

# Effect of sorghum consumption on health outcomes: a systematic review

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**Context:** Sorghum, an ancient grain originating in Africa, may have health-protective properties that could encourage its consumption among those who do not traditionally consume it. **Objective:** The aim of this systematic review was to evaluate the health effects associated with the consumption of sorghum among humans. **Data Sources:** Academic databases were searched for relevant studies published between 1985 and November 2015. **Study Selection:** Nineteen studies – 13 interventional and 6 observational – were identified for inclusion. **Data Extraction:** Participant characteristics, study country, health outcomes, main findings, and study quality were reported. **Results:** Studies were divided into those that investigated the effect of sorghum on chronic disease and those that investigated other effects of sorghum on health. There was evidence that the consumption of sorghum attenuated blood glucose responses and decreased the expression of markers of oxidative stress. Sorghum was also observed to be a suitable ingredient for the formulation of oral rehydration solutions and showed potential for use as a medical adjunct to boost immune responses in HIV-positive patients. **Conclusions:** The implication is that sorghum may have attributes superior to those of other staple grains, indicating its potential for innovative uses in commercial foods. More work is required to elucidate the health effects of sorghum when consumed by population groups that have not been traditional consumers of the grain.

## INTRODUCTION

Cereals and pseudocereals, consumed throughout the world, are responsible for approximately 35% of daily dietary energy intake.<sup>1</sup> Recent meta-analyses have determined that the risk of coronary heart disease,<sup>2</sup> cardiovascular disease,<sup>3</sup> and type 2 diabetes<sup>4</sup> is significantly reduced among individuals who consume at least 2 servings of whole grains per day compared with those who consume none. It is also reported that consumption of a diet low in whole grains is the fourth most prominent dietary risk factor contributing to the global burden of disease.<sup>5</sup> At the community level, popular

diets such as the high-protein Paleo diet recommend the avoidance of all grains,<sup>6</sup> contrary to messages in the dietary guidelines established by health authorities.<sup>7,8</sup>

The focus of these dietary guidelines is to translate scientific research into evidence-based advice for the population. Policy documents such as the most recent revision of the Australian Dietary Guidelines<sup>7</sup> and the Australian National Food Plan emphasize the importance of a sustainable food system to future-proof production practices.<sup>9</sup> Because grain-based products form an integral part of the global diet, promoting the consumption of grains that are particularly tolerant to fluctuations in environmental conditions is socially and

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Key words: cereal, chronic disease, grain, human, sorghum.

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commercially desirable. This, coupled with the ongoing consumer demand for gluten-free ancient grains,<sup>10</sup> has encouraged research efforts to explore the health benefits of a range of grains, including sorghum.

Originating in northeastern Africa,<sup>11</sup> sorghum (*Sorghum bicolor* [L.] Moench) is a gluten-free grain<sup>12</sup> that is drought tolerant<sup>13</sup> and consumed as a dietary staple in parts of Africa and Asia.<sup>14</sup> In contrast, in the United States and Australia, sorghum is used predominantly as an animal feed, with only a small quantity used for the manufacture of human foods.<sup>11</sup> This is despite the presence of bioactive compounds such as proanthocyanidins, 3-deoxyanthocyanidins, and flavones,<sup>15</sup> which have been purported to inhibit the growth of cancer cells in vitro<sup>16,17</sup> and to induce anti-inflammatory effects,<sup>18</sup> albeit in animal models. These compounds are not present in all varieties of sorghum,<sup>19</sup> but if the unique health benefits associated with them could be replicated in humans, there may be increased consumer engagement, facilitating opportunities to develop new sorghum-based products for the human food supply. An important issue is the need to process sorghum to facilitate human consumption, which has implications for researchers and manufacturers.

Previous research has explored the health benefits of sorghum, but most of it has focused on animal models and in vitro studies. Some reviews have investigated specific compounds, such as phytochemicals,<sup>20,21</sup> or the effect of processing on the composition of the grain.<sup>22</sup> Others have provided a general overview of nutritional composition and have examined the health implications of the compounds identified.<sup>23,24</sup> The broad conclusion is that human studies are needed to accurately define the health properties of sorghum.

There is currently a small body of evidence investigating the effect of sorghum consumption on human health outcomes. Systematic reviews of these studies can provide valuable insights into potential health benefits attributed to sorghum as well as guidance for future human intervention studies. The aim of this review is to evaluate the evidence for health effects associated with the consumption of sorghum in the human diet.

## METHODS

A systematic literature review was performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.<sup>25</sup> The protocol, including search strategies, inclusion criteria, quality assessment, and method of analysis, was registered with PROSPERO (International Prospective Register of Systematic Reviews; <http://www.crd.york.ac.uk/PROSPERO>), registration number CRD42015024024, prior to commencement.

## Inclusion and exclusion criteria

Owing to the paucity of human studies investigating effects of sorghum consumption, any studies that explored an association between sorghum consumption and health outcomes in humans were considered. A health outcome was defined as a measurable effect on a biologically or physiologically relevant parameter in humans. This could include (but was not limited to) the impact of sorghum consumption on disease biomarkers, anthropometric measures, mortality, and morbidity. The definition did not include bioavailability or digestibility of nutrients from sorghum. Studies investigating these characteristics were excluded from the review.

Original research published in the English language after January 1985 was included. Articles were excluded if they did not appear in a peer-reviewed journal or if they were review articles or conference abstracts. A single author (T.S.) conducted the search and selected the articles.

*Intervention/exposure.* To be eligible for inclusion, at least one group of participants within the study must have been consuming sorghum as part of the diet. The sorghum could be present in native form (grain sorghum), processed form (refined, milled, cooked, etc), or extracted form (such as the germ or endosperm) or included as an ingredient in a food product. Studies were excluded if a range of foods (including sorghum) were included as part of the intervention diet, unless the effect of sorghum could be separated from the effect of the other factors in the diet.

*Comparison group.* The study was excluded if the control group was also exposed to sorghum, unless one of the following was applicable: (1) the study had a cross-over design with 2 distinct periods (1 in which sorghum was included in the diet and 1 in which it was absent from the participants' diet); or (2) the study was an observational study that made between-group comparisons on the basis of the frequency of and/or the quantity of sorghum consumption or compared a pre-test (prior to sorghum consumption) period with a post-test (after sorghum consumption) period.

If the control/comparison group was exposed to an alternative source of nutrients (eg, in an intervention study), these nutrients had to be in the form of a food to enable valid comparisons between the control group and the intervention/sorghum group.

*Study design.* Experimental and observational studies conducted over all time frames were considered. A summary of the participants, interventions, comparisons,

### Box 1. PICOS criteria for inclusion and exclusion of studies

Parameter	Description
Population	Males and females of any age, health status, socioeconomic status, and geographic location
Intervention/exposure	Consumption of sorghum in its raw form (grain sorghum), processed form (refined, milled, cooked, etc), extracted form (such as the germ or endosperm), or included as an ingredient in a food product
Comparison	Control/comparison groups that did not consume sorghum. If the control/comparison group was exposed to an alternative source of nutrients (eg, in an intervention study), these nutrients must have been in the form of a “food” to enable valid comparisons to be made
Outcomes	Effect of sorghum on health outcomes
Study design	No restrictions on study design

outcomes, and study design (PICOS) criteria is presented in [Box 1](#).

### Search terms and strategy

The following search terms were used: “sorghum,” “human,” “health,” “diet,” “benefit,” “subject,” and “intervention.” Combinations of these terms were joined with the Boolean operator “AND” to identify relevant articles during the search phase, performed in October and November 2015. The same set of search terms was used to identify relevant articles in the following databases: Agricola, Cambridge Journals Online, Cochrane Library, CINAHL, MEDLINE, PubMed, SAGE Journals Online, ScienceDirect, Scopus, SPORTDiscus, SpringerLink, Web of Science, and Wiley Online.

Initially, one author screened the titles of the articles for inclusion. The abstracts of potentially suitable articles were then reviewed. The full text of each potentially eligible article was retrieved and saved for further analysis. After two authors assessed the full text independently, articles were either included in the review or excluded on the basis of the predefined criteria. The reference lists of the articles included for review were also examined for additional articles, which were then assessed using the same eligibility criteria.

### Data extraction

A summary table was developed prior to the commencement of the review and contained categories relevant to the review. Intervention and observational studies were summarized separately. Study design, participant characteristics, country in which the study was performed, health outcomes, main findings, and study quality were included in the summary tables. Both the control diet and the intervention diet were reported for intervention studies. Inclusion criteria and the method used to assess dietary intake were reported for observational studies. For studies that met all eligibility criteria, the necessary data were extracted into one of the

mentioned tables by one author (T.S.) and then verified by a second author (E.B.).

### Quality assessment

Two approaches were used for quality assessment. First, the design of each included study (eg, randomized control trial, case-control study, or cohort study) was identified and recorded. The National Health and Medical Research Council levels of evidence criteria<sup>26</sup> were then used to assign a ranking to each of these studies. Next, the internal validity and the risk of bias among individual studies were assessed using the Health Canada quality appraisal tool.<sup>27</sup>

This tool enables intervention and observational studies to be assessed separately, with a possible score of 0 to 15 generated for intervention studies and 0 to 12 for observational studies. A point was scored for each “yes” response to the equally weighted questions that comprise the tool. Studies that scored at least 8 of 15 and 7 of 12 for intervention and observational studies, respectively, were high quality, while those scoring below these thresholds were low quality. Intervention studies were assessed on the basis of inclusion/exclusion criteria, group allocation, blinding, attrition, exposure/intervention, health effects, statistical analysis, and potential confounders. The same set of criteria, apart from group allocation and randomization, was assessed for observational studies. Instead, the quality appraisal tool for observational studies assessed the comparability of study groups at baseline.

The criteria included in the Health Canada tool were grouped together under the broad categories of “reporting” and “internal validity.” The categorization of criteria as either reporting or internal validity was guided by existing quality rating tools, such as the study quality checklist developed by Downs and Black,<sup>28</sup> which provides clear guidance about which criteria should be incorporated into these categories. Furthermore, the distinction between reporting and internal validity provided a transparent overview of the key elements that underpin the quality of individual

**Table 1** Questions and potential responses to assess reporting of the composition of sorghum

Category	Question	Response
Sorghum variety	Was the variety specified? If yes, what was the variety?	Yes/no Variety
Sorghum processing	Was the sorghum processed? If yes, how?	Yes/no/not reported Processing technique
Chemical analysis	Was a chemical analysis performed? If yes, are the results reported?	Yes/no/not reported Yes/no/not applicable

studies and enabled comparisons to be made across studies and, more broadly, across the body of literature.

Finally, the composition of sorghum was considered. Plant foods are known to differ in their nutritional composition because of genetic and environmental factors.<sup>29</sup> This may result in different health outcomes because of the varying composition of sorghum used in each individual study. Additionally, the degree of processing and the consumption of certain components of the grain may also have varying effects on health outcomes.<sup>22</sup> Thus, the variety of sorghum used in the study, the type of processing (if any) of the grain, and whether a chemical analysis of the grain (to determine nutritional composition) was performed were all reported. These factors provide a means of exploring the quality of the reporting in relation to the composition of sorghum used in each study (Table 1).

### Method of analysis

Because of the range of health outcomes being assessed, it was not possible to perform a meta-analysis. Instead, broad patterns were observed and used to group together specific health outcomes associated with the consumption of sorghum, such as chronic disease prevention. The data generated from studies investigating similar outcomes were synthesized at a group level rather than an individual level and were examined from a qualitative perspective, although the analysis incorporated quantitative estimates for studies that reported estimated effect sizes. Characteristics of the sorghum product that may have influenced health outcomes (such as processing), as well as compounds that may have been potentially responsible for generating these effects, were also explored in detail. Studies that were rated of higher quality (on the basis of the Health Canada appraisal tool) guided the discussion and underpinned the formulation of recommendations for future research.

## RESULTS

The systematic searches of the scientific databases resulted in the retrieval of a total of 1782 articles. After screening and eliminating articles that did not meet the eligibility criteria, 15 articles were included in the final

review (Figure 1). The reference lists of included articles were searched manually, resulting in 4 additional articles that met the eligibility criteria. The combination of electronic and manual searches led to the inclusion of 13 intervention studies and 6 observational studies.

### Quality assessment

Using the Health Canada Quality Appraisal tool, the quality of the intervention and observational studies was summarized separately in descending order (Table 2<sup>30–42</sup> and Table 3,<sup>43–48</sup> respectively). The overall scores for intervention studies ranged from 4 (low) to 12 (high), with the average being 7.5 (low). The overall scores for observational studies ranged from 3 (low) to 9 (high), with the average score being 7 (high). More broadly, 11 studies were classified as high quality, with the remaining 8 being of low quality. Among intervention studies, the scores obtained in the reporting component were generally superior to the internal validity scores, while the scores for these components among the observational studies were equivalent.

Information relevant to the composition of sorghum was poorly reported, with fewer than one-quarter of the studies stating the variety of sorghum used in the study and fewer than one-third performing an analysis of the composition of the grain (Table 4). Processing of sorghum was reported in 12 of the 19 studies, with all but 1 of these 12 also stating the processing method.

### Data extraction

The range of health outcomes assessed included the effect of sorghum consumption on blood glucose responses (5 studies), oral rehydration (5 studies), cancer (3 studies), a debilitating condition known as “nodding syndrome” that affects children (2 studies), growth (1 study), immune function (1 study), oxidative stress (1 study), and celiac disease (1 study). These studies were categorized dichotomously as studies investigating the following types of outcomes (Table 5): health outcomes associated with chronic diseases, such as type 2 diabetes and cancer, and other health outcomes associated with sorghum consumption, eg, treatments for conditions such as dehydration.

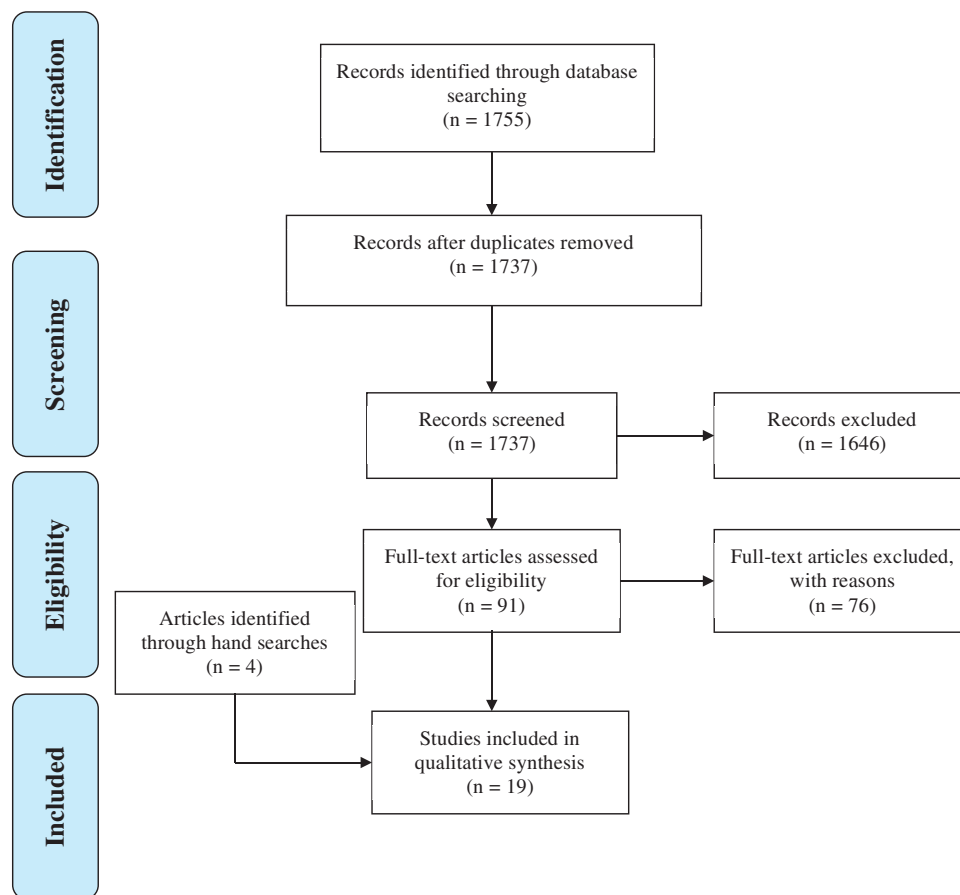


Figure 1 PRISMA flowchart of study selection process

Table 2 Summary of the overall quality of intervention studies (high or low), the classification of study design as per National Health and Medical Research Council (NHMRC) level of evidence guidelines, and the scores associated with reporting, internal validity, and overall study quality. The average scores for these components across all intervention studies are provided for comparison

Reference	Quality	NHMRC level of evidence	Reporting score (n/8)	Percentage of reporting elements satisfied (%)	Internal validity score (n/7)	Percentage of internal validity elements satisfied (%)	Total score (n/15)
Khan et al. (2015) <sup>30</sup>	High	II	8	100	4	57	12
Molla et al. (1989) <sup>31</sup>	High	II	7	88	3	43	10
Kenya et al. (1989) <sup>32</sup>	High	II	7	88	2	29	9
Mustafa et al. (1995) <sup>33</sup>	High	II	6	75	2	29	8
Abdelgadir et al. (2005) <sup>34</sup>	High	III-2	5	63	3	43	8
Poquette et al. (2014) <sup>35</sup>	High	III-2	5	63	3	43	8
Prasad et al. (2015) <sup>36</sup>	High	III-2	5	63	3	43	8
Lepage et al. (1989) <sup>37</sup>	Low	II	5	63	2	29	7
Pelleboer et al. (1990) <sup>38</sup>	Low	III-2	6	75	1	14	7
Mani et al. (1993) <sup>39</sup>	Low	III-2	4	50	2	29	6
Ayuba et al. (2014) <sup>40</sup>	Low	II	3	38	2	29	5
Prasad et al. (2016) <sup>41</sup>	Low	II	5	63	0	0	5
Lakshmi & Vimala (1996) <sup>42</sup>	Low	III-2	2	25	2	29	4
Average score or percentage	Low	–	5.2	65	2.2	32	7.5

*Health outcomes associated with chronic diseases.* Of the studies that investigated the effect of sorghum consumption on blood glucose responses, 3 were of high quality and 2 of low quality. After consumption of

sorghum, glucose and insulin responses were decreased by up to 26% and 55%, respectively,<sup>35</sup> compared with responses after consuming control foods such as wheat, maize, or rice. In addition, the glycemic index and



**Table 3 Summary of the overall quality of observational studies (high or low), the classification of study design as per National Health and Medical Research Council (NHMRC) level of evidence guidelines, and the scores associated with reporting, internal validity, and overall study quality. The average scores for these components across all observational studies are provided for comparison**

Reference	Quality	NHMRC level of evidence	Reporting score (n/6)	Percentage of reporting elements satisfied (%)	Internal validity score (n/6)	Percentage of internal validity elements satisfied (%)	Total score (n/12)
Zheng et al. (1993) <sup>43</sup>	High	III-2	4	67	5	83	9
Sewram et al. (2014) <sup>44</sup>	High	III-2	5	83	4	67	9
Gao et al. (2011) <sup>45</sup>	High	III-2	4	67	4	67	8
Foltz et al. (2013) <sup>46</sup>	High	III-2	4	67	4	67	8
Ciacchi et al. (2007) <sup>47</sup>	Low	IV	2	33	3	50	5
Tumwine et al. (2012) <sup>48</sup>	Low	III-2	2	33	1	17	3
Average score or percentage	High	–	3.5	58	3.5	58	7

**Table 4 Summary of the frequency with which included studies reported information pertinent to the composition of sorghum**

Reporting criterion	No. of studies that reported (n/19)	Percentage of studies that reported
Sorghum variety <sup>a</sup>	4	21
Processing of sorghum (method of processing <sup>b</sup> )	12 (11)	73 (92)
Performance of a chemical analysis <sup>c</sup>	6	32

<sup>a</sup>Varieties included red, red (tannin free), white (tannin free), narango, serena, bari, diri, and M35-1.

<sup>b</sup>Refers to the number or percentage of studies that reported the processing method (eg, milling, boiling, etc) among those that reported the sorghum had been processed.

<sup>c</sup>All studies that reported performing a chemical analysis also published the results from these analyses.

glycemic load of sorghum-based foods (apart from sorghum roti) were lower than those of equivalent wheat-based foods.<sup>36</sup>

Three high-quality case-control studies investigated the risk of esophageal, oral, and gastric cancers associated with dietary and lifestyle factors. The purpose of these studies was to identify factors that appeared to impart risk or protection, with the findings proving to be highly inconsistent. The results corresponding to sorghum consumption (after adjusting for potential confounders such as age, tobacco use, and alcohol use) suggested that individuals consuming the highest quantity in a cohort from Shanxi province in China were up to 5% less likely to develop esophageal cancer,<sup>45</sup> while individuals in the Eastern Cape of South Africa were 54% more likely to experience this outcome.<sup>44</sup> Risk of gastric cardia cancer increased by 1% for those consuming sorghum, while risk of gastric noncardia cancer decreased by 12% (gastric cardia cancer occurs at the point where the esophagus connects to the stomach [cardia], while gastric noncardia cancer is found in all other areas of the stomach).<sup>45</sup> Finally, sorghum consumption was associated with a 65% increased risk of oral cancer among hospitalized patients in Beijing.<sup>43</sup>

**Table 5 Categorization of outcomes identified through the systematic review**

Prevention of chronic disease	Other sorghum-associated outcomes
Blood glucose responses	Oral rehydration
Cancer	Nodding syndrome
Oxidative stress	Immune function
	Growth
	Celiac disease

Another study of high quality explored the impact of tannin-free sorghum on markers of oxidative stress. Two hours after the consumption of pasta containing 30% red sorghum, a 24% increase (compared with baseline) in the level of plasma polyphenols was recorded.<sup>30</sup> In contrast, the consumption of wheat pasta generated a 1% decrease in plasma polyphenols over this same time period.<sup>30</sup> In addition, a 34% increase in superoxide dismutase activity was recorded after the consumption of red sorghum pasta, compared with an increase of 0.7% after the consumption of wheat pasta. Finally, a marker of protein oxidation, protein carbonyl, decreased by 26% after red sorghum consumption but increased by 8% after wheat pasta consumption.

**Other health outcomes.** Three high-quality and 2 low-quality studies assessed the efficacy of using sorghum as part of an oral rehydration solution (ORS) for children with acute diarrhea. Compared with children treated with the standard World Health Organization (WHO) ORS, children treated with sorghum ORS consumed between 16%<sup>37</sup> and 42%<sup>31</sup> less ORS in the first 24 hours. This relative decrease in intake persisted over the entire period that children were treated with ORS. Treatment with sorghum ORS also decreased stool output by up to 40%<sup>37</sup> in comparison with WHO ORS treatment and decreased the average duration of diarrhea.

A high-quality case-control study conducted in Uganda<sup>46</sup> and 3 separate low-quality case-control

studies (results were pooled) conducted in South Sudan<sup>48</sup> attempted to identify underlying risk factors for the onset of nodding syndrome, a rare condition that affects the physical and neurological development of children and is characterized by paroxysmal episodes of head nodding.<sup>46</sup> In Uganda, the consumption of red sorghum was associated with a 40% increased risk of nodding syndrome, but this was not statistically significant.<sup>46</sup> The consumption of the serena variety of sorghum in South Sudan was associated with a statistically significant 5-fold increased risk of nodding syndrome.<sup>48</sup> There did not appear to be a statistically significant effect of consuming any other variety of sorghum in the same population group.<sup>48</sup>

Immune function in HIV-positive patients, growth among children, and safety for individuals with celiac disease were assessed in 3 separate low-quality studies. The consumption of a traditional preparation of sorghum (Jobelyn) in conjunction with antiretroviral therapy augmented the increase in CD4<sup>+</sup> T-cell counts beyond the increase seen with antiretroviral therapy alone.<sup>40</sup> The supplementation of traditional diets with sorghum was associated with an increase in height and weight among female children but no discernible differences among male children.<sup>41</sup> Finally, it was established that sorghum was a safe alternative for patients with celiac disease, with no gastrointestinal or nongastrointestinal symptoms observed after consumption.<sup>47</sup>

*Data presentation.* A summary of intervention and observational studies exploring the effect of sorghum consumption on outcomes associated with chronic disease is presented in Table 6 and Table 7, respectively. Similarly, Table 8 and Table 9 present a summary of intervention and observational studies that explore other health outcomes associated with the consumption of sorghum in the human diet.

## DISCUSSION

### Health outcomes associated with chronic diseases

The review of the literature suggests sorghum possesses nutritional properties that could facilitate a role in the management of chronic diseases. The favorable glycemic responses induced by the consumption of sorghum were similar in magnitude to the relative glucose attenuation induced by grains rich in  $\beta$ -glucan, such as oats and barley.<sup>49</sup> This has implications for food manufacturers and their choice of ingredients when products are developed for consumers who display health-conscious behaviors. In contrast, evidence from studies investigating a relationship between sorghum consumption and the risk of gastric and esophageal cancer,

estimated to be responsible for 14% of global cancer deaths annually,<sup>50</sup> is ambiguous. There appeared to be a stronger relationship between the consumption of sorghum and a reduction in the expression of markers of oxidative stress. Similar effects have been seen after the consumption of plant foods, such as fruit and vegetables,<sup>51</sup> suggesting that sorghum may possess functional bioactive compounds that can impart health benefits.

The mix of research described in this review was further scrutinized to identify the manner in which health benefits from consumption of sorghum appear to be maximized. In particular, factors that may have influenced outcomes, such as degree of processing, food composition, dose, and exposure time, need to be explored, as these variables have implications for manufacturing and for generation of health benefits.

*Blood glucose response.* The type of food and the degree of processing may have contributed to the efficacy of blood glucose and insulin attenuation seen after the consumption of sorghum-based products. Whether consumed as part of traditional foods, such as flatbread, porridge, dhokla, and roti, or as foods more commonly consumed in the Western diet, such as pasta, biscuits, and muffins, the attenuation of blood glucose after sorghum consumption persisted. This suggests that the matrix of nutrients present within sorghum remains active even after the grain is processed.

The favorable glycemic responses may have been facilitated by the presence and digestibility of starch. Previous in vitro research showed a reduction in starch digestibility of flatbreads prepared from sorghum<sup>52</sup> and an inverse correlation between starch digestibility and the sorghum content of pasta.<sup>53</sup> Levels of slowly digestible and resistant starch were higher in muffins prepared from sorghum than in wheat muffins and may have contributed to the attenuation of blood glucose and insulin responses.<sup>35</sup> Assessments of the starch content were absent from other reviewed studies. This should be addressed in future research order to establish how starch present within the matrix of the grain may affect glycemic responses.

The elevated dietary fiber content of sorghum (compared with that of wheat,<sup>36,42</sup> rice,<sup>36,42</sup> and maize<sup>34</sup>) may also have contributed to the observed glucose and insulin responses. An inverse relationship between dietary fiber content and glycemic response was apparent in 2 studies.<sup>36,42</sup> This association was absent when sorghum was compared with millet (*Panicum miliaceum*), which had less dietary fiber than sorghum but induced more significant improvements in blood glucose and insulin responses.<sup>34</sup> This suggests that other compounds present in the grain, such as polyphenols

**Table 6 Characteristics of intervention studies exploring the effect of sorghum consumption on outcomes related to chronic disease**

Reference	Study design	Participants <sup>a</sup>		Country	Control diet	Intervention diet	Health outcome	Main findings	Quality <sup>b</sup>
		Intervention group	Control group						
Khan et al. (2015) <sup>30</sup>	RCT	n = 20 Age = 23.5 y M = 30%	n = 20 Age = 23.5 y M = 30%	Australia	100% semolina pasta	Semolina pasta with 30% whole-grain red sorghum (tannin free) or 30% whole-grain white sorghum (tannin free)	Oxidative stress	Levels in red sorghum pasta group at baseline: plasma total polyphenols (216.90 mg GAE/L), total antioxidants (297.08 μmol/l), SOD activity (10.16 U/ml), and protein carbonyl (38.01 nmol/L). Levels at 120 min: plasma total polyphenols (269.4 mg GAE/L), total antioxidants (375.44 μmol/l), SOD activity (13.66 U/ml), and protein carbonyl (28.23 nmol/L) (all $P < 0.05$ ). The net change (levels at 120 min minus levels at 0 min) in plasma polyphenol concentration, antioxidant capacity, SOD activity, and protein carbonyl content was greater than the net change in these levels for the control pasta (all $P < 0.05$ )	High
Abdelgadir et al. (2005) <sup>34</sup>	Comparative	n = 10 Age = 50.2 y M = 40%	n = 10 Age = 50.2 y M = 40%	Sudan	Maize acida (porridge)	Sorghum kisra (flatbread) and sorghum acida (porridge)	Blood glucose response	AUC (glucose) for sorghum flatbread, sorghum porridge, and maize porridge was 389.3, 296.1, and 392, respectively (no stats). AUC (insulin) for sorghum flatbread, sorghum porridge, and maize porridge was 2950.6, 2418, and 4367, respectively (no stats)	High
Poquette et al. (2014) <sup>35</sup>	Comparative	n = 10 Age = 25.1 y M = 100%	n = 10 Age = 25.1 y M = 100%	USA	Whole-grain wheat muffin	Whole-grain sorghum muffin	Blood glucose response	Plasma glucose (insulin) response to sorghum muffins was reduced at 45, 60, 75, 90, and 120 (at 15, 30, 45, 60, 75, and 90) min (all $P < 0.05$ ) compared with response to wheat muffins.	High

(continued)



Table 6 Continued

Reference	Study design	Participants <sup>a</sup>		Country	Control diet	Intervention diet	Health outcome	Main findings	Quality <sup>b</sup>
		Intervention group	Control group						
Prasad et al. (2015) <sup>36</sup>	Comparative	n = 10 Age = 25.6 y	n = 10 Age = 25.6 y	India	Wheat roti (unleavened flatbread), wheat coarse rawa upma (thick porridge), wheat fine rawa upma, rice poha (flattened flakes), wheat pasta, and wheat biscuits	Sorghum multigrain roti, sorghum coarse rawa upma, sorghum fine rawa upma, sorghum flakes poha, sorghum pasta, and sorghum biscuits	Blood glucose response	Compared with the wheat muffin, the sorghum muffin reduced mean glucose and insulin responses by 25.7% (3863 to 2871 mg/dL) and 55.2% (3029 to 1357 mg/dL), respectively (both $P < 0.05$ ) Compared with the respective control, a lower GI was obtained for sorghum coarse upma ( $P < 0.05$ ), sorghum poha, and sorghum pasta (both $P < 0.01$ ). The GI of sorghum upma, sorghum poha, sorghum pasta, and sorghum biscuits was lower than that for the control ( $P < 0.01$ ). Sorghum roti had a higher GI than wheat roti ( $P < 0.05$ )	High
Mani et al. (1993) <sup>39</sup>	Comparative	n = 5 Age > 40 y	n = 5 Age > 40 y	India	50 g of glucose	Sorghum containing 50 g of available carbohydrate	Blood glucose response	No significant differences in blood glucose response between sorghum and glucose at 1 h or 2 h ( $P > 0.05$ )	Low
Lakshmi & Vimala (1996) <sup>42</sup>	Comparative	n = 6 Age range: 45–60 y M = 50%	n = 6 Age range: 45–60 y M = 50%	India	Wheat missi roti, rice upma, rice dhokla (fermented and fried grain)	Whole and dehulled sorghum missi roti, semolina upma, dhokla	Blood glucose response	Mean plasma glucose rose by 21.9 mg/dL, 20.3 mg/dL, and 26.6 mg/dL after 1 h among those consuming whole sorghum (missi roti, semolina upma, and dhokla, respectively). In comparison, mean plasma glucose rose by 30.8 mg/dL, 30.8 mg/dL, and 35.8 mg/dL after 1 h among those consuming wheat missi roti, rice semolina upma, and rice dhokla, respectively	Low

Abbreviations: AUC, area under the curve; GAE, gallic acid equivalent; GI, glycemic index; GL, glycemic load; SOD, superoxide dismutase; RCT, randomized control trial.

<sup>a</sup>Unless specified, age refers to the mean age of participants and M represents the proportion of male participants. Where M is absent, gender was not specified.

<sup>b</sup>Quality of the studies (high or low) was based on the Health Canada Quality Appraisal Tool: high ( $\geq 8$ ) and low ( $\leq 7$ ).

**Table 7 Characteristics of observational studies exploring the effect of sorghum consumption on outcomes related to chronic disease**

Reference	Study design	Participants <sup>a</sup>		Country	Inclusion criteria	Dietary assessment method	Health outcome	Main findings	Quality <sup>b</sup>
		Cases	Controls						
Zheng et al. (1993) <sup>43</sup>	Case-control	n = 404 Age range: 18–80 y	n = 404 Age range: 18–80 y	China	All oral cancer patients admitted to 1 of the 7 hospitals in Beijing	FFQ	Cancer	Compared with consumption of sorghum <1 ×/mo, consumption of sorghum 1–2 ×/mo and ≥3 ×/mo was associated with an 89% and 65% higher chance, respectively, of esophageal cancer diagnosis (both <i>P</i> > 0.05).	High
Gao et al. (2011) <sup>45</sup>	Case-control	ESCC group: n = 600 Age = 58 y M = 63% GCA group: n = 599 Age = 61 y M = 82% GNCA group: n = 316 Age = 57.5 y M = 76%	n = 1514 Age = 59 y M = 73%	China	Aged at least 20 y; from Taiyuan, Linfen, Jinzhong, Changzi, or Xinzhou; recently diagnosed with cancer of the esophagus or stomach; no previous treatment. Tumor treatment had to be performed at the Shanxi Cancer Hospital, and diagnoses had to be confirmed histologically by pathologists	Interviews	Cancer	Prior to 1984, consumption of sorghum as the primary staple was associated with a 5% risk reduction for ESCC, a 12% risk reduction for GNCA, and 1% risk increase for GCA (all <i>P</i> > 0.05). After 1984, consumption of sorghum as the primary staple was associated with a 1% risk reduction for ESCC and a 101% risk increase for GCA (both <i>P</i> > 0.05). No case of sorghum consumption in GNCA patients has been reported since 1984	High
Sewram et al. (2014) <sup>44</sup>	Case-control	n = 670M = 50%	n = 1188M = 52%	South Africa	Incident cases of squamous cell carcinoma of the esophagus diagnosed at 1 of the 3 major public referral hospitals in the Eastern Cape Province of South Africa	Interviews	Cancer	Compared with those who never consumed sorghum, males and females who consumed sorghum <2 ×/wk had a 64% and 98% increased risk of developing esophageal cancer, respectively (both <i>P</i> < 0.05). No significant association found between higher intakes of sorghum and esophageal cancer	High

**Abbreviations:** ESCC, esophageal squamous cell carcinoma; FFQ, food frequency questionnaire; GCA, gastric cardia adenocarcinoma; GNCA, gastric noncardia adenocarcinoma.

<sup>a</sup>Age refers to the mean age of participants and M represents the proportion of male participants. Where age is absent, the mean age or age range was not expressed. Where M is absent, gender was not specified in the study.

<sup>b</sup>The quality of the studies (high or low) was based on the Health Canada Quality Appraisal Tool: high (≥7) and low (≤6).

**Table 8 Characteristics of intervention studies exploring other health outcomes associated with the consumption of sorghum**

Reference	Study design	Participants <sup>a</sup>		Country	Control diet	Intervention diet	Health outcome	Main findings	Quality <sup>b</sup>
		Intervention group	Control group						
Molla et al. (1989) <sup>31</sup>	RCT	n = 35 Age = 29.4 mo	n = 42 Age = 28.7 mo	Bangladesh	WHO glucose ORS	Sorghum-based ORS	Oral rehydration	After the first 24 h, ORS intake was 140 mL/kg for the sorghum group vs 240 mL/kg for the glucose group ( $P < 0.001$ ). Stool output for the sorghum group was 215 mL/kg compared with 343 mL/kg for the glucose group ( $P < 0.001$ )	High
Kenya et al. (1989) <sup>32</sup>	RCT	n = 48 Age = 13 mo M = 100%	n = 50 Age = 11 mo M = 100%	Kenya	WHO glucose ORS	Sorghum-based ORS	Oral rehydration	After the first 24 h, ORS intake was 177 mL/kg for the sorghum group vs 214 mL/kg for the glucose group ( $P < 0.05$ ). No significant difference in stool output or diarrhea duration was observed	High
Mustafa et al. (1995) <sup>33</sup>	RCT	n = 34 Age = 18.1 mo M = 100%	n = 30 Age = 14 mo M = 100%	Sudan	WHO glucose ORS	Sorghum-based ORS	Oral rehydration	Duration of diarrhea (46.7 h) and ORS intake (2419.8 mL) in the sorghum group were lower than respective values (735.5 h and 3487.5 mL) in the glucose ORS group (both $P < 0.05$ )	High
Lepage et al. (1989) <sup>37</sup>	RCT	n = 50 Age = 10.7 mo M = 100%	n = 50 Age = 9.6 mo M = 100%	Rwanda	WHO glucose ORS	Sorghum-based ORS	Oral rehydration	Mean duration of diarrhea after starting rehydration was less for sorghum ORS group (26 h) than for WHO ORS group (38.8 h) ( $P < 0.01$ ). Total stool output was 134.5 g/kg for the sorghum group and 225.4 g/kg for the WHO ORS group, and ORS intake was 185.5 mL/kg for the sorghum ORS group and 284.2 mL/kg for the WHO ORS group (both $P < 0.05$ )	Low
Pelleboer et al. (1990) <sup>38</sup>	Comparative	n = 34 Age = 13 mo M = 65%	n = 30 Age = 12.5 mo M = 57%	Nigeria	WHO glucose ORS	Whole grain sorghum-based ORS	Oral rehydration	Duration of diarrhea was 92 h for sorghum ORS and 81 h for WHO ORS ( $P = 0.79$ )	Low
Ayuba et al. (2014) <sup>40</sup>	RCT	n = 27 Age range: 18–67 y Jobelyn: n = 8 Age range: 18–67 y	n = 16 Age range: 18–67 y Jobelyn: n = 8 Age range: 18–67 y	Nigeria	Not specified	Jobelyn	Immune function	CD4 <sup>+</sup> T-cell counts did not differ between the ART and ART + Jobelyn groups at baseline. At 6 and 12 wk, the group consuming Jobelyn in conjunction with ART showed an increase in CD4 <sup>+</sup> T-cell counts ( $P < 0.001$ ) compared with the group that received ART alone. CD4 <sup>+</sup> T-cell counts in the group that received Jobelyn alone increased at 12 wk ( $P < 0.01$ ) compared with baseline levels	Low
Prasad et al. (2016) <sup>41</sup>	RCT	n = 133 Age = 11.2 y (males) Age = 10.0 y (females) M = 41%	n = 129 Age = 11.07 y (males) Age = 9.9 y (females) M = 54%	India	Regular rice diet	Sorghum upma or khichide (breakfast) and roti (lunch)	Growth	Relative to the control group, height and weight increased by a greater proportion among females consuming sorghum. Relative to the control group, height and weight increased by a smaller proportion among males consuming sorghum. No statistical comparison was made	Low

Abbreviations: ART, antiretroviral therapy; ORS, oral rehydration solution; RCT, randomized control trial; WHO, World Health Organization.

<sup>a</sup>Age refers to the mean age of participants and M represents the proportion of male participants. Where M is absent, gender was not specified in the study.

<sup>b</sup>The quality of the studies (high or low) was based on the Health Canada Quality Appraisal Tool: high ( $\geq 8$ ) and low ( $\leq 7$ ).

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**Table 9 Characteristics of observational studies exploring other health outcomes associated with the consumption of sorghum**

Reference	Study design	Participants <sup>a</sup>	Country	Inclusion criteria	Dietary assessment method	Health outcome	Main findings	Quality <sup>b</sup>
		Cases	Controls					
Foltz et al. (2013) <sup>46</sup>	Case-control	n = 51 Age = 11.6 y M = 55%	Uganda	Village controls: n = 49 Age = 8.5 y M = 44% Household controls: n = 44 Age = 8.1 y M = 45%	Previously developmentally normal children aged 5–15 y with nodding episodes as well as another neurological abnormality	Interviews	Consumption of red sorghum (tannin content not stated) was associated with a 40% increased likelihood of displaying nodding syndrome ( $P > 0.05$ )	High
Ciacchi et al. (2007) <sup>47</sup>	Pre-test/post-test	n = 2 M = 0%	Italy	n = 2 M = 0%	None stated	None stated	Antitransglutaminase levels at baseline were 2.3 $\mu$ L and 3.4 $\mu$ L for the 2 patients. Levels 7 d after the last sorghum intake were 2.7 $\mu$ L and 3.5 $\mu$ L, respectively (no stats)	Low
Tumwine et al. (2012) <sup>48</sup>	Case-control	n = 82 <sup>c</sup>	South Sudan	n = 84	Cases with head nodding, head nodding and seizures, and seizures only	Interviews by key informants	Consumption of tannin-containing sorghum (serena) was associated with a 522% increased risk of experiencing nodding syndrome	Low

<sup>a</sup>Age refers to the mean age of participants and M represents the proportion of male participants. Where age is absent, the mean age or age range was not expressed in the study. Where M is absent, gender was not specified in the study.

<sup>b</sup>The quality of the studies (high or low) was based on the Health Canada Quality Appraisal Tool: high ( $\geq 7$ ) and low ( $\leq 6$ ).

<sup>c</sup>Three separate case-control studies were performed in neighboring villages. The results from all 3 are pooled together here.

(found in high concentrations in millet and sorghum<sup>54</sup>) and protein, may have affected glycemic outcomes.<sup>55</sup> Despite this, the presence of these compounds was not evaluated in any studies investigating glycemic responses and should be explored in future research.

Factors such as the ratio of amylose to amylopectin, the degree of starch gelatinization, and particle size are known to influence glycemic responses and have been shown to vary between whole and refined grains.<sup>56</sup> This was reflected by the consumption of whole-grain sorghum generating smaller net changes in blood glucose responses than products made from dehulled sorghum, wheat, or rice.<sup>42</sup> Similarly, muffins prepared from whole-grain sorghum significantly decreased the glucose and insulin response compared with whole-grain wheat muffins.<sup>35</sup> It would be advisable for future studies investigating glycemic responses to report the degree of processing the grain has undergone in order to evaluate the effect of processing on glycemic responses.

The favorable glycemic responses attributed to the consumption of sorghum suggest that the release of glucose into the bloodstream is more gradual. This is supported by the glycemic index of sorghum-based foods, which ranges from 45 for sorghum poha<sup>36</sup> (a dish of flattened, flaked grain) to 77 for roasted sorghum bread.<sup>39</sup> These values were superior to those of the corresponding control meal and provide further evidence that the matrix of nutrients present within the grain plays a synergistic role in generating positive outcomes. Future research should build on this evidence by focusing on the effect of sorghum consumption on satiety, which has been articulated by traditional sorghum consumers in Africa<sup>20</sup> but has yet to be scientifically validated.

Means of determining the serving size of sorghum-based and control meals varied from matching on the basis of carbohydrate content<sup>34,39,42</sup> to matching on a mass basis.<sup>36</sup> Although the comparison of the glycemic responses to foods with an equivalent carbohydrate load provides more robust scientific evidence at the population level, it is conceivable that individuals would be more likely to consume or substitute foods on a mass basis. Sorghum appeared to generate superior glycemic responses to wheat when equivalent serving sizes were consumed.<sup>36</sup> This has implications for future research methods and the translation of results to a broader population level.

An absence of standardization in the number of time intervals and overall timeframe used to calculate the incremental values for area under the curve is likely to explain part of the variability in the magnitude of blood glucose responses seen across the literature. Despite this heterogeneity, the results consistently showed that the consumption of sorghum induced

smaller peaks<sup>34,35,39,42</sup> and smaller overall changes<sup>34,35</sup> in blood glucose responses than did the consumption of control foods.

The attenuation of blood glucose responses was observed in healthy subjects<sup>35</sup> as well as in those with type 2 diabetes.<sup>34,39,42</sup> The observation of these positive outcomes across these population groups suggests the consumption of sorghum could contribute to health benefits for a wide range of individuals. Specifically, substituting sorghum for currently popular dietary grains such as wheat, rice, and maize may lead to more favorable control of blood glucose and insulin. This has implications for researchers and food manufacturers alike.

*Cancer.* Research in animal and in vitro models has shown that polyphenolic compounds present in whole-grain sorghum can inhibit the proliferation of breast cancer cells<sup>57,58</sup> and gastrointestinal cancer cells.<sup>59</sup> The 3 case-control studies investigating gastric, oral, and esophageal cancer did not specify if patients consumed whole or refined sorghum.<sup>43-45</sup> This may have contributed to the variability in cancer outcomes, since some individuals consumed whole-grain sorghum, rich in protective compounds, while others consumed refined sorghum devoid of such compounds.

The relative abundance of these polyphenols also depends on both environmental and genetic factors,<sup>20</sup> which varies depending on the geographical origin of sorghum. The case-control studies were conducted in China<sup>43,45</sup> and South Africa,<sup>44</sup> which suggests that different varieties of sorghum with unique nutritional compositions were consumed by the populations under study. Without a detailed chemical analysis, it is impossible to know the nutritional composition and associated phytochemical content of the specific sorghum consumed. Future work should endeavor to characterize the phytochemical composition of the sorghum used in a study in order to gain insight into the potential role of the specific compounds present.

There appeared to be an inverse relationship between frequency of sorghum consumption and risk of oral<sup>43</sup> and esophageal cancer,<sup>44</sup> particularly among females.<sup>44</sup> It is not possible to ascertain the quantity of sorghum needed to achieve a reduction in risk, since these studies focused on the frequency of sorghum intake, rather than the quantity. Despite this, frequency was not measured in a uniform manner, ranging from daily, monthly, or “staple” consumption.<sup>45</sup> A definition of “staple” was not provided, and thus it is conceivable that the ambiguity associated with this term led to inconsistent interpretations by study participants. This may have resulted in vastly different sorghum consumption levels being combined, decreasing the

precision of estimates linking sorghum consumption to cancer outcomes.

A potential weakness of the case-control studies, as well as a potential reason behind the ambiguous results, was the reliance on self-reported dietary consumption and time lag between actual consumption and data collection (up to 15 years).<sup>45</sup> Dietary intake was collected through a food frequency questionnaire,<sup>43</sup> validated by the Chinese Institute of Nutrition, or estimated through interviews conducted by nursing staff.<sup>44,45</sup> Since the cancer had already been diagnosed, retrospective questionnaires provided the solitary means of ascertaining dietary consumption prior to the onset of the cancer. Although the interviews were structured to allow nursing staff to conduct them, it is conceivable that employing trained dietitians would have generated richer information, such as type of sorghum (porridge, flat bread, etc) and the quantity consumed. This information would have provided insight into historical food consumption, which has particular relevance for sites such as the stomach, mouth, and esophagus, which are directly exposed to food and the associated nutrients on a regular basis.

The adjustment for confounders such as tobacco smoking and alcohol consumption provides a degree of assurance that the resulting empirical results were robust. However, because of the observational rather than experimental design of these studies, it is impossible to infer a cause-and-effect relationship between sorghum consumption and cancer outcomes. Moreover, the consumption of other grains such as wheat, rice, or millet was not associated with a change in cancer risk,<sup>44</sup> suggesting that grains may not play a significant role in the etiology of cancers of the stomach and esophagus. Instead, it was shown that a healthy dietary pattern comprised of sorghum, green leafy vegetables, green legumes, fruit, and meat had a protective effect against esophageal cancer, particularly in females.<sup>44</sup> This reflects the importance of understanding that dietary risk factors are more appropriately analyzed in the context of whole diets rather than individual foods.

The relatively large samples recruited for entry into these case-control studies suggest that the findings would be quite robust. However, the total number of individuals consuming sorghum within these studies was quite small when compared with the size of the overall sample. This may explain the wide confidence intervals in these studies. It also reflects the challenge in assessing the effect of sorghum consumption on cancer outcomes, namely the difficulty in finding population groups that have consumed the grain on a regular basis.

The role of sorghum in the etiology of stomach, oral, and esophageal cancer is still unclear. Further understanding could be gained through research focusing



on the mechanistic basis behind purported effects in both animal and in vitro models. Concurrently, the incidence of cancer in population groups known to consume sorghum should be monitored over time (longitudinal studies) to provide insight into potential protective effects.

**Oxidative stress.** Elevated levels of free radicals in the human body contribute to oxidative stress, which has been implicated in the onset of cancer, arthritis, and degenerative diseases.<sup>51</sup> Compounds with antioxidant properties provide protection against these free radicals, with whole-grain sorghum, particularly the red, brown, and black varieties, being rich sources of phytochemicals that have antioxidant activity.<sup>20</sup> Pasta with a red sorghum content of 30% was shown to have a phenolic content approximately 4-fold higher than that of pasta prepared from wheat. Consumption of this pasta generated a significant reduction in oxidative stress, which is likely attributable to this elevated phenolic content.<sup>30</sup> Future research should focus on identifying these phenolic compounds in order to gain a deeper understanding of their bioactivity and potential functionality when incorporated into food products.

The randomized control trial of Khan et al.<sup>30</sup> provided compelling evidence that the consumption of tannin-free red sorghum decreased the expression of markers of oxidative stress. Moreover, the crossover design facilitated comparison of results among the same set of individuals, providing a robust framework for comparing outcomes. Furthermore, the acute reduction in markers of oxidative stress within a healthy cohort suggests that the compounds responsible for this effect are potent antioxidants. Future work should attempt to replicate and extend these findings by observing the effect of sorghum consumption over longer time periods and among unhealthy cohorts. These results would have broader implications for manufacturers of sorghum-based products and for the potential marketing strategies that could be used to engage consumers.

### Other health outcomes

While the majority of commercial interest is focused on the impact of sorghum consumption on outcomes related to chronic disease, there is a parallel body of literature that investigates health outcomes among population groups that consume sorghum on a regular basis. The majority of this research focuses on individuals in the developing world and the effect of sorghum consumption on acute infant dehydration and diarrhea, nodding syndrome, immune function among HIV-positive patients, and adolescent growth and

development. The safety of sorghum as a gluten-free food is also explored.

**Oral rehydration.** Dehydration among infants living in developing countries, commonly induced by diarrhea, is a significant public health issue, particularly since diarrhea is the second most common cause of death among children aged of 1 to 59 months.<sup>60</sup> Treatment methods are improving, with water and electrolyte ORS advocated by the WHO as an effective means of assisting recovery. Difficulties in accessing WHO ORS for remote communities, however, is concerning. This has spawned research exploring the efficacy of using grains, such as sorghum, for preparation of ORS.

The WHO has articulated an optimal osmolarity for ORS that was adjusted in 2003 to align with clinical best practice. The 5 studies investigating the role of sorghum as a potential component of ORS were all performed prior to this amendment, meaning that the efficacy of sorghum-containing ORS in comparison with that of the current WHO ORS is difficult to ascertain. Nonetheless, when compared with the previous WHO ORS, the sorghum ORS appeared to be at least as effective (and often superior) at facilitating rehydration.

There appeared to be a tendency for a smaller volume of sorghum ORS than WHO ORS to be consumed.<sup>31–33,37</sup> This may partially explain the decrease in overall output of stools observed in this group.<sup>31–33,37</sup> Furthermore, it was postulated that the presence of starch in the sorghum preparation resulted in a smaller osmotic penalty in the intestinal lumen than did the glucose molecules in the glucose-based solution.<sup>61</sup> This enables more water molecules to be transported across the intestinal lumen, providing enhanced opportunities to recover water and leading to improved recovery outcomes.

The range of definitions used by individual studies to define recovery from diarrhea may have contributed to the variation in results. Half of the studies showed that sorghum ORS significantly decreased the average duration of diarrhea by at least 12 hours,<sup>33,37</sup> while the other half noted a nonsignificant increase in the average duration of diarrhea, up to a maximum of 11 hours.<sup>32,38</sup> In addition, recovery time appeared to vary widely, with standard deviations of over 20 hours across the sorghum and WHO ORS groups. These findings reflect the complex interactions involved in recovery from diarrhea and the need to implement a clear framework for what constitutes recovery.

Differences in participant recruitment may provide an additional explanation for the range of findings. To be eligible for inclusion, the duration of diarrhea prior to study commencement was capped at 72 hours by 4 of the 5 studies. In contrast, Pelleboer et al.<sup>38</sup> allowed

participants to have experienced diarrhea for up to 14 days prior to entry. The findings suggest that sorghum ORS is less effective at inducing recovery from chronic diarrhea than from acute diarrhea. This should be further investigated in clinical settings.

The premise behind investigating sorghum as a potential ORS component was to identify its efficacy in assisting recovery from dehydration in communities that may not have reliable access to WHO ORS. Additionally, these communities may not have access to equipment that can be used to refine grain, meaning that they would be reliant on whole-grain sorghum. The absence of reporting on both the type of sorghum and the degree of processing among studies investigating the efficacy of food-based ORS is therefore a limitation. This shortcoming should be rectified in future work, particularly since sorghum is readily available in large areas of sub-Saharan Africa, where diarrhea is responsible for over 20% of infant deaths in certain areas.<sup>60</sup> The inclusion of sorghum in ORS preparations is therefore a sensible alternative that should be further explored to ensure sorghum-based ORS is at least as efficacious as the current WHO ORS preparation.

*Nodding syndrome.* The underlying cause of nodding syndrome is currently unclear, although various lifestyle, dietary, and environmental factors have been identified as possible etiological factors. Populations native to Uganda and South Sudan, who have shown susceptibility to this illness, are known to consume sorghum on a regular basis. Despite this, there was no evidence to suggest that the consumption of red sorghum<sup>48</sup> or 3 varieties of sorghum native to South Sudan had a significant impact on the number of individuals who experienced nodding syndrome.<sup>46</sup> In contrast, there appeared to be an increased risk of developing nodding syndrome among individuals who consumed the serena variety of sorghum, which was introduced as emergency food aid by the World Food Programme<sup>48</sup> but was not well accepted by local farmers because of its color and bitter taste.<sup>62</sup> This suggests the presence of undesirable compounds that could be evaluated in future research. The findings could provide insight into compounds that may be implicated in the etiology of nodding syndrome.

The difficulty in designing a study to determine the cause of nodding syndrome stems from the multifaceted etiology of this illness. The use of case-control studies was therefore a valuable method for gaining insight into the influence of potential causes. Furthermore, the matching of cases with appropriate controls enabled risk factors such as consumption of serena sorghum to be identified and explored. The exploratory nature of this research, however, did not provide sufficient scope

to identify the effect of consuming different quantities of sorghum on nodding syndrome outcomes. This, along with other risk factors, such as the presence of the parasitic nematode *Onchocerca volvulus* and exposure to wartime chemicals,<sup>46</sup> should be further investigated in future research.

*Immune function.* The practice of using traditional preparations for medicinal purposes is gaining increased support from the WHO, particularly for conditions such as HIV infection, usually treated with antiretroviral therapy. Antiretroviral therapy is available to only about 37% of HIV-positive patients living in Africa,<sup>63</sup> providing impetus for the identification of easily accessible traditional preparations with similar levels of efficacy. Jobelyn, a commercially available dietary supplement prepared from sorghum, is one such example, but it requires rigorous scientific examination before it can be approved as a medicinal compound.

Over a 12-week intervention period, the consumption of Jobelyn significantly increased the CD4<sup>+</sup> T-cell count in HIV-positive patients.<sup>40</sup> The results showed that Jobelyn augmented the effect of antiretroviral therapy alone. Although the mechanism of action is unclear, previous *in vitro* research showed that Jobelyn triggers antiviral immune responses by stimulating the production of natural killer cells and chemokines.<sup>40</sup> These promising findings should be explored across a larger sample to elucidate the efficacy of Jobelyn. This has implications for the management of illnesses such as HIV infection in geographic locations where there is limited access to medications available in more affluent countries.

*Growth.* Although sorghum is used as a dietary staple in parts of Africa and Asia, only 1 study has investigated the impact of sorghum consumption on outcomes related to growth and weight gain in children. Over an 8-month intervention period, the female group consuming sorghum exhibited an increased rate of growth and weight gain in comparison with the control group. In contrast, the male control group showed an increased rate of growth and weight gain compared with the group consuming sorghum.<sup>41</sup> These results may simply have been indicative of a catch-up effect caused by differences in baseline height and weight of the respective female and male study populations.<sup>41</sup> It is therefore difficult to attribute the height and weight outcomes in these children to the consumption of sorghum.

Future studies should investigate the effect of sorghum consumption in children considered overweight or obese. If the results from this type of study were favorable, they could provide a unique marketing point and act as an incentive for food manufacturers to

develop sorghum-based products. This would have broader implications for public health advocates and consumer adoption of sorghum into the diet.

**Celiac disease.** Sorghum was considered safe for individuals with celiac disease, although the methodology on which this outcome was based was not clearly presented. The levels of antitransglutaminase antibodies (generated in response to the presence of gluten) were not reported as frequently as was stated in the method. Although the reported levels of these antibodies were within a normal range, they were not measured immediately after the sorghum consumption period. If antibody levels remained within a normal range immediately after the consumption of sorghum, there would be compelling evidence that it is safe for individuals with celiac disease. In future work, these measurements must be reported in a clear and transparent manner. In addition, the gold standard for determining negative consequences associated with food consumption and celiac disease is gastroscopic examination for the presence of villous atrophy, but this was not performed at any stage.

The use of pre- and postintervention measures to determine outcomes related to celiac disease represents the lowest form of scientific evidence. Intervention studies are generally performed when very little is known about possible outcomes. They are used to gain insight into possible relationships. Therefore, to ensure sorghum is safe for patients with celiac disease, long-term studies should be conducted. Additionally, research should focus on identifying and characterizing the types of protein present in sorghum.

The small sample ( $n=2$ ) showed the exploratory nature of the research and a weakness of the study. This work provides a foundation from which to work, particularly since these 2 individuals were known to have celiac disease, and as such it is likely that sorghum would be safe for other individuals with similar conditions. Further work should investigate the protein composition of sorghum so that it can be compared with that of other grains regarded as safe for individuals who cannot tolerate gluten.

### Limitations of the review

The majority of studies focus on traditional foods that are not commonly consumed as part of the diet in regions such as Australia, Europe, and the United States. The effect of sorghum consumption on outcomes relevant to chronic disease in the developed world, where grains are commonly consumed as bread, pasta, and breakfast cereals, is difficult to infer. Without a clear understanding of the health effects of sorghum

processed into such foods, conclusions about the efficacy of sorghum as a potential health food will be limited.

The studies included in this literature review explore the health benefits of sorghum in isolation. Many foods, however, are not eaten individually but are consumed as part of a broader diet. The external validity of these studies is therefore questionable because the effect of consuming sorghum as part of a broader diet was not considered. It is not known how the consumption of sorghum within the context of a diet will affect health outcomes or whether the health effects identified in this review will still persist. This area requires more research, particularly in the discipline of nutrition, which focuses on the overall effect of dietary patterns on health outcomes.

A key limitation identified in this review is the absence of clear reporting of the physiochemical and nutritional composition of the food under study. Without knowing the nutrients contained in a food, it is very difficult to pinpoint the compound responsible for generating a particular effect. Although this is a simplistic view, it is often ignored in many quality-rating tools, which seek to categorize the overall quality of a study. When there is an absence of understanding of how particular compounds interact to generate a particular health outcome, it would be valuable to know the nutritional composition of the food to gain insight into the compounds potentially responsible for this outcome. This is often ignored in studies of food, despite the need to characterize the ingredient or food prior to submitting health claims.

### Recommendations for future research

Future studies should aim to extend the current body of knowledge about the potential health benefits associated with sorghum. This includes an exploration of the extent to which hormones are affected by the consumption of sorghum, particularly those related to glucose and insulin responses and the associated effects on satiety. In addition, animal and in vitro studies suggest that sorghum has properties that could help fight cancerous cells by inhibiting their ability to regenerate and grow. This is likely related to the anti-inflammatory effects identified in this review and should be explored in human studies to quantify any potential benefits.

It is well established that the nutritional composition of plant-based foods such as sorghum can differ because of environmental and genetic factors. Bearing this in mind, studies that aim to investigate the effect of consuming plant foods should also report the physiochemical and nutritional composition of the food in question, since this can change depending on

processing. This suggestion is most relevant to intervention studies, where intake of the test food can be controlled, rather than observational studies, where participants have more freedom regarding the consumption of foods in their diet.

Future studies investigating the potential health benefits of sorghum should include independent tests of the composition of sorghum in order to improve understanding of the compounds that may be responsible for health outcomes. This would include the determination of various bioactive compounds in sorghum to understand their potential functionality in a human cohort. This is particularly relevant for food manufacturers, since food products rich in unique bioactive compounds may provide a point of differentiation in the market and be capable of generating additional returns through their sale to consumers.

From a commercial perspective, future work must explore the viability of incorporating sorghum into the food supplies of cultures that do not currently consume it on a regular basis. This would provide monetary value for manufacturers as well as insight into the potential for public health initiatives to leverage the desirable health properties of sorghum. Similarly, any benefits that can be attributed to the consumption of sorghum become redundant (to public health outcomes or commercially) if a sustainable supply of the grain cannot be secured. These considerations require additional work into the future.

## CONCLUSION

Despite playing a significant role in Africa and Asia as a staple grain, sorghum has only recently emerged as a potential human food source in the developed world. Research related to its desirable agronomic and nutritional properties is currently building the evidence base to determine its functional potential. Although the discipline of nutrition focuses on developing an understanding of whole foods and the importance of the complete diet for health outcomes, identifying individual compounds provides basic insight into the potential functional properties of a food. Compounds present within sorghum, particularly starch, dietary fiber, and phytochemicals, have been found to elicit desirable glycemic responses and reduce oxidative stress, which has implications for chronic disease. In addition, other uses of sorghum as an ORS component, as an adjunct to treatment for immune deficiencies in HIV-positive patients, and as a gluten-free food, showcase an array of nutritional benefits. Research aimed at translating these qualities to consumers and food manufacturers will contribute to the base of evidence that supports the inclusion of sorghum in the human food supply.

## Acknowledgments

*Funding/support.* The Grains Research and Development Corporation and the Rural Industries Research and Development Corporation provided one author (T.S.) with scholarships. Neither of these bodies had a role in the design, performance, or final approval of the review.

*Declaration of interest.* The authors have no relevant interests to declare.

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