread and pasta, as base products for modification [10]. Fresh noodles enriched with fiber-rich fractions contribute to food convenience due to improved nutritional quality, reduced cooking time, and acceptable cooking quality [11]. A product with a changed composition is in greater demand if there is an acceptance of the product as a carrier of the added ingredient [12]. Therefore, the motives for selecting pasta as a food product that is convenient to use may be crucial in assessing the acceptance of a product with a modified composition, i.e., pasta with added fiber. Adding various sources of fiber to pasta can result in lowering calorie intake by manipulating starch degradation [6,13]. Moreover, product modifications can worsen its physical, chemical, and sensory properties and these properties are vital for consumers' acceptance [14,15]. Consequently, in recent years, dietary fiber has been used in improving pasta [16–21].

The food industry aimed to enhance the overall nutritional balance of carbohydrate-rich foods by raising their dietary fiber content at the cost of readily digestible carbohydrates. Moreover, the food industry can use the physicochemical properties of fiber to enhance some properties of their products, such as viscosity, texture, sensory characteristics, and shelf-life [6]. Furthermore, fiber-enriched pasta could be produced by increasing the content of dietary fiber by several percent in a regular semolina-based pasta formulation, leading to acceptable products with matching characteristics of texture and color compared to commercial products [22]. Thus, both consumers and the food industry may benefit from enriching cereal products with dietary fiber components [23,24].

Thus, the aim of the current study was two-fold: (1) to identify consumer segments based on pasta selection motives and (2) to examine differences between the identified segments in terms of the perception of pasta and pasta with added fiber, and information on the food label.

2. Materials and Methods

2.1. Data Collection Process

The sample used in the study (N = 1013) was obtained through a cross-sectional quantitative survey, being part of a Bioproduct project. The following paper discusses selected findings from a larger study [25,26]. The sample was selected using the following criteria: the representativeness of the population of Poland according to voivodship and the quota character by gender, education, and place of residence. All subjects of the study were 21+. Only those respondents who met other recruitment criteria, i.e., made their own or cooperative food purchase, participated in the study. A professional market research agency was used to conduct interviews with respondents. The interviews were performed on a face-to-face basis at respondents' homes. Moreover, the ESOMAR (European Society for Opinion and Marketing Research) code of conduct was respected and the CAPI (computer-assisted personal interview) technique was employed.

2.2. Description of Questionnaire

The questionnaire in the study comprised a few main sections and discussed issues, such as: (A) the importance of pasta selection motives ("How important are the following factors for you when purchasing pasta?", where 1 = not important at all and 5 = very important) (items are presented in Table 1) as well as (B) the lifestyle self-assessment ("How do you assess yourself in terms of your lifestyle?", where 1 = I totally disagree and 5 = I totally agree) (statements are presented in Table 4). In order to evaluate (C) the consumers' opinion regarding pasta, and the importance of food information, including the significance of information on the pasta label, the following questions were asked: "To what extent do you agree with the following statements on pasta?", "To what extent do you agree with the following statements?", where 1 = I totally disagree and 5 = I totally agree; and "How important is the following information on the pasta label for you?", where 1 = not important and 5 = very important (statements are presented in Tables 5 and 6). Finally, in order to identify opinions on cereal products with added fiber and opinions on pasta with added fiber compared to the same pasta without added fiber, the questions were worded as follows: "To what extent do you agree with the following statements about grain products with added fiber?" and "Please compare pasta with added fiber to the same pasta without fiber", where 1 = I totally disagree and 5 = I totally agree (items are presented in Tables 7 and 8).

2.3. Statistical Analysis

Analysis of the statements' reliability in a question regarding the motives for pasta choice was performed using the Cronbach coefficient alpha. The value of the Cronbach coefficient alpha = 0.908 confirmed the right choice of questions for factor analysis (FA). The factors obtained via the FA explained 59.6% of the total variation. Particular factors were qualified based on the minimum value of factor loadings determined at 0.5, with the factor adequate for the requirements of factor analysis as studied by the Kaiser-Mayer-Olkin measure (KMO). The KMO value, indicating collective correlation of variables, was 0.922, which clearly validated the rationale behind employing the variable reduction method. Table 1 presents the identified factors that were used for cluster analysis.

Table 1. Factor analysis (FA) referring to consumers' use of pasta selection motives; varimax rotated factor loadings percentage of explained variance (N = 1013, Poland).

Pasta Selection Motives	Factor 1 The Sensory Motives and Availability	Factor 2 The Marketing Motives	Factor 3 The Convenience and Familiarity
Taste	0.774	.	.
Use-by date/shelf life	0.718	.	.
General appearance	0.701	.	.
Personal or family preference	0.671	.	.
Price	0.626	.	.
Availability	0.606	.	.
Color	0.518		
Quality label	.	0.748	.
Place of purchase	.	0.748	.
Seller's opinion	.	0.724	.
Nutritional value	.	0.675	.
Manufacturer/brand	.	0.63	.
Shorter cooking time	.	.	0.806
Knowledge of the product	.	.	0.703
Information on the packaging	.	.	0.617
Package size	.	.	0.593
The variance explained/% explained variance	41.8	11.9	5.9

Consumers were divided into segments in a two-stage process. The first stage consisted in performing a cluster analysis using hierarchical methods. The second stage included a cluster analysis based on non-hierarchical method k-means with initial cluster seeds, which emerged using the hierarchical method. Four well-separated clusters were achieved (Table 2).

Moreover, the mean values of opinions between pairs of clusters were compared by means of a post-hoc test (Waller-Duncan k-ratio t-test). Taking the motives for choosing pasta into account, consumers in segment No. 1 valued sensory motives and availability most. In the case of segment No. 2, the most important were the sensory motives and availability, and the least importance compared to other segments was attached to the convenience and familiarity. For the consumers in segment No. 3, the most important were the convenience and familiarity and the marketing motives were the least important. In the case of segment No. 4, the marketing motives were rated lower than in the case of segment No. 1, whereas the least importance was attached to the sensory motives and availability.

Table 2. Characteristics of the identified segments according to the motives of pasta selection; the mean ratings of the segments on the classification variables.

Pasta Selection Motives	Segment 1	Segment 2	Segment 3	Segment 4	*p*-Value
The Sensory Motives and Availability	3.84 [b]	4.29 [a]	2.97 [c]	1.55 [d]	<0.0001
The Marketing Motives	4.40 [a]	2.45[c]	1.68 [d]	3.20 [b]	<0.0001
The Convenience and Familiarity	4.05 [b]	1.58 [d]	4.46 [a]	2.22 [c]	<0.0001

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

The statistical analysis was carried out using the SAS 9.4 statistical package (SAS Institute, Cary, NC, USA).

3. Results

3.1. Description of the Sample and Clusters

As previously indicated, the non-hierarchical k-means clustering method led to the identification of four clusters: Quality-oriented (cluster 1), sensory-oriented (cluster 2), convenience-oriented (cluster 3), and neutral (cluster 4) clusters. Socio-demographic variables, such as gender, age, education, size of the place of residence, and subjective assessment of the financial situation, were used to profile the clusters (Table 3). However, variables, such as gender and age, did not significantly influence the profile of the clusters. The independence χ^2 test was used to assess the diversity of profile features between clusters. The characteristics of the study sample are shown in Table 3.

Segment No. 1 (quality-oriented; N = 245; 24.2%) comprised more than 1/3 people with secondary education (35.51%), and every 5th respondent surveyed had higher education (20.41%), which is slightly less than in segment No. 2. In total, 40.0% of the respondents in segment No. 1 declared rural areas as their place of residence, and 15.1% of people also resided in a city of more than 500,000 inhabitants, which is the highest percentage compared to the other segments. Taking income into consideration indicates that more than half of the surveyed respondents (53.47%) reported that they can afford some but not all of their expenses, and 1/4 reported that (26.53%) income allows them to meet only basic needs.

In segment No. 2 (sensory-oriented; N = 221; 21.8%), more than 1/3 of the surveyed (36.2%) were respondents with secondary education and more than 1/4 of the surveyed (26.2%) were respondents with higher education. It should be noted that this represented the largest percentage compared to the other segments. Taking into account the place of residence indicated that, as in the case of segment No. 4 (described later), almost 4/5 of the respondents lived in rural areas (38.5%) and 1/4 (24.0%) lived in a town of less than 50,000 inhabitants. Only every 10th respondent (10.4%) declared that they live in a city with a population between 101,000 and 300,000, which is the lowest percentage compared to the other segments. Taking into account the subjective assessment of the financial situation, it was indicated that half of the surveyed individuals (52.0%) declared that they could afford some but not all expenses, and 18.6% stated that their income allowed them to meet only basic needs, while a similar percentage (19.0%) of the surveyed individuals claimed that they could afford everything, and in this category of assessment, this group of respondents was the most numerous in comparison with the other segments.

Table 3. Socio-demographic characteristics of the consumers surveyed (N = 1013, Poland).

Variables	Total Sample	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	p-Value
Sex						0.7759
female	53.4	55.5	54.8	52.3	51.7	
male	46.6	44.5	45.2	47.7	48.3	
Age						0.1902
up to 30 years	20.9	19.2	22.1	21.3	21.2	
31–40 years	17.9	21.2	22.6	16.3	13.3	
41–50 years	16.0	15.5	10.9	17.1	19.0	
51–60 years	18.9	18.8	19.5	17.1	19.9	
over 60 years	26.3	25.3	24.9	28.2	26.6	
Education						0.0001
elementary	6.1	6.5	3.2	3.2	9.7	
vocational	29.4	25.7	26.2	27.8	35.4	
secondary	36.5	35.5	36.2	42.6	33.5	
Bachelor's Engineer	9.5	11.8	8.2	11.1	7.5	
Higher	18.5	20.5	26.2	15.3	13.9	
Place of residence						<0.0001
village	38.4	40.0	38.5	36.5	38.4	
Town below 50,000	16.3	10.2	24.0	7.4	21.5	
Town from 50,000 to 100,000	13.9	9.4	15.4	13.9	16.3	
City from 101,000 to 300,000	18.7	17.5	10.4	29.2	18.1	
City from 301,000 to 500,000	5.8	7.8	3.6	9.3	3.6	
City over 500,000	6.9	15.1	8.1	3.7	2.1	
Opinion on family income						<0.0001
Is not sufficient at all	5.7	4.5	6.8	4.6	6.7	
Enables to meet only basic needs	26.8	26.5	18.6	24.1	34.1	
We can afford some, but not all expenses	53.5	53.5	52.0	64.3	47.4	
We can afford everything	11.1	12.2	19.0	5.1	9.1	
We can afford everything, and in addition we can put some money aside	2.9	3.3	3.6	1.9	2.7	

χ^2 test of independence, p-value < 0.05—differences between groups are significant.

In segment No. 3 (convenience-oriented; N = 216; 21.3%), more than 2/5 of the respondents (42.59%) declared secondary education. Consideration of place of residence indicated that more than one-third (36.57%) were rural residents and almost one-third (29.17%) lived in a city of 101,000 to 300,000 residents. This segment was dominated by people assessing their income as allowing them to meet some but not all of their expenses (64.35%).

In segment No. 4 (neutral; N = 331; 32.7%), individuals with secondary education and vocational education comprised approximately 70% of respondents in this segment (35.4% and 33.5%, respectively). Almost 40% of the respondents were residents of rural areas (38.4%), every 5th respondent declared that they live in a town of less than 50,000 residents (21.5%), and a much smaller percentage of respondents declared a city of 101,000 to 300,000 residents as their place of residence (18.1%). The subjective assessment of the financial situation indicated that almost half of the individuals surveyed (47.4%) said they could afford some but not all of their expenses, and more than a third (34.1%) said their family income allowed them to meet only basic needs.

To sum up, the socio-demographic characteristics indicated that in the quality-oriented and sensory-oriented segments, there were more individuals with higher (the sum of bachelor's and higher) education than in the other segments, and in the convenience-oriented segment, there were more individuals with secondary education. One-third of the convenience-oriented segment were inhabitants of cities of 100,000–300,000, whereas in the sensory-oriented and neutral segments, the majority of respondents lived in villages and towns of up to 50,000 inhabitants (the sum of villages and towns of up to 50,000 inhabitants—about 60%). Consumers in the quality-oriented segment and the sensory-oriented segment rated their financial situation as the best one.

Table 4 shows the self-assessment of lifestyle in the study group. Consumers in the quality-oriented segment perceived themselves mainly as caring for their own health, paying great attention to the naturalness of food, physically active, and with high ecological awareness to a greater extent compared to the other segments. The sensory-oriented segment reported high levels of agreement with most of the lifestyle statements; however, statements describing their lifestyle as physically active and with high ecological awareness reported lower levels of agreement compared to both quality-oriented and convenience-oriented consumers.

Table 4. Description of segments based on the self-assessed lifestyle of the surveyed.

Statements	Mean	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	*p*-Value
Family-oriented	4.05	4.39 [a]	4.19 [b]	4.31 [ab]	3.53 [c]	<0.0001
Valuing tradition	3.96	4.34 [a]	3.90 [b]	4.21 [a]	3.54 [c]	<0.0001
Caring for their own health	3.82	4.06 [a]	3.90 [b]	3.82 [b]	3.58 [c]	<0.0001
Involved in professional work	3.57	3.91 [a]	3.66 [b]	3.73 [ab]	3.14 [c]	<0.0001
Attaching great importance to the naturalness of food	3.57	4.07 [a]	3.55 [b]	3.66 [b]	3.13 [c]	<0.0001
Physically active	3.57	3.91 [a]	3.45 [c]	3.74 [b]	3.27 [d]	<0.0001
Highly concerned about environment	3.37	3.81 [a]	3.21 [c]	3.49 [b]	3.05 [d]	<0.0001

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

The convenience-oriented segment, like the sensory-oriented segment, achieved high levels of agreement with most of the statements describing lifestyles, while in the case of the statements about being family oriented and involved in professional work, the level of agreement did not differ from the segment that included quality-oriented and sensory-oriented consumers.

Respondents from the neutral segment were least likely to agree with most of the proposed lifestyle statements compared to the other segments.

3.2. Opinions on Pasta and Information on the Food Label

In Table 5, respondents' opinions on pasta are presented. Respondents in the quality-oriented segment largely agreed with most statements related to general opinions about pasta and food label information. Only for the statement "the taste of pasta is more important to me than its health benefits" did respondents indicate equal agreement compared to those in the sensory-oriented and convenience-oriented segments.

Table 5. Profile of segments according to statements on pasta and information on food labels.

Statements	Mean	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	*p*-Value
Information on product packaging is very important to me	3.52	3.86 [a]	3.26 [c]	3.67 [b]	3.32 [c]	<0.0001
I compare information on product labels before I decide which product to choose	3.35	3.72 [a]	3.21 [b]	3.27 [b]	3.22 [b]	<0.0001
I compare labels to choose products with the highest nutritional value	3.28	3.65 [a]	3.15 [cb]	3.05 [c]	3.22 [b]	<0.0001
I purchase more expensive pasta, because I think that the price goes along with the quality	3.36	3.9 [a]	3.19 [b]	3.25 [b]	3.12 [b]	<0.0001
In order to improve the health-promoting benefits, fiber can be added to the pasta	3.34	3.69 [a]	3.31 [b]	3.38 [b]	3.08 [c]	<0.0001
The taste of pasta is more important to me than its health-promoting benefits	3.21	3.30 [ab]	3.14 [bc]	3.35 [a]	3.09 [c]	0.004
It is vital to consume enough pasta	2.97	2.97 [ab]	2.86 [b]	2.87 [b]	3.09 [a]	0.004

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

With respect to agreement with two statements, i.e., (1) In order to improve the health-promoting benefits, fiber can be added to the pasta and (2) it is important to consume enough pasta, the level of agreement was similar in sensory-oriented and convenience-oriented segments. Additionally, regarding the statement "Information on product packaging is very important to me", respondents from the sensory-oriented and neutral segments had the same lowest level of agreement compared to the other segments.

Segment No. 3 with convenience-oriented consumers reported a high level of agreement (i.e., not much lower than segment No. 4) with the statement "Information on product packaging is very important to me". Regarding the statement "I compare labels to choose products with the highest nutritional value", respondents from this segment indicated the lowest level of agreement compared to the quality-oriented and neutral segments. However, this level did not differ from the level of agreement expressed by respondents from the sensory-oriented segment.

Respondents in the neutral segment had the lowest level of agreement with the statement "In order to improve the health-promoting benefits, fiber can be added to the pasta as compared to all segments". "The taste of pasta is more important to me than its health-promoting benefits" also had a low level of agreement, but this was similar to the level of agreement expressed by the sensory-oriented segment.

The opinions on the information placed on pasta labels are shown in Table 6. The three most important pieces of information were price, shelf life, and the name of the product. The quality-oriented segment showed the highest ratings for most of the information on the pasta label compared to the other segments.

Table 6. Profile of segments in terms of statements referring to information on the pasta label.

Statements	Mean	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	*p*-Value
price	4.29	4.71 [a]	4.42 [c]	4.53 [b]	3.73 [d]	<0.0001
shelf life	4.27	4.74 [a]	4.46 [b]	4.54 [b]	3.61 [c]	<0.0001
product name	4.08	4.67 [a]	4.16 [b]	4.12 [b]	3.56 [c]	<0.0001
weight	3.96	4.59 [a]	3.75 [c]	4.11 [b]	3.53 [d]	<0.0001
cooking time	3.91	4.53 [a]	3.52 [c]	4.37 [b]	3.40 [c]	<0.0001
product composition	3.85	4.66 [a]	3.64 [b]	3.63 [b]	3.51 [b]	<0.0001
producer	3.84	4.56 [a]	3.66 [b]	3.79 [b]	3.45 [c]	<0.0001
information on health effects	3.77	4.61 [a]	3.50 [c]	3.71 [b]	3.36 [c]	<0.0001
calorific value	3.72	4.56 [a]	3.47 [b]	3.48 [b]	3.41 [b]	<0.0001
information on the fiber content	3.63	4.46 [a]	3.38 [b]	3.37 [b]	3.32 [b]	<0.0001
quality label	3.61	4.55 [a]	3.41 [b]	3.24 [c]	3.29 [bc]	<0.0001
recipes for pasta dishes	3.39	4.13 [a]	2.56 [d]	3.63 [b]	3.22 [c]	<0.0001

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

A comparison of segment No. 2 and segment No. 3 (sensory-oriented, convenience-oriented) indicates that some of the information on the pasta packaging was of similar importance to consumers in these segments in choosing foods, i.e., shelf life, product name, producer.

The quality label, on the other hand, was significantly more important to consumers in the sensory-oriented segment compared to the convenience-oriented segment. For consumers in the convenience-oriented segment, price, weight, cooking time, and information on health effects were significantly more important compared to the sensory-oriented segment.

Compared to all segments, the neutral segment rated the following information lowest: price, shelf life, product name, weight, and producer. Information on health effects was also rated lowest by consumers in the neutral segment, but it was not significantly different from the rating in the sensory-oriented segment.

3.3. The Importance of Adding Fiber to Cereal Products

Table 7 presents respondents' opinions on the importance of enriching cereal products with fiber. They showed strong agreement with the opinions that such products facilitate a healthy lifestyle and can lower the negative consequences of an inadequate diet. For opinions regarding cereal products with added fiber, the quality-oriented segment significantly indicated the highest level of agreement for all statements. On the other hand, the neutral segment significantly indicated the lowest level of agreement with most of the given statements. Only the statement "The addition of fiber to cereal products worsens their taste" was rated significantly lowest by respondents in the sensory-oriented segment compared to all other segments. Respondents from this segment also rated the statement "I can prevent disease by eating such products regularly" significantly lower compared to the convenience-oriented segment but significantly higher than respondents from the neutral segment.

Table 7. Profile of the segments in terms of statements referring to cereal products with added fiber.

Statements	Mean	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	*p*-Value
They facilitate a healthy lifestyle	3.70	4.09 ^{a}	3.65 ^{b}	3.77 ^{b}	3.37 ^{c}	<0.0001
May lower the negative consequences of an inadequate diet	3.61	4.04 ^{a}	3.63 ^{b}	3.73 ^{b}	3.18 ^{c}	<0.0001
I can prevent disease by consuming such products regularly	3.52	4.02 ^{a}	3.37 ^{c}	3.66 ^{b}	3.16 ^{d}	<0.0001
There is a need to add fiber to cereal products	3.52	3.94 ^{a}	3.48 ^{b}	3.54 ^{b}	3.20 ^{c}	<0.0001
The addition of fiber to bread and pasta raises their calorific value	2.96	3.34 ^{a}	2.99 ^{b}	3.09 ^{b}	2.34 ^{c}	<0.0001
The addition of fiber to cereal products worsens their taste	2.95	3.12 ^{a}	2.58 ^{c}	2.94 ^{b}	3.06 ^{ab}	<0.0001

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

Consumers' views on the pasta with added fiber and pasta without added fiber are presented in Table 8. It shows that the respondents most frequently indicated the statement that pasta with added fiber is more expensive compared to pasta without the addition of fiber. Moreover, in their opinion, pasta enriched with fiber is healthier and more nutritious as well as less calorific when compared to pasta without added fiber.

Table 8. Profile of segments in terms of statements referring to pasta with added fiber compared to the same pasta but without fiber.

Statements	Mean	Quality-Oriented 1	Sensory-Oriented 2	Convenience-Oriented 3	Neutral 4	*p*-Value
Is more expensive	3.68	4.07 ^{a}	3.48 ^{b}	4.08 ^{a}	3.25 ^{c}	<0.0001
Is healthier	3.61	4.09 ^{a}	3.59 ^{c}	3.78 ^{b}	3.14 ^{d}	<0.0001
Has a higher nutrient content	3.52	3.99 ^{a}	3.36 ^{c}	3.64 ^{b}	3.20 ^{d}	<0.0001
Is less calorific	3.50	3.96 ^{a}	3.51 ^{b}	3.57 ^{b}	3.10 ^{c}	<0.0001
Is more difficult to find in shops	3.42	3.71 ^{a}	3.38 ^{b}	3.51 ^{b}	3.18 ^{c}	<0.0001
Has a better taste	3.31	3.95 ^{a}	2.76 ^{c}	3.31 ^{b}	3.21 ^{b}	<0.0001
Looks worse	2.94	3.18 ^{a}	2.54 ^{c}	2.89 ^{b}	3.04 ^{ab}	<0.0001
Has a more visually attractive packaging	2.94	2.86	2.96	3.06	2.91	0.45

Means with the same letter are not significantly different; ANOVA post-hoc Waller-Duncan K-ratio t Test.

With respect to pasta with increased fiber levels, the highest significant levels of agreement were again observed in the quality-oriented segment for most statements. For the statement that pasta with increased fiber is more expensive compared to pasta without added fiber, the highest levels of agreement were obtained in the quality-oriented and convenience-oriented segments. In contrast, neutral respondents significantly indicated the lowest ratings for statements that pasta with increased fiber content is more expensive, healthier, has higher nutrient content, is lower in calories, and is harder to be found in stores compared to pasta without increased fiber.

Regarding better taste and worse appearance of pasta with increased fiber compared to pasta without fiber, respondents from the sensory-oriented segment indicated the lowest significant ratings of agreement. Information regarding the visually attractive packaging of pasta without fiber compared to pasta with increased fiber was equally important to respondents from all separated segments.

4. Discussion

The variances in the factors influencing the choice of staple foods [10,27] should be taken into consideration while researching the acceptance of reformulated foods. Consequently, the research was designed to determine consumer groups according to their pasta selection motives.

4.1. Motives for Choosing Pasta

The obtained results showed that the information found on product packaging was important to respondents and that they compared the information on the labels of different foods before making a choice. This information was particularly essential to those in the quality-oriented segment compared to the other segments. Literature research confirms that the details on the packaging of a cereal product [28–30], including the information on the label, is significant for buyers [10,31]. In relation to pasta, becoming familiar with the information provided on the labels of food products, and perceiving oneself as a person who cares about health contributed to declaring a willingness to consume pasta with the addition of fiber [32]. However, surveys also showed that consumers do not always refer to the information presented on the packaging, e.g., because they are in a hurry, or the information is too detailed. Moreover, some consumer groups, namely athletes, consumers with health conditions, and those who attach great importance to a healthy lifestyle, may find appropriate food labeling useful [33].

At the same time, it should be emphasized that price and expiration date were among the two most important pieces of information indicated on the label. Similarly, as indicated earlier, these pieces of information were paramount for respondents from the quality-oriented segment. They also declared to a greater extent that they buy more expensive pasta, because in their opinion, the price of the product is adequate to its quality. The importance of price in a food choice is also confirmed by other literature studies [34–36]. In the case of information indicating the expiration date, the literature shows that consumers place a high value on the expiration date/shelf life and suitability for consumption [33,37]. Besides, freshness [38–40] and food safety [41,42] are important for consumers. Furthermore, information on packaging, including best-before dates, can be a kind of confirmation of food safety [43–45].

4.2. Choosing Pasta with Added Fiber

Regarding the fiber content of pasta, the subjects of the study declared that it was worth increasing fiber levels to increase the health-promoting benefits of the product. Again, quality-oriented consumers agreed the most, while neutral consumers agreed least with the above-mentioned opinion. When it comes to the addition of fiber to cereal products in general, the most important aspects indicated by respondents were the facilitation of a healthy lifestyle and the reduction of the adverse effects of a poor diet. Again, quality-oriented consumers agreed with this statement to the greatest extent, while neutral consumers agreed to the least extent.

It is estimated that consumers will increasingly make a food choice based on health-related motives. This is due to their value system in which health is ranked high [46–48]. The positive perception of health among some consumers results from their pro-healthy diet, which is rich in plant-origin foods (fruit and vegetables) [49–52]. Views on the health concerns resulting from the presence of fiber in the product are supported by the literature [53–55]. Adding dietary fiber to the pasta enables the creation of products with enhanced nutritional value [56] to meet market demands for healthier food choices [57]. Added-fiber grain products appear to be a useful tool for whole-grain avoiders to increase cereal fiber intakes, as this group is unlikely to accept whole-grain sensory properties [58].

Our study indicated that pasta with added fiber in consumers' opinion is more expensive but also healthier compared to pasta without added fiber. The health aspect was mainly emphasized by quality-oriented consumers. On the other hand, both quality-oriented and convenience-oriented consumers paid attention to the higher price. Consumers in the sensory-oriented segment, in relation to cereal products with increased fiber content, were the least likely to agree that the addition of fiber worsened their taste compared to the other segments, and in relation to pasta with increased fiber content, the least likely to agree that it looked worse compared to pasta without fiber. However, with respect to the taste of pasta with added fiber, these consumers were more cautious, as they were least likely to agree that it has a better taste compared to pasta without added fiber. The cited opinions may indicate that sensory-oriented consumers do not quite like the taste of this pasta, while at the same time, they do not mind that it may have a characteristic darker color and lumps/spots that at the same time visually indicate the presence of fiber (and presumably so they have a visual guarantee/confirmation at the same time that the fiber is there).

Studies in the literature indicate that expectations and sensory experiences are involved in the overall assessment of product quality [59]. Moreover, it has been emphasized many times in the literature that taste plays a major role in food choice [60,61], and for cereal products [62–64], including pasta, it was also noted that it was an important selection factor [65]. The literature also indicates that spaghetti fortified with fiber had good overall acceptability, and could represent a healthy product with good technological and sensory properties [21]. Some consumers favored the fortified sample over the control one, including pasta, and some of them would pay more for the fortified products [66]. Generally, consumers showed less acceptance of a modified pasta when a product had a more intense darker color, and bitter or more sour taste. Acceptance grew among consumers who tend to purchase unconventional pasta [67].

Consumers in the sensory-oriented segment participating in our study were also the least likely to report paying attention to recipes for pasta dishes on the label, which may indicate that this segment may most likely have their own well-tried recipes and does not need this type of information on the label. In contrast, recipes for pasta dishes were important to consumers in the quality-oriented and convenience-oriented segments.

Literature studies indicate that consumers are looking for recipes for dishes [68]; however, their availability is important, e.g., recipes on websites are of particular interest due to their ease of use [69]. In the future, online databases providing consumers with, among other things, recipes for various types of dishes in order to compose interesting and nutritious meals from the consumer's perspective may be of interest [70].

4.3. Practical Implications, Strengths and Limitations

The practical implications of our findings for practitioners in the cereal industry as well as for policy makers are that their efforts to influence the consumption of those products should include tailoring them to the specific consumers they aim to target. While developing food products, efforts should be aimed at enhancing the health value of food consumers perceive as convenient and easy to use.

The strength of our results lies in a relatively large sample of the Polish population. Nevertheless, the findings have their limitations. The sample comprised consumers solely or jointly contributing to grocery shopping of a household. Furthermore, the data used in the study was prone to bias. The first concerns the self-declared information obtained from the survey that may be inaccurate due to the unnatural circumstances imposed by the questionnaire itself. Furthermore, the real circumstances in where the choice of pasta is made and the use of products themselves rather than using the questionnaire would reflect the environment where a purchasing decision is made. However, due to the size of the sample as well as logistic and economical limitations, research using the real products or labels was impossible.

For the abovementioned reasons, the findings in this study should be used with caution when cultural differences may occur. Despite these flaws, our study provides new insights into the motives behind pasta selection.

5. Conclusions

Finding out about consumers' motivations and demand for cereal products, including pasta, may be beneficial for manufacturers to design new types of food and devise marketing strategies, which will result in developing a practical and revised approach to attract consumers who want to promote their health, well-being, and quality of life.

There are numerous opportunities for further developments on the market of cereal products with added fiber, e.g., relatively positive opinions on the significance of enhancing fiber in the diet, the acceptance of adding fiber to pasta, and consumer awareness of the beneficial properties of fiber for health. However, it is important to keep in mind which consumer group the fiber pasta is targeted at, because the consumers' belonging to a particular segment influence what factors are taken into account when making purchasing decisions. Moreover, regarding the fiber content of pasta, quality-oriented consumers agreed the most, while neutral consumers agreed least with the opinion indicating that it was worth increasing fiber levels to increase the health-promoting benefits of the product.

The results of the study can provide valuable insights for those involved not only in nutrition education but also directly for producers and processors operating on the food market. Therefore, these findings are of significance for those involved in the public nutrition sector as well as for those responsible for preparing well-targeted marketing messages. The conclusions may constitute invaluable insights for those devising educational initiatives and campaigns.

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nutrients

Communication

Consensus, Global Definitions of Whole Grain as a Food Ingredient and of Whole-Grain Foods Presented on Behalf of the Whole Grain Initiative

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Abstract: Proposed global definitions of whole grain as an ingredient and whole grain food are presented by the authors on behalf of the Whole Grain Initiative. Whole grains are an important pillar of healthy and sustainable diets. Internationally accepted credible definitions of whole grains as food ingredients and whole-grain foods are necessary to ensure that all global stakeholders have shared standards, and that consumers find them clear, credible, and useful. Based on widely accepted, existing definitions and new developments, the Definitions Working Group of the global Whole Grain Initiative, with experts from academia, government agencies and industry, developed definitions for global application. The key statements of the definition documents are as follows: "Whole grains shall consist of the intact, ground, cracked, flaked or otherwise processed kernel after the removal of inedible parts such as the hull and husk; all anatomical components, including the endosperm, germ, and bran must be present in the same relative proportions as in the intact kernel" and "A whole-grain food shall contain at least 50% whole-grain ingredients based on dry weight. Foods containing 25–50% whole-grain ingredients based on dry weight, may make a front-of-pack claim on the presence of whole grain but cannot be designated 'whole grain' in the product name". The definition documents have been ratified by the leading international scientific associations in this area. We urge that these consensus Whole Grain Initiative definitions be adopted as the basis for definitions used by national regulatory authorities and for health promotion organisations worldwide to use in nutrition education and food labelling.

Keywords: whole grain; whole-grain food; definition; ingredient; labelling

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1. Introduction

1.1. Whole Grains—Dietary Recommendations, Rationale, and Intake

Increased intake of whole grains in population studies is consistently associated with a lower all-cause mortality and with reduced risk of lifestyle-related diseases such as cardiovascular diseases, type 2 diabetes and colon cancer [1,2]. Consequently, consumption of whole grains is recommended in dietary guidelines worldwide [3,4]. Recommendations range from generic advice to include eating a variety of grain-based foods, mostly whole-grain and/or products high in cereal fibre, to more quantitative recommendations. In the United States, dietary guidelines advise to consume at least 3 servings/day, equating, for example, to 3 slices of whole-grain bread containing approximately 48 g whole grain, in order to make half your grains whole grains [5]. In Denmark, an intake of at least 75 g whole grains/10 MJ is recommended. Sweden recommends 70 g and 90 g of whole grains for women and men, respectively [6]. Because nearly all people in every country include one or more varieties of cereal grain in their diet, substituting whole grains for refined grains should be less challenging than introducing new a new food group into the diet, and an important step for improved public health (or reduced rates of non-communicable diseases).

In contrast, average dietary intake of whole grains in almost all countries is well below recommended levels, thus the fibre, nutrients and phytonutrients they contain are not part of the diet [7–12]. This deficit has the potential to contribute to chronic diseases and to their attendant high health costs, which must be shouldered by individuals and governments [13–15].

Increased intake of whole grains is also aligned with the shift to plant-based diets occurring throughout the world, outlined in recommendations for healthy and sustainable eating patterns. Guidelines for sustainable diets tend to suggest a higher intake of whole grains than is currently recommended by national organisations. For example, the EAT–Lancet Commission on healthy diets from sustainable food systems recommends an intake of 232 g whole grains/day—corresponding to 11 servings/slices of bread [16]. Increasing the consumption of fruits, vegetables and whole grains and decreasing red meat consumption remain key population objectives of many national dietary guidelines. A modelling study on healthfulness and sustainability of national and global food-based dietary guidelines indicated that healthy, mainly plant-based diets from sustainable food systems have a major impact on sustainability and contribute to a larger extent to health benefits than the diets recommended in current national dietary guidelines [17]. This emphasises the need for, and urgency of, actions that contribute to an increased intake of whole grains.

1.2. Trends in Consumption, Consumer Perceptions, and Desires for Labelling

The market for whole-grain foods and ingredients is growing worldwide. Growth is noted for a number of formerly less well-known grains, including quinoa, amaranth, spelt, teff and millet, although their consumption remains minor compared with the major cereal grains of wheat, rice and maize. Manufactured products with whole grains are increasingly entering new markets, such as Southeast Asia and Latin America. Due to this trend, Malaysia [18] and Brazil [19] recently published definitions for whole-grain foods.

Whole-grain consumption remains, on average, significantly below recommended levels, despite the growth in availability of whole-grain foods. Although the taste of whole-grain products may be appreciated by more consumers over time, raising the content of whole grains in products may result in a lower appreciation by some. This is particularly true when consumers are not familiar with the taste and colour of whole grains. In order to capitalise on the positive image of whole grains, some food manufacturers may highlight the presence of low levels of whole grains through on-package images or textual messages front-of-pack. Although such statements may be factually correct, a study showed that consumers may misinterpret such messages as signifying the presence of higher amounts of the highlighted ingredient than is actually present [20]. For example, consumer organisations in Europe and Brazil expressed the need for high levels of whole grains and non-misleading labelling for whole-grain foods front-of-pack [21,22]. In recent years, front-of-pack labelling has been recognised by the WHO as an important policy tool for promoting healthy diets and preventing obesity and diet-related non-communicable diseases [23]. As a result, it has become a key issue in debates on regulations for nutrition and health-related labelling.

1.3. The Need for Globally Accepted Definitions for Whole Grains as a Food Ingredient and for a Whole-Grain Food

At the 6th International Whole Grain Summit, Vienna, 13–15 November 2017, key goals and actions were identified to contribute to an increased intake of whole-grain products. To carry out the action points, the Whole Grain Summit participants agreed to work together in the global "Whole Grain Initiative" [24]. The Whole Grain Initiative gathered an international working group on definitions, with over 40 expert members from academia, government agencies and industry from Asia, Europe, North and Latin America, Oceania and Africa, to realise the first goal—"*to reach consensus on a global definition of whole grain (as raw material) and on the definition of a whole-grain food*". The group considered widely accepted definitions as well as new developments in breeding, processing technologies, and markets worldwide as well as the needs and wishes of consumer organisations with regard to whole grain-related regulations and labelling. Actions by regulatory authorities currently developing their own whole-grain definitions were also included in deliberations.

The development of the global Whole-Grain Food definition with input from stakeholders from around the world is not intended to denigrate refined or enriched refined grains in any way. Data from nationally representative dietary intake surveys consistently shows that consumption of whole grains is well below recommendations, despite reported health benefits of higher whole-grain intake. It is recognised that dietary guidance may include allowances for enriched grain intake, but because enriched and refined grain intake is not a shortfall in the diet, the focus of this definition is to promote whole grains. The whole-grain food definition described in this paper serves multiple purposes, but, ultimately, all are intended to promote public health and consumer confidence.

2. The Global Definition of Whole Grains as a Food Ingredient

2.1. General Remarks

Definitions of whole grains as a raw material and a food ingredient are included in food regulations in many countries. The existing definitions are aligned, namely that whole grains shall consist of the intact or processed edible components of the kernel, including the endosperm, germ, and bran, which must be present in the same relative proportions as in the intact kernel [25,26]. However, differences exist regarding the grains included and allowed processes. The core statement of the proposed definition is shown in Box 1. The full definition document is included in the Supplementary Materials (Document S1). The key points of the definition—the meaning of the terms kernel, endosperm, bran and germ, the grains to be included and processing aspects—are outlined below.

Box 1. Whole Grain Initiative—Definition of Whole Grain as a Food Ingredient.

> Whole grains shall consist of the intact, ground, cracked, flaked or otherwise processed kernel after the removal of inedible parts such as the hull and husk. All anatomical components, including the endosperm, germ, and bran must be present in the same relative proportions as in the intact kernel.

In cereal science and technology, and in milling, the bran includes the aleurone layer, whereas in botanical definitions the aleurone layer is considered to be part of the endosperm. The term kernel in the definition is used for many widely consumed grains, such as wheat, maize, rice, barley and rye. Other commonly used terms include seed, berry, groats and simply 'grain'. Additional terms, both in English and other languages, may be used as well. As stated in the definition, the use of the term wholemeal may be legally protected in some jurisdictions and may be equivalent to whole grain. The use of the term wholemeal versus whole grain should be checked within local contexts.

2.2. Grains to Be Included

All currently accepted definitions include cereal grains of the *Poaceae* grass family and, in many cases, also selected pseudocereals. Pseudocereals are defined as fruits or seeds of non-grass species that are consumed in a similar way to cereals because their nutritional profiles, preparation and uses are similar to cereal grains. Most definitions do not specify in detail the species of grains included. The definition of the Cereals & Grains Association (C & G Association, formerly AACC International) provided a list of the cereal grain species with all edible cereal grains known at that time, as well as the following three widely used pseudocereals: amaranth, buckwheat and quinoa [25]. Considering that the whole grains of all these species contain higher levels of dietary fibre and other beneficial compounds than their refined counterparts, and taking into account the benefit of global harmonisation of whole-grain definitions, the same broad range was adopted in a previous collaborative definition developed by the Healthgrain European Union Integrated Research Project, with input from a large number of universities and industries in Europe [26]. Oilseeds, pulses and legumes differ substantially from cereal grains in their anatomy and composition, and are not included in any definitions nor in dietary recommendations for whole grains [3].

Some other organisations do provide similar lists showing examples of sources of whole grain [27,28]. In Denmark and Sweden, evidence of health benefits of specific grain species is required. Therefore, only wheat (including spelt), rye, oats, barley, maize, rice, millet and sorghum are listed as whole grain. The consensus global definition presented here allows for the addition of newly developed species of cereal grains, when they are accepted by the relevant authoritative groups. For example, the recently launched Tritordeum species obtained by crossing durum wheat with the wild barley *Hordeum chilense,* is currently grown and included in products sold in Australia and Europe. Such developments through breeding can improve both nutrient content and consumer acceptance, and these grain species should be included in whole grain definitions [29].

In dietary guidelines, pseudocereals are usually included in the grains and grain product categories. Amaranth, buckwheat, (including both common buckwheat and tartary buckwheat) and quinoa are mentioned in a number of definitions and are the most common pseudocereals consumed. Their inclusion also increases the number of gluten-free whole-grain options available for individuals with coeliac disease. These 'established' pseudocereals are listed in the Annex of the global definition. Including the pseudocereals into the Annex allows for the addition of new pseudocereals without changing the definition.

The pseudocereal area is dynamic and the working group was required to consider seeds which are sometimes called whole grains. For example, while chia is often mentioned, its nutrient profile with ~40% dietary fibre is, contrary to amaranth, buckwheat and quinoa, far outside the range found in cereal grains [30]. Two other seeds were suggested for inclusion, djulis and jitoumi. Djulis (*Chenopodium formosarum*) is also called red quinoa and is related to quinoa (*Chenopodium quinoa*), but currently produced at a very small scale [31]. Jitoumi (*Euryales Semen*, *Euryale ferox*) are the seeds of the pricky waterlily, currently used in parts of India and China as food, but detailed compositional and health-related data are currently not available. Considering all available information, it was concluded that there are currently no convincing arguments for addition of grains other than the three pseudocereals currently included in the Annex. As more innovation in the area emerges, the Annex may be updated.

The Annex also includes: "The anatomical components of pseudocereals, being dicotyledons, are different from those of the monocotyledonous cereal grains. As for cereal grains, all edible anatomical parts of processed pseudocereals must be present in the same relative proportions as in the intact seed".

2.3. Processing Aspects

All existing whole grain definitions require that the edible components of the grain are present in their original proportions when the grains have been processed. Most grains need to be processed before consumption, which may include steps such as cleaning (e.g., removal of stones, stems, etc.), removing inedible parts (e.g., hull/husk), and both dry (e.g., milling) and wet (e.g., malting, sprouting, fermenting) processing to make the grains more stable for storage, palatable, and often with the side effect of improving nutrient bioavailability.

In most commonly applied milling processes, endosperm, bran and germ fractions are separated for later recombination. When a long shelf life is required, the germ and bran fraction are usually heated to help stabilise and reduce rancidity, followed by recombination with the endosperm from a different batch of grain. In most large flour milling plants, a wide range of varieties of the same grain species are processed and grains from these varieties may be intermingled before or during processing. Therefore, the endosperm, bran and germ of the recombined whole-grain flour may originate from different varieties or at least batches.

Many producers of consumer products also practice 'recombination'—then usually called reconstitution—where the various fractions are recombined to the specified proportions at their point of use, compared with at the mill. Some national regulations, including from Denmark and Spain, do not allow reconstitution instead of recombination at the mill. In discussions in and outside the Working Group, proponents of this restriction mentioned that consumers may consider reconstituted whole-grain flour as inauthentic. However, reconstitution may result in lower costs and may create opportunities for improving taste and texture. For example, bakeries in the EU HealthBread project recombined the softened bran fraction after a long pre-fermentation [32]. Both recombination and reconstitution, as well as other new processes, are allowed by the consensus definitions provided that manufacturing practices to ensure quality are applied. The goal is safe and taste-acceptable whole-grain products created from processes not limited to grinding, cracking and flaking mentioned in previous definitions of whole grain. For fermentation, malting, and sprouting, the definition presented here has adopted the conditions set by C & G Association [25] and the Healthgrain Forum [33], which stipulate nutrient values have not diminished and—for malting and sprouting—that the length of the sprout should not exceed kernel length.

Mycotoxins, agrochemicals, and microbial contaminants tend to be concentrated in the outer pericarp layer. The option for removal of a minor part of the grain kernel is included in some definitions (Healthgrain [26], Germany, Switzerland, and Denmark). The Healthgrain definition states "*small losses of components—that is, less than 2% of the grain/10% of the bran—that occur through processing methods consistent with safety and quality are allowed*". Considering the large variations that might occur world-wide regarding the specific grain type or variety, and local regulations or constraints, no quantitative limit is included in the global definition, but—as stated in the definition document (Supplementary Document S1): "*allowable limits for the percentage removed should be evidence-based and should be kept to a minimum*".

3. The Global Definition of a Whole-Grain Food

3.1. General Remarks

Definitions of traditional whole-grain foods, such as bread, pasta and biscuits, have been in place already for many years in a number of countries. Current definitions, however, lack consistency. For example, amongst countries, the minimum percentage of whole-grain flour required for labelling bread as whole grain varies between 50 and 100% of the flour. For biscuits and pasta products, similar variations can be found [33]. Consumer acceptability of products with high levels of whole grains has limits and may be a reason why manufacturers choose lower levels of whole grains in a number of foods.

In response to the growing interest in mentioning 'whole grain' on food labels of a wide range of products, the C & G Association proposed a first generic definition in 2013, as follows: *a whole grain food product must contain 8 grams or more of whole grain per 30 grams of product* [25]. In 2017, the Healthgrain Forum proposed the following definition with a similar minimum level of whole grain: $\geq$30% whole-grain ingredients, but on a dry-weight basis, enabling products with a high moisture content to be defined as a whole-grain product. Products required more whole-grain than refined-grain ingredients [33], setting an effective threshold of >50% for products based on 100% cereal flour. The latter addition was based on the current definition in Denmark [34] and concerns expressed by the European Consumer Organisation Bureau Européen des Unions de Consommateurs (BEUC), the umbrella group for 46 independent consumer organisations from 32 countries in Europe [13]. New generic definitions were issued in Malaysia in 2020 [18] and in Brazil in 2021 [19], and are being discussed in a range of other countries. The publication of a global consensus definition endorsed by leading international scientific associations in this area may contribute to harmonisation of definitions world-wide. Box 2 shows the core statements of the Whole Grain Initiative definition. The full definition document is included in the Supplementary Materials (Document S2).

Box 2. Whole Grain Initiative Definition of a Whole-Grain Food

I. Definition of a whole-grain food

A whole-grain food shall contain at least 50% whole-grain ingredients based on dry weight

II. Requirements for designating the presence of 'whole grain' front-of-pack

Foods containing a minimum of 25% whole-grain ingredients based on dry weight, may make a front-of-pack claim on the presence of whole grain but cannot be designated 'whole grain' in the product name. *

* The decision to include "and at least 8 g/serving" in addition to "a minimum of 25% whole-grain ingredients based on dry weight" should be left to national authorities.

3.2. A Generic Definition Based on Dry Weight

There is a growing array of whole-grain products, but they vary widely in their proportion of whole-grain ingredients. Grain-based food products have moisture levels varying from less than 5% for dry biscuits to about 90% for grain-based alternatives for milk and yoghurt.

Unfortunately, regulation on labelling is limited or absent in some jurisdictions and labelling of whole-grain content of food is further complicated by the wide variety of foods and particularly the amount of water present in the final product. The amount of water in a whole-grain product is important because it impacts the overall weight, making it hard to directly compare the amount of whole grains in a dry product compared with a wet or cooked product, if water content is not taken into account. Therefore, a generic definition, based on setting a minimum level of whole grains on a dry-weight basis, was considered as the most realistic option for the global definition.

As stated in the definition, the dry weight of a food or ingredient is the weight of the food after its moisture content has been subtracted from its total weight. The content of whole grains is the dry weight provided by all whole-grain ingredients expressed as a percentage of the total dry weight of the food product. This percentage (to be used for the definition) may be based on analysis, or on calculations with accepted data for the ingredients, such as presented in food composition databases.

The percentage of whole grains to be designated on the pack should be based on local regulations, such as the widely used Quantitative Ingredient Declaration system (QUID), also included in the Codex Standard 1, 1985, Section 5.1: Quantitative ingredients declaration [35]. For products with a high moisture content, the percentage of whole grains based on dry weight will be higher than the percentage based on QUID. This practice—calculation of the percentage of whole grains for the definition based on dry weight and calculation for labelling according to the QUID system—has already been followed for over 20 years in Denmark and Sweden [28]. An example of these calculations is presented in the Supplementary Materials (Document S3).

3.3. A Whole-Grain Food—At Least 50% Whole-Grain Ingredients Based on Dry Weight

In the Healthgrain Forum definition, at least 30% whole grain on a dry weight basis is required, and levels of refined-grain ingredients should not be higher than those of whole-grain ingredients. However, with the Healthgrain definition, a whole-grain product may contain on a dry-weight basis 30% whole grain and, for instance, 70% starch. In the currently presented consensus definition, with at least 50% whole grains, the sum of whole-grain ingredients will be the majority of the product on a dry-weight basis. This is important to minimise the potential for consumer confusion. Foods with a low percentage content of whole grains cannot be labelled as a whole-grain food. It is recognised that ≥50% whole grains may be difficult for products containing high amounts of other ingredients, such as pizza with toppings and some bakery products. However, given the aim of the project is to encourage whole-grain intake to improve health outcomes, it may be argued that such foods should not be considered "whole-grain", and this may encourage reformulation of current products to meet higher standards. Previously, gradual changes in composition have been applied successfully [36]. As outlined in detail below, foods containing a minimum of 25% whole-grain ingredients based on dry weight, may make a front-of-pack claim on the presence of whole grains. For foods with low levels of other ingredients, such as bread and pasta the ≥50% threshold is below the (near) 100% level of whole grains required in many national regulations.

In line with our aim of stimulating the intake of whole grains, the definition document states that national regulations and definitions, which require a greater proportion of whole grains in a product, will prevail, whereas in countries with existing definitions that permit less than 50% for labelling a product as a 'whole-grain food', a change in regulations and the adoption of the proposed definition is strongly encouraged.

In whole-grain foods, especially those with high levels of grains, the percentage of whole grains may vary considerably; when only grains are present, a whole-grain food may contain at least 50%, and up to 100% whole-grain ingredients based on dry weight. Reporting the percentage of whole grain in a product in any front-of-pack labelling is strongly recommended in the definition, for ensuring fair practices in the food trade and ease of consumer comparison among and between products. This is required in the recent definitions in Malaysia [18] and Brazil [19].

3.4. Minimum Level for Mentioning Whole Grain Front-of-Pack: 25% Whole-Grain Ingredients Based on Dry Weight

The presence of whole grains in a product is often highlighted with pictures of grains as part of front-of-pack labelling. Such pictures have been criticised by consumer organisations for potentially misleading consumers, for instance when a product contained only 15% whole grain by weight, and considerably more added sugar [21] without any indication front-of-pack. The definition working group agreed that the mentioning of whole grain front-of-pack should only be allowed when a dietarily or nutritionally meaningful amount was present. Based on the following considerations, the level of 25% whole grain based on dry weight was chosen:

- The first whole grain food recommendation was based on the United States Dietary Guidelines for Americans, including the guidance to make 'half your grains whole'. The first whole grain health claim allowed by the U.S. FDA defined a whole-grain product eligible for a claim around whole-grain bread with 51% whole-grain wheat flour [37]. Because 1 slice (serving) of whole-wheat bread has 16 g whole grain, one-half of the full serving of whole grain would be 8 g. The 8 g whole grain, which was used in most early epidemiological studies examining the relationship between whole grain and health outcomes, was considered as the minimum meaningful amount of whole grain deserving of mention front-of-pack.
- This 8 g whole grain/serving is currently widely recommended as a minimum level, for example, in the regulation in Malaysia [18], the recommendation by the UK-based Institute of Grocery Distribution [28], the whole grain stamp systems outlined below of the Whole Grains Council (WGC) [27], and the Australian Grains & Legumes Nutrition Council (GLNC) [38]. The GLNC states the following: *To carry GLNC certification a product must (. . .) contain at least 8 g whole grain per manufacturer serve AND at least 25% whole grain ingredients.* For the WGC, 8 g per serving or 25 g/100 g (depending

on the country) is the minimum level for using a stamp, whereas for calling a food a whole-grain food, at least half of the grain ingredients have to be whole. The stamps indicate both the % whole grain of all grain components and the amount of whole grain per serving or per 100 g. The whole grain intake recommendation of 48 g is the extrapolation of the average number of servings of grain per day in the U.S. (6 servings), and if each serving delivers 8 g whole grain, then the daily recommendation is 48 g whole grain.

- When using the relatively small serving sizes as recommended by the USDA and the Whole Grains Council [27], and following the criteria of the GNLC, 8 g whole grain per serving corresponds to ~25–30 g whole grain/100 g.
- Serves or serving sizes are defined differently in different countries. Therefore, in order to avoid confusion in a global definition, the minimum amount of whole-grain ingredients is expressed as a percentage.

Finally, the combination of at least 50% whole-grain ingredients for whole-grain foods and at least 25% for inclusion of "whole grain" in front-of-pack labelling is in line with regulations, recommendations by Codex, and other authoritative bodies. These organisations require two levels of a nutrient in a food (such as "source of" and "high" dietary fibre), where the amount required for the "high" qualification is twice the amount required for "source of". For whole-grain foods we propose that there is application of the same approach as complying with the 'source of' and 'high in' descriptors, which is unique. Currently, no precedent exists for applying regulatory standards associated with nutrients onto food groups. The dual levels will also address both the need for a high whole-grain level in whole-grain foods, as expressed by consumer organisations, and for a lower but meaningful minimum level for inclusion of whole grain in front-of-pack labelling to attract consumers not accustomed to higher levels of whole grains in food.

4. Final Remarks

Both the Whole Grain Ingredient and Whole-Grain Food definitions have been ratified by the leading international cereal science associations, including the C & G Association, the Healthgrain Forum, and the International Association for Cereal Science and Technology (ICC). The Whole Grain Initiative's definitions working group, in collaboration with the Whole Grain Initiative leadership team, is working across countries and regulatory authorities to advocate for adoption of these definitions globally. There are numerous reasons why whole-grain intake remains low in most regions across the globe, and the members of the WGI are committed to reducing the barriers. The consensus definitions presented here seek to improve consumer confidence in the integrity of the label and help support consumers in selecting foods with evidence-based health benefits, while providing aspirational targets for food manufacturers wishing to describe their products as a "whole-grain food" and highlight the whole-grain content on labels. The adoption of the Whole Grain Initiative consensus whole grain definitions is strongly encouraged and should serve as a reference point for national regulatory authorities.

Supplementary Materials: The following are available online at: https://www.mdpi.com/article/10.3390/nu14010138/s1. Document S1, Definition of whole grain as food ingredient. Document S2, Definition of a whole-grain food. Document S3, Calculation of percentage of whole-grain ingredients based on dry weight.

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Communication

Terminology Matters: Advancing Science to Define an Optimal Pulse Intake

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Abstract: Confusion around the terms "legumes" and "pulses" has been a long-standing problem among consumers, health professionals, and researchers in the United States. The Food and Agricultural Organization defines pulses as legumes that are harvested solely as dry grain and include beans, peas, chickpeas, and lentils. For the first time ever, the 2020–2025 Dietary Guidelines for Americans recognized and used the terminology "pulses." Correct terminology usage is important to build a solid research foundation that is specific to pulses, primarily because of their unique nutritional attributes that impact health differently than other legumes. Future widespread conformity and standardized use of a definition and categorization system around pulses versus legumes in research would allow for an improved interpretation of science and a better understanding of current research gaps. Clarity around these gaps could enhance and improve dietary recommendations, including the ability to refine our current understanding of the optimal daily or weekly intake of pulses at which health benefits are maximized.

Keywords: pulse; beans; peas; chickpeas; lentils; legumes

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1. Introduction

The improper usage of and confusion around the terms "legumes" and "pulses" has been a pervasive problem among consumers, health professionals, and researchers in the United States [1–3]. Even the primary source of federal dietary advice, the Dietary Guidelines for Americans (DGA), used the term "legumes" for decades where the term "pulses" would have been more accurate. However, for the first time, the 2020–2025 Dietary Guidelines for Americans [4] used the terminology "pulses," which they defined as the dried edible seeds of legumes including beans, peas, and lentils. The name of the vegetable subgroup previously called the "legumes (beans and peas)" subgroup was also changed to the "beans, peas, and lentils" subgroup in order to better reflect the foods included in the subgroup. Prior iterations of the DGA commonly referred to this food group as "legumes (beans and peas)" with no other clarification or references to the term "pulses" [5]. In a recent article by Didinger and Thompson [3], the ambiguity over terminology and the importance of understanding that pulses are a distinct subclass of legumes both nutritionally and functionally is described. There is little doubt that global harmonization of the terminology would allow for clearer dietary messages that may have significant public health impact, but the terminology is also important to build a solid research foundation that is specific to pulses, primarily because of their unique nutritional attributes that impact health differently than other legumes. The main objective of this communication is to demonstrate how widespread conformity and standardized use of the definition and language around pulses in research would have a broader bearing on the interpretation of the science and lead to a better understanding of the significant research gaps. Clarity around these gaps could enhance and improve dietary recommendations, including the ability to refine our current understanding of the optimal daily or weekly intake of pulses at which health benefits are maximized.

2. Pulses as a Distinct Class of Legumes

Although they are frequently used interchangeably, the terms "legume" and "pulse" have distinct meanings. The term "legume" broadly includes any edible parts of plants in the Fabaceae and Leguminosae family, including the leaves, stems, pods, and seeds of the plant. When used generally, this term encompasses all types of legumes including soybeans, peanuts, fresh green beans and peas, and pulses. Legumes are often split into two subcategories: oilseed legumes (peanuts and soybeans) and non-oil seed legumes. Non-oil seed legumes include pulses and freshly harvested garden vegetable varieties of legumes such as green peas, snap peas, and green beans, which are mostly consumed whole including both the pod and seeds. "Pulse" is the term used specifically for describing non-oilseed dry, nutritionally dense, edible seeds of legumes and includes dry beans, dry peas, chickpeas, and lentils. Unlike other legumes, pulses remain on plants to dry before harvesting [6]. The Food and Agriculture Organization recognizes 11 types of pulses: dry beans, dry broad beans, dry peas, chickpeas, cow peas, pigeon peas, lentils, Bambara beans, vetches, lupins, and pulses nes ('not elsewhere specified' or minor pulses that do not fall into one of the other categories). Commonly consumed pulses in the U.S. [7] include dry beans such as pinto, black, and kidney beans and dry peas (e.g., yellow or green peas), chickpeas, and lentils, but there are hundreds of varieties of pulses (e.g., mung beans, lupin, cowpeas, and fava beans) produced and consumed globally [6].

When conducting and reporting research regarding the health or nutritional benefits of legumes, it is important to specify the type of legume used in the study because each type has different nutritional properties. For example, oilseed legumes (peanuts and soybeans) are higher in fat and lower in dietary fiber than other types of legumes such as green beans, green peas, or pulses. Due to their dried state, pulses have a unique nutritional profile. Pulses contain about 7 to 10 g of protein per serving (~100 g or $\frac{1}{2}$ cup cooked) depending on the pulse type [8,9]. They also comprise 50–65% carbohydrate including resistant starch, soluble, and insoluble fiber and have a low glycemic index. Pulses contain a vast array of phytochemicals and other bioactive components [10]. They are highly nutrient dense and, as such, are considered a significant dietary source of many nutrients such as complex carbohydrate, protein, fiber, folate, iron, magnesium, and potassium and are a good source of many other nutrients such as choline, zinc, selenium, phosphorus, and thiamin [8,9]. Significant improvements in nutrient intakes at levels around 100 g or $\frac{1}{2}$ cup cooked per day of pulses have been observed in several population-based studies [7,11–14].

Despite the significant nutritional differences between pulses and other legumes, "legumes" is the terminology more commonly used in the research literature to describe pulses, even if other legumes such as soy and peanuts are excluded from consideration. There is substantial ambiguity in legume and/or pulse research since the definitions and types of legumes vary widely among studies and the term "pulses" has not been commonly used to describe this type of legume despite their clear distinction from the broader legume class.

3. Strengthening Pulse Research by Using Less Ambiguous Terminology

3.1. Prospective Cohort Studies and Randomized Controlled Trials

There is considerable evidence from observational or prospective cohort studies and randomized controlled trials (RCTs) showing the consumption of pulses is associated with positive health outcomes, such as reduced risk factors for cardiovascular disease, hypertension, diabetes, overweight or obesity, and colorectal and prostate cancers [8,15–21]. Several systematic reviews and meta-analyses (SRMA) have been conducted that summarize empirical evidence from many prospective cohort studies and RCTs including the dose or amount of legumes or pulses that elicit a particular response or health outcome [15–21]. Much of this research, however, could be strengthened by using less ambiguous terminology or by conducting research that focuses solely on pulses rather than the broader class of legumes.

In 2017, a review of SRMAs by Viguiliouk et al. [20], for example, included both prospective cohort studies and RCTs that examined the effect of dietary pulse or legume intakes on cardiometabolic outcomes. At that time of this review, there were no SRMA-conducted targeting pulses specifically; thus, data analysis included SRMAs of studies that included all legumes (pulses, soybean, soy products, peanuts, fresh peas, and fresh beans). In these prospective cohort studies, for SRMAs that included all legumes and not only pulses, a reduced risk of coronary heart disease was observed at legume intakes of four >100 g servings of pulses per week. For other outcomes such as cardiovascular, diabetes, and stroke risk, the associations remain uncertain and require further study. For RCTs where the focus was specifically targeting pulses (only dry beans, peas, lentils, and chickpeas), a decrease in cardiometabolic risk facts (e.g., HbA1c and LDL-cholesterol and body weight) at pulse intakes of 120–132 g/day (0.5–0.75 cups/day, the equivalent of about one serving/day) was observed. In one of the SRMAs reviewed, a reduction in blood pressure was achieved with a relatively high average dose of ~162 g/day (0.8 cups per day) of pulses, an amount well above current recommendations [19].

In a more recent umbrella review of SRMAs using prospective cohort studies, the associations between legumes or pulses and cardio metabolic disease outcomes were investigated. Study results showed that pulses with or without other legumes were associated with a decreased incidence of cardiovascular disease, coronary heart disease, hypertension, and obesity when comparing the highest intake of pulses with the lowest intake [21]. Although the studies specified that the exposure was "legumes," the legumes were not differentiated by type or included types other than pulses such as soy beans, soy products, peanuts, fresh green peas, or fresh beans. However, the authors explain that the indirectness of exposure was not considered in the analysis since >50% of the studies included were from countries (mostly from Europe and North America) where pulses are consumed in much larger quantities than soy or soy products. The assumption is that the associations observed were likely due mostly to pulse intake; however, more directed research on pulses without other legumes would remove the uncertainty in estimated exposure. Moreover, associations were assessed by comparing lowest to highest quantiles of intake; thus, optimal doses of pulses were difficult to ascertain since there was a wide range of intakes when comparing the lowest to highest levels of intake.

Both epidemiological and clinical trial evidence point towards positive health benefits of consuming pulses; however, epidemiological evidence could be more directed specifically at pulses; many of the studies include other legumes or use the terminology "legumes" when it would really be more correct and specific to use the terminology "pulses." Differing dietary exposures (e.g., pulses with and without other legumes, various pulse types, and pulse flours) make it difficult to compare and combine studies. Prospective cohort studies rely mostly on food frequency questionnaires; therefore, dietary exposures are only semi-quantitative and, thus, only an estimate of dietary (pulse) exposure is possible, making it difficult to ascertain an optimal dose for a specified effect [15,16,20,21]. In recent years, there has been significant advancement in the availability of innovative pulse products, such as pulse pastas, pulse veggie patties, and pulse flours. As these innovative products continue to emerge and consumers begin to more frequently include them in the diet, there is a need for consideration as to how these will be captured in food frequency questionnaires and other dietary survey methods in the future. Furthermore, vegetables including pulses are consumed in food mixtures as often as they are eaten separately [4,7]. Quantifying pulses using standard recipes for food mixtures may contribute to over or underestimating pulse consumption as they are largely dependent on the accuracy of the food and nutrient composition databases and self-reported estimates of intake. Consumers often are unaware of specific ingredients in the foods they consume including pulse type or amount. Advancing the science in this area requires better dietary data collection methods and improvements in databases to correctly classify, quantify, and more accurately capture pulse or legume type, all of which are impacted by how researchers and consumers define pulses or legumes.

3.2. Population-Based Dietary Surveys

Population-based data from dietary surveys constitute another way legumes and pulses have been studied [7,11–14,22]. Dietary surveys are used to inform dietary recommendations including DGA by providing data on trends in intake, dietary patterns, and nutrient intakes. They are also used for monitoring dietary intakes in the population and to guide research; however, most studies have focused on the broader category of legumes with little to no data on pulses specifically.

In 2009, the National Health and Nutrition Examination Survey (NHANES) was one of the first to assess intakes of pulses in the U.S. [7], with several others that followed including studies conducted on the Canadian Community Health Survey to describe pulse intakes in the Canadian population [11–15]. The most important and consistent finding that emerged from these few population-based studies, however, is that that diet quality is improved on days when pulses are consumed [7,11–14]. This improvement in diet quality is notable when $\frac{1}{2}$ cup (~100 g) or more of pulses are consumed, and significantly higher intakes of many nutrients, especially fiber, are observed at all levels of consumption when comparing pulse consumers with non-consumers [7,11,13]. The Canadian study takes this one step further and evaluated the diets in comparison to dietary reference intakes for many of the nutrients; the results showed that a greater proportion of the population met the reference intake on days when pulses were consumed compared to days when they were not [13]. These data suggest that not only is dietary quality better on days when pulses are consumed but pulse consumers were more likely to meet dietary intake recommendations for several key nutrients.

To our knowledge, there is little or no pulse consumption data similar to the population based dietary surveys in the U.S. or Canada. This is a significant research gap, especially when considering the nutritional implications in countries where nutrient intakes are well below recommended levels. What little is known about global pulse intakes, particularly in low-income or middle-income countries, comes from per capita supply or the availability of pulses for use as food as an estimate of the average consumption but does not provide any useful data on the impact of pulse consumption on nutrient intakes or diet quality [9].

Even though dietary surveys can provide critical data for monitoring nutrient intakes, estimating intakes of specific foods, and identifying dietary patterns, they have similar limitations to other types of epidemiological pulse or legume research (e.g., prospective cohort studies) including reliance on self-reported dietary intakes, as discussed above. As with other types of pulse research, clearer definitions and classification of pulses and legumes could also improve the estimation of pulse intake from these surveys.

4. Categorization of Pulses and Optimal Intake

Without a doubt, the inclusion of the terminology "pulses" defined as dry beans, peas, and lentils in the 2020–2025 DGA is a step towards recognizing the unique characteristics of pulses separately from other legumes; however, there is still room for more clarity in the DGA [4]. For example, green soybeans (edamame) are included in the vegetable subgroup "beans, peas, lentils" despite being the only non-pulse included in the subgroup. Green (snap) peas and green beans (string beans/snap beans) are both legumes, but green peas are placed in the "starchy vegetable" subgroup and green beans are placed in the "other vegetable" subgroup even though they have similar compositions. DGA also do not include chickpeas often referred to as garbanzo beans as a separate pulse type in their definition of a pulse, which could also contribute to confusion as it does not recognize chickpeas as the separate botanical group it is and does not fully align with the FAO's definition of a pulse [6].

When considering individual dietary patterns in the most recent DGAs, foods in the "beans, peas, lentils" subgroup can be considered either a vegetable or a protein to meet recommended intakes [4]. Despite some confusion in the U.S. guidelines, this is even more persistent in dietary guidance across the globe even though the terminology "pulse" is more commonly used and understood [23]. The inconsistency is really in the placement of pulses in the diet; for example, some countries place pulses in a "fruit and vegetable" category while others place pulses in a "meat and meat alternate" category. Much of these inconsistencies might be a reflection in differences in dietary patterns or in the manner pulses are usually consumed [23]. For example, in some African and Asian countries, pulses are a staple food consumed almost every day, whereas in the U.S., Canada, and Europe, pulses are more typically consumed as an occasional side dish or soup and often in place of other vegetables [7,24].

There is also little consensus globally about what constitutes a pulse serving size or the recommended frequency of pulse consumption [23]. In the U.S., there has been some rather significant changes in the recommendations over time [4,24,25]. The most recent 2020–2025 DGAs recommend 1.5 cup equivalents of beans, peas, and lentils per week for individuals following a 2000-calorie healthy U.S.-style dietary pattern or a 2000-calorie healthy Mediterranean-style dietary pattern. For individuals following a 2000-calorie healthy vegetarian dietary pattern, the DGAs recommend 3 cup equivalents of beans, peas, and lentils per week [4]. The 2005 DGA [25] specified 3 cups of legumes (beans and peas) per week as the recommended level of intake for all individuals (i.e., not only one subset of individuals such as vegetarians) based on their contributions of nutrients that were limiting in the diets of Americans (e.g., potassium, folate, and fiber); however, in 2010, this recommendation decreased to 1.5 cups of legumes per week with no apparent justification [24]. There is a rather complex history of how DGAs have evolved over time with a shift towards more science-based recommendations and, perhaps, this explains to some extent why recommendations for pulses (or legumes) have changed [26]. With that in mind, there is little doubt that scientific evidence will be the basis for any change in current recommendations. While limited in scope, the more recent literature that is available has suggested that positive health outcomes are observed at pulse intakes of around $\frac{1}{2}$ cup or 100 g per day, which is higher than the amount currently recommended by the DGA for individuals following a healthy U.S.-style and healthy Mediterranean-style dietary pattern. More directed research on pulses specifically using consistent pulse terminology and better agreement about where pulses fit into the context of a healthy dietary pattern would provide a stronger basis for defining optimal intakes for health and ensure dietary guidance is recommending that American's consume the most optimal amounts.

5. Future Directions

Despite the research gaps and limitations of the existing literature, population-based consumption data show improvements in diet quality on days when pulses are consumed [7,11–14]. Other epidemiological evidence demonstrates associations between pulse intake and health outcomes and clinical evidence shows positive metabolic response to diets containing pulses [15–21]. Furthermore, the studies support health benefits from consuming at least $\frac{1}{2}$ cup cooked (~100 g) of pulses per day, which suggests that intakes above 1.5 cups per week may be more optimal [7,11,13,20]. Less than 10% of the U.S. population meets recommendations for fiber, and many of the key nutrients in pulses such as potassium, magnesium, and choline were noted by the DGA 2015 committee as nutrients of concern [5]. This alone supports increasing pulse consumption as one potential strategy towards achieving healthier dietary patterns. Another potential strategy is shifting towards more plant-based diets by substituting some or most of the animal protein with plant sources such as pulses. This is often referred to as a flexitarian approach and is increasingly popular for its perceived health benefits, but more research on flexitarian diets that incorporate pulses is needed. Our market place continues to expand with a plethora of innovative ways pulses are incorporated into a variety of foods. The unique composition of pulses makes them well suited for incorporation into pastas, cereals, snack foods, soups, and beverages. These innovative food technologies could play a role in overcoming hurdles to increase pulse consumption making pulse-based food more palatable and nutritious.

Additional research specifically directed at pulses apart from the broader legume category is warranted. Long-term clinical trials assessing pulse exposure within well-controlled diets will add to the body of evidence around the optimal intake of pulses at which health benefits are maximized. Future research from national food intake surveys including modeling studies that quantify the impact of pulse ingredients as additions and/or replacements in multi-component foods will be important to further capture the impact of pulses on nutrient intakes from these foods. Modeling studies rely on the placement in the context of a healthy diet (e.g., pulses can be counted as both a vegetable or a protein) and how pulses are defined. Advancing the science in this area requires better data collection methods and improvements in databases in order to more accurately capture and quantify the intake of specific pulses. Identifying and correctly classifying legumes and pulses will advance all types of research in this area, refine dietary recommendations, and improve public health.

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