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Anaemia prevalence may be reduced among countries that fortify flour

Jonathan S. Barkley[1,2], Kathleen S. Wheeler[1,2] and Helena Pachón[1,2]*

[1]*Food Fortification Initiative, 1599 Clifton Road, Atlanta, GA 30322, USA*

[2]*Hubert Department of Global Health, Rollins School of Public Health, Emory University, 1518 Clifton Road North East, Atlanta, GA 30322, USA*

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Abstract

The effectiveness of flour fortification in reducing anaemia prevalence is equivocal. The goal was to utilise the existing national-level data to assess whether anaemia in non-pregnant women was reduced after countries began fortifying wheat flour, alone or in combination with maize flour, with at least Fe, folic acid, vitamin A or vitamin B_{12}. Nationally representative anaemia data were identified through Demographic and Health Survey reports, the WHO Vitamin and Mineral Nutrition Information System database and other national-level nutrition surveys. Countries with at least two anaemia surveys were considered for inclusion. Within countries, surveys were excluded if altitude was not consistently adjusted for, or if the blood-draw site (e.g. capillary or venous) or Hb quantification method (e.g. HemoCue or Cyanmethaemoglobin) differed. Anaemia prevalence was modelled for countries that had pre- and post-fortification data (*n* 12) and for countries that never fortified flour (*n* 20) using logistic regression models that controlled for time effects, human development index (HDI) and endemic malaria. After adjusting for HDI and malaria, each year of fortification was associated with a 2·4 % reduction in the odds of anaemia prevalence (PR 0·976, 95 % CI 0·975, 0·978). Among countries that never fortified, no reduction in the odds of anaemia prevalence over time was observed (PR 0·999, 95 % CI 0·997, 1·002). Among both fortification and non-fortification countries, HDI and malaria were significantly associated with anaemia ($P < 0·001$). Although this type of evidence precludes a definitive conclusion, results suggest that after controlling for time effects, HDI and endemic malaria, anaemia prevalence has decreased significantly in countries that fortify flour with micronutrients, while remaining unchanged in countries that do not.

Key words: Fortification: Wheat flour: Maize flour: Enrichment: Micronutrients: Hb

Anaemia continues to be an important public health problem in many regions of the world, and there has been a little decrease in the global prevalence in recent years[1]. It is a major public health problem in many regions, particularly low- to middle-income countries with prevalence exceeding 40 %[2] for pre-school children in Central and West Africa, East Africa and Southern Africa, South Asia, and Oceania, and for non-pregnant and pregnant women of reproductive age in Central and West Africa and South Asia[1]. Compared with 1995, 2011 estimates of the prevalence of anaemia declined by 5 % points or less, from 47 to 43 % in pre-school children, 33 to 29 % in non-pregnant women (NPW) and 43 to 38 % in pregnant women[1]. Nutritional causes of anaemia include Fe and other nutrient deficiencies, while non-nutritional causes include malaria, infections and haemoglobinopathies[2].

Food fortification can address many of the nutritional causes of anaemia. That is, the risk for anaemia is lowered if foods are fortified[3] with nutrients known to influence Hb synthesis such as the minerals Cu, Fe, Se and Zn, and the vitamins A, B_2, B_6, folic acid (B_9), B_{12} and E[4]. A meta-analysis of efficacy trials has indicated that fortifying food with Fe increases Hb levels and decreases the prevalence of anaemia[5]. Currently, eighty-one countries mandate fortification of wheat flour alone or in combination with maize flour[6]. Fe and folic acid, the synthetic form of folate (vitamin B_9), are the combinations of fortificants most commonly used.

The evidence on the effectiveness of flour fortification for reducing anaemia is inconsistent. Ten publications were reviewed that summarise studies completed in twelve countries reporting Hb levels before and after initiation of flour fortification; inconsistent methodology across the studies precluded completing a meta-analyses of their results[7]. The nutrients added to wheat and maize flour in these studies included Fe, Zn and vitamins A, B_1, B_2, B_3, B_6, B_{12} and folic acid. Notably, in eight of the countries, the recommended Fe compounds[8] were used. The post-fortification measurement was conducted as early as 6·5 months after fortification began in one Australian study[9] and as late as 8 years

Abbreviations: DHS, Demographic and Health Surveys; HDI, human development index; NPW, non-pregnant women; PR, prevalence OR.

* **Corresponding author:** H. Pachón, fax +1 404 727 9745, email helena.pachon@emory.edu

after fortification began in Bushehr province in Iran[10]. A total of twenty-three subgroup analyses were reported. Of them, eleven reported an increase in Hb levels after flour fortification began. The increase ranged from 1 g/l in Brazilian pregnant women[11] to 21 g/l in Tajik children[12]. Of the total subgroups, twelve showed a decrease in Hb levels after fortification began, or no change in relation to a control group (nine analyses)[13]. In summary, the evidence from effectiveness trials is equivocal on whether fortification of flour with one or several nutrients improves Hb.

The objective of the present study was to use nationally representative anaemia surveys to assess whether anaemia prevalence was reduced in NPW after countries began fortifying wheat flour, alone or in combination with maize flour, with at least Fe, folic acid, vitamin A or vitamin B_{12}.

Methods

No identifying information of human subjects was used; thus, the present study was exempt from Institutional Review Board review.

Survey collection and determining anaemia prevalence

Nationally representative anaemia surveys of NPW were identified through Demographic and Health Surveys (DHS)[14], the WHO Vitamin and Mineral Nutrition Information System database[15], Multiple Indicator Cluster Surveys[16] and internet searches. The total number of NPW with measured Hb values and the proportion with anaemia were abstracted from each survey report. Anaemia proportions specific to NPW were not always reported in the final DHS reports; thus, data files were used to determine these values among countries with DHS (Table 1). To be consistent with DHS methodology, the anaemia variables were weighted as described by DHS[17] and Hb values between 0 and 60 g/l were considered implausible values for calculation and excluded. Altitude-adjusted Hb is included as a variable in the DHS data files and was used to determine anaemia prevalence. Anaemia prevalence was calculated as the proportion of NPW with Hb $<$ 120 g/l.

Inclusion/exclusion criteria

To ensure data consistency within a country, surveys were excluded if altitude was not consistently adjusted for (i.e. if one survey was adjusted for altitude and another was not), if different cut-offs were used to define anaemia, or if either the blood-draw site (i.e. venous or capillary) or the Hb-quantification method (i.e. HemoCue or Cyanmethaemoglobin) differed.

Countries were included in the analysis if at least two nationally representative anaemia surveys were conducted on NPW and met the inclusion criteria. Countries with flour-fortification programs were included if at least one anaemia survey was available before fortification was implemented, at least one survey was available at least 2 years after fortification was implemented, and the above criteria were met. A country was considered a ‘fortification country’ if wheat flour was fortified either alone, or in combination with maize flour, with at least Fe, folic acid, vitamin A or vitamin B_{12} (Table 1). Non-fortification countries were included if at least two surveys were available, they met the inclusion criteria, and no mandatory flour fortification was ongoing during the survey period.

Data collection of covariates

To control for factors associated with anaemia, data on the human development index (HDI) and malaria were collected. HDI data were obtained from the UN Development Program[18]. HDI is a single statistic that combines life expectancy, education and income indices into a composite value that represents a county’s social and economic development. HDI values range between 0 and 1; higher values are indicative of greater social and economic development. If an index was not available from the same year of a nutrition survey, then the index value from the closest available year ($\pm$ 4 years) was used (Table 1). A cross-sectional assessment of countries with endemic malaria was obtained from the WHO’s 2011 global malaria report[19] (Table 1).

Statistical analysis

Anaemia prevalence ratios were studied using logistic regression models separately for countries that fortified and for those that did not. A continuous exposure variable was used for countries that fortified and countries that never fortified. For countries with data during the pre- and post-fortification periods, exposure was coded as years since fortification was implemented ((before (negative values) or after (positive values)). For countries that never fortified, exposure was similarly coded as years since baseline (positive values), where baseline was defined as the year of the first available anaemia survey. Data were managed in Excel. In addition to the exposure variable, each model included HDI and endemic malaria (dummy coded 0/1). Modelling anaemia prevalence using the events/trials format of logistic regression allowed the sample sizes of each survey to be taken into account. All analyses were conducted using SAS 9.3 (SAS Institute, Inc.). Prevalence ratios were reported along with their corresponding 95 % CI, and an α level of 0·05 was used to determine statistical significance.

Results

Characteristics of data sets

Anaemia data from two countries with pre- and post-fortification data (El Salvador[20–23] and Guatemala[24–26]) and seven countries that never fortified (Azerbaijan[27,28], Guinea[14,29], Liberia[14,30], Mozambique[14,31], Sri Lanka[32,33], Vanuatu[16,34] and Vietnam[35,36]) were excluded because they did not meet the inclusion criteria. Table 1[6,14,37–67], therefore, summarises data from fortification countries that met the inclusion criteria

Table 1. Summary of country characteristics, survey results and covariate values for fortification (*n* 12) and non-fortification (*n* 20) countries that conducted nationally representative anaemia surveys on non-pregnant women (NPW)

			Fortification implementation		Survey					
Country	Grains fortified*	Nutrients added*	Year	Source	Year	Source	Np. of NPW	Anaemia prevalence (%)	HDI†	Endemic malaria‡
Bolivia	Wheat	B_1, B_2, B_3, B_9, Fe	1998	Pena-Rosas & Sinclair[37]	1998	DHS§[14]	2514	27·1	0·62	1
					2003	DHS[14]	4510	30·6	0·65	1
					2008	DHS[14]	4422	34·5	0·66	1
Costa Rica	Wheat, maize	B_1, B_2, B_3, B_9, Fe	1997	Pena-Rosas & Sinclair[37]	1982	Ministerio de Salud[38]	434	20	0·62	1
					1996	Rodriguez *et al.*[39]	820	18·6	0·71	1
					2008	Ministerio de Salud[40]	870	9·9	0·75	1
Fiji	Wheat	B_1, B_2, B_3, B_9, Fe, Zn	2005	National Food and Nutrition Centre[41]	2004	National Food and Nutrition Centre[41]	749	40·3	0·69	0
					2010	National Food and Nutrition Centre[42]	869	27·6	0·7	0
Honduras	Wheat	B_1, B_2, B_3, B_9, Fe	1997	Pena-Rosas & Sinclair[37]	1996	Ministerio de Salud Pública *et al.*[43]	1001	25·8	0·56	1
					2001	DHS[14]	3589	14·7	0·56	1
					2006	DHS[14]	17 354	18·5	0·59	1
					2012	DHS[14]	20 298	14·9	0·63	1
Indonesia	Wheat	B_9, Fe, Zn	2001	FFI database[6]	1997	Frankenberg & Thomas[44]	7598	33·8	0·54	1
					2000	Strauss *et al.*[45]	9881	36·6	0·54	1
					2007	Strauss *et al.*[46]	11 212	23·9	0·54	1
Jordan	Wheat	A, B_1, B_2, B_3, B_6, B_9, B_{12}, D, Fe, Zn	2002	FFI database[6]	2002	DHS[14]	1220	28·2	0·65	0
					2007	DHS[14]	3329	39·1	0·7	0
					2009	DHS[14]	3075	31·1	0·7	0
Mexico	Wheat, maize	B_9, Fe	1996	FFI database[6]	1988	Martínez *et al.*[47]	4025	15·4	0·65	1
					1998	Ministerio de Salud[48]	16 497	20	0·72	1
					2006	Ministerio de Salud[49]	20 480	16·4	0·75	1
					2012	Ministerio de Salud[50]	18 118	11·6	0·78	1
Nicaragua	Wheat	B_1, B_2, B_3, B_9, Fe	1997	Darnton-Hill *et al.*[51]	1993	Ministerio de Salud[52]	1730	33·6	0·48	1
					2000	Ministerio de Salud[53]	2083	22·3	0·53	1
					2003	Ministerio de Salud[54]	402	15·3	0·57	1
					2004	Ministerio de Salud[54]	413	9·4	0·57	1
					2005	Ministerio de Salud[54]	431	9·2	0·57	1
Peru	Wheat	B_1, B_2, B_3, B_9, Fe	1997	Darnton-Hill *et al.*[51]	1996	DHS[14]	1478	32·8	0·68	1
					2000	DHS[14]	4987	29·6	0·68	1
					2004	DHS[14]	20 146	25·2	0·7	1
					2009	DHS[14]	18 028	20·2	0·72	1
					2010	DHS[14]	18 023	20·1	0·73	1
					2011	DHS[14]	18 017	16·3	0·74	1
					2012	DHS[14]	19 562	16·5	0·74	1
Philippines	Wheat	A, Fe	2004	FFI database[6]	1982	Food and Nutrition Research Institute[55]	4439	27	0·56	1
					1987	Food and Nutrition Research Institute[56]	1632	38·9	0·58	1
					1993	Food and Nutrition Research Institute[57]	1691	24	0·58	1
					1998	Food and Nutrition Research Institute[58]	6012	34·3	0·61	1
					2008	Food and Nutrition Research Institute[59]	4202	20·7	0·64	1
Senegal	Wheat	B_1, B_2, B_3, B_6, B_9, B_{12}, Fe, Zn	2009	FFI database[6]	2005	DHS[14]	4088	58·2	0·44	1
					2009	DHS[14]	5610	63·3	0·46	1
					2011	DHS[14]	5182	53·8	0·47	1
Uzbekistan	Wheat	B_1, B_2, B_3, B_9, Fe, Zn	2005	FFI database[6]	1996	DHS[14]	4031	61·2	0·62	1
					2008	Northrop-Clewes *et al.*[60]	2580	34·4	0·64	1
Armenia	None	NA	NA	NA	2000	DHS[14]	5968	12·5	0·65	0
					2005	DHS[14]	5904	24·2	0·7	0

Table 1. *Continued*

			Fortification implementation		Survey					
Country	Grains fortified*	Nutrients added*	Year	Source	Year	Source	Np. of NPW	Anaemia prevalence (%)	HDI†	Endemic malaria‡
Benin	None	NA	NA	NA	2001	DHS[14]	1803	64·6	0·38	1
					2006	DHS[14]	2869	59·9	0·41	1
Burkina Faso	None	NA	NA	NA	2003	DHS[14]	2327	51·7	0·3	1
					2010	DHS[14]	4561	46·1	0·33	1
Cambodia	None	NA	NA	NA	2000	DHS[14]	2720	56·3	0·44	1
					2005	DHS[14]	6409	44·5	0·5	1
					2010	DHS[14]	7385	43·4	0·53	1
Cameroon	None	NA	NA	NA	2004	DHS[14]	4549	44·2	0·45	1
					2011	DHS[14]	7054	38·4	0·49	1
Egypt	None	NA	NA	NA	2000	DHS[14]	5275	26·7	0·59	1
					2005	DHS[14]	4368	38·3	0·63	1
Ethiopia	None	NA	NA	NA	2005	DHS[14]	3399	23·9	0·32	1
					2011	DHS[14]	9676	15	0·39	1
India	None	NA	NA	NA	1999	DHS[14]	2968	50·4	0·46	1
					2006	DHS[14]	88 719	53·2	0·52	1
Lesotho	None	NA	NA	NA	2004	DHS[14]	2221	33·1	0·43	0
					2009	DHS[14]	3087	26·5	0·45	0
Madagascar	None	NA	NA	NA	1997	DHS[14]	2846	41·7	0·43	1
					2004	DHS[14]	1293	45·7	0·47	1
					2009	DHS[14]	7610	35·1	0·49	1
Malawi	None	NA	NA	NA	2004	DHS[14]	1246	45·8	0·36	1
					2010	DHS[14]	4186	28·8	0·41	1
Maldives	None	NA	NA	NA	2001	Ministry of Health[61]	1287	49·6	0·59	0
					2007	Ministry of Health[62]	1284	15·4	0·66	0
Mali	None	NA	NA	NA	2001	DHS[14]	1874	59·7	0·27	1
					2006	DHS[14]	2520	57·7	0·32	1
Nepal	None	NA	NA	NA	1998	Ministry of Health[63]	3437	66·7	0·4	1
					2006	DHS[14]	1039	38·9	0·44	1
					2011	DHS[14]	5796	34·4	0·46	1
Rwanda	None	NA	NA	NA	2005	DHS[14]	3302	25·1	0·38	1
					2008	DHS[14]	3925	17·5	0·41	1
					2010	DHS[14]	4370	16·7	0·43	1
Tajikistan	None	NA	NA	NA	2003	Branca *et al.*[64]	2042	41·2	0·58	0
					2009	Ministry of Health[65]	2138	24·2	0·61	0
Tanzania	None	NA	NA	NA	2005	DHS[14]	6057	47	0·4	1
					2010	DHS[14]	6166	38·6	0·47	1
Timor- Leste	None	NA	NA	NA	2003	DHS[14]	3745	31·5	0·46	1
					2009	DHS[14]	2817	16·6	0·55	1
Zambia	None	NA	NA	NA	1998	Luo *et al.*[66]	1498	38·3	0·38	1
					2003	MOST *et al.*[67]	623	29·1	0·4	1
Zimbabwe	None	NA	NA	NA	2006	DHS[14]	5598	37·4	0·35	1
					2011	DHS[14]	5789	28·2	0·39	1

HDI, human development index; DHS, Demographic and Health Surveys; FFI, Food Fortification Initiative; NA, not applicable.
* Information obtained from most recently available data in FFI's database[6].
† HDI closest to the year the survey was conducted was obtained from a UN Development Program report[18]. All values are between 0 and 1, where 1 represents higher social and economic development.
‡ Endemic malaria was obtained from the WHO's 2011 global burden of malaria report[19], where 0 represents not endemic and 1 represents endemic.
§ All anaemia prevalence from DHS were calculated using the data files and analysis guidelines provided through the DHS Website.

(*n* 12) and from countries that did not fortify and met the inclusion criteria (*n* 20).

Modelling

Adjusting for HDI and malaria, each year of flour fortification was associated with a 2·4 % decreased odds of anaemia (prevalence OR (PR) 0·976, 95 % CI 0·975, 0·978; Fig. 1). Among countries that never fortified, no reduction in anaemia over time was observed (PR 0·999, 95 % CI 0·997, 1·002). In both models, HDI and malaria were significantly associated with anaemia, but with differing directions of association ($P<0·001$). HDI was inversely associated with anaemia among fortification countries such that a unit increase was associated with a large reduction in the odds of anaemia (PR 0·040, 95 % CI 0·036, 0·045); however, endemic malaria was also associated with reduced anaemia odds (PR 0·546, 95 % CI 0·522, 0·571). Among countries that never fortified, endemic malaria was positively associated with odds of anaemia (PR 2·805, 95 % CI 2·703, 2·911), and increasing HDI was also associated with increased anaemia odds (PR 3·890, 95 % CI 3·443, 4·394).

Discussion

The purpose of the present study was to use existing data sources to examine anaemia trends in NPW among countries that fortified wheat flour, alone or in combination with maize flour, and among those that did not. We found that after controlling for endemic malaria and HDI, significant reductions in anaemia prevalence were only observed among countries that initiated fortification. Among countries that fortified, each year of fortification was associated with a 2·4 % reduction in the odds of anaemia compared with each previous year. Although this type of evidence precludes a definitive conclusion, overall, the results suggest that flour fortification may be able to significantly reduce anaemia burden at the population level.

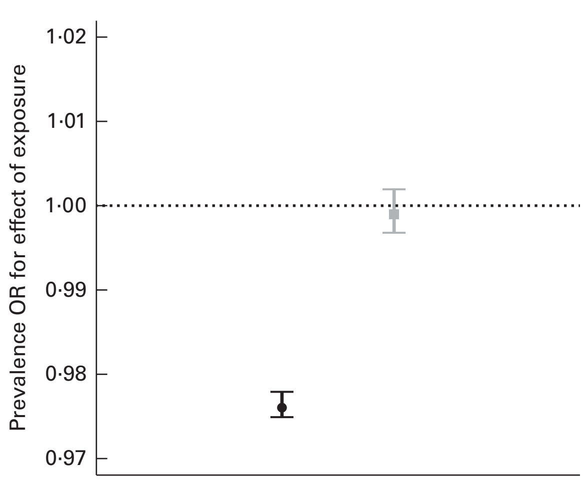

Fig. 1. Prevalence OR and 95 % CI for the effect of exposure on anaemia prevalence in non-pregnant women after controlling for human development index and endemic malaria. Exposure was coded as years since fortification was implemented for fortification countries (●, *n* 12) and year since baseline survey for non-fortification countries (■, *n* 20).

The reduction in anaemia prevalence in NPW found in the present study is consistent with the small (4 % points) global reduction in anaemia observed between 1995 and 2011 in NPW[1]. This small reduction is also consistent with the fact that fortification can only address nutritional causes of anaemia, such as Fe deficiency[68] or other nutrient deficiencies.

However, the conclusion that fortification can significantly lower the burden of anaemia at a population level contradicts findings from a desk review[69]. Hurrell *et al.*[69] reviewed the design of flour-fortification programs and concluded that most countries that fortify with Fe use non-recommended forms with low bioavailability that would not be sufficient to lower anaemia prevalence at the population level (*n* 50 of 78). Among the twelve fortification countries that were included in the analyses, seven currently use a higher-bioavailability Fe compound recommended by the WHO[8]. Since a greater proportion of countries that fortify using higher bioavailability Fe compounds were included in the present study, this may help explain why reductions in anaemia prevalence were observed. Fe levels and flour consumption among the included countries may have also influenced this result. In addition, Hurrell *et al.*[69] noted that compliance to fortification programs is often low and can play a contributing role to non-improvement over time. However, the present analysis did not assess the contributing effect of fortification compliance.

The present study attempted to address non-nutritional causes of anaemia by controlling for HDI and endemic malaria. HDI, composed from life expectancy, education and income indices, synthesises social and economic development – two underlying causes of anaemia[70] – into a single statistic. As expected, increased social and economic development (HDI) was inversely associated with anaemia prevalence in countries that initiated flour fortification. However, surprisingly, increased HDI was positively associated with anaemia among non-fortification countries. This unexpected result may be explained in part by differences in regional representativeness between the two groups of countries. As presented in Table 1, the non-fortification countries were more representative of Africa and tended to have lower HDI than the fortification countries. Since HDI values tended to be low in non-fortification countries (mean 0·46) compared with fortification countries (mean 0·63), it is possible that these values were not able to adequately capture differences in economic and social development between countries. Thus, among the non-fortification countries included in this analysis, large improvements in a macro index such as HDI would be probably necessary to capture population shifts in living conditions that would relate to improved nutrition and concomitant reductions in anaemia. Although endemic malaria was positively associated with anaemia among non-fortification countries, it was unexpectedly associated with decreased anaemia prevalence among fortification countries. This inverse effect may be partially explained by the fact that in a country that fortifies, those with malaria are also likely to consume fortified foods and are therefore getting more nutrients in their diets. Thus, in these countries, malaria status may not be as strong of a predictor of anaemia prevalence. This result may be further explained by the geographic representativeness of the countries, in addition to limitations due to how malaria was coded. African countries tend to have larger anaemia burdens due to malaria, infections, inflammation and hook worms. In regions where these non-nutritional anaemia causes play a role, food fortification would be expected to have less effect. Countries that fortified were more representative of the Americas (Table 1), which has a much lower malaria burden than Africa. Specifically, 83 % of confirmed reported malaria cases occurred in Africa, while only 4 % occurred in the Americans[19]. The graduations in endemic malaria exposure cannot be captured by the current 0/1 dummy variable coding, and thus, this may explain why the expected association was not observed among the fortification countries. This dummy coding was employed since poor malaria surveillance systems exist for many countries[19]. Unlike HDI, endemic malaria was assessed at one point in time (based on a 2011 WHO global malaria report[19]), and thus was not able to account for temporal changes in disease risk. However, since no significant impact was made on reducing global malaria prevalence between 1992 and 2002[71], and the malaria endemic countries as identified by WHO's malaria reports (only available since 2008) have remained largely unchanged, using a one-time assessment for malaria was likely acceptable. Nevertheless, in future investigations, employing more categories to represent graduations of malaria burden would be preferable. Other issues, such as the seasonality of malaria and differential participation rates, may have also influenced the malaria results among countries that fortified. Malaria has a lower disease burden during dry seasons[19]; thus, each survey's results could be biased depending on the season and the disease status (malaria or non-malaria) of those who agreed to provide blood samples.

There are both advantages and limitations to the present study that are important to recognise for future investigations that further explore these associations. This analysis was able to account for elapsed time through the use of continuous exposure variables (years since fortification implementation for fortification countries, and years since baseline survey for non-fortification countries). Countries that have been fortifying for a longer time are more likely to see reductions in anaemia simply because the intervention has had more time to take effect. Thus, considering exposure in this way can lead to more valid results than simply comparing countries that fortify to those that do not. The main advantage is that analyses were restricted to nationally representative surveys and an attempt was made to ensure data quality and consistency by excluding surveys that were not comparable within countries. In cases where raw data files were available for the countries, consistent adjustments for altitude were made so that data were not unnecessarily excluded.

However, the fact that exclusions were made may have influenced the results. As mentioned, two and seven countries were excluded from the fortification and non-fortification groups, respectively, because they did not meet the inclusion criteria. The most common reason for exclusion (n 7) was that both the blood-draw and Hb-quantification methods differed between surveys. It has been shown that each of these factors can influence reported anaemia prevalence[72]; thus, for future comparisons, it would be helpful if surveys followed consistent methodology over time. DHS were the most common source for anaemia data (Table 1) and consistently used capillary blood and the HemoCue method to measure Hb. Thus, if other investigations similarly followed consistent methodology, more accurate comparisons could be made between and within countries.

A main limitation of the present study was the small sample size. This limited the number of covariates that could be adjusted for in the analyses and may have led to biased associations. Residual confounding could still be present either from imprecision/measurement errors associated with covariates we adjusted for or from those that could not be considered in the present study. A final limitation worth noting is the generalisability of the results. Due to data availability, most non-fortification countries were from Africa (n 14 of 20), while most countries that initiated fortification were from Latin America (n 6 of 12). Due to these differences, a single model that matched a non-fortification country to a fortification country was not viable, and instead two separate logistic models were run. Using this approach still allows for conclusions to be made about each group of countries, and effects due to unmeasured or unknown confounders were likely similar within each group because the fortification and non-fortification countries were generally from the same region. Furthermore, despite small sample sizes, the CI obtained for the measures of effect between both groups of countries were narrow, suggesting good precision of the estimates.

In conclusion, after adjusting for important factors associated with anaemia, flour fortification was associated with decreased anaemia prevalence in NPW. Since efforts were made to control for other factors associated with anaemia, this observation is encouraging. Evidence that low bioavailable Fe compounds are typically used, as stated by Hurrell *et al.*[69], suggests there is room to improve Hb concentration through Fe fortification. Of the eighty-one countries that mandate fortification of wheat flour alone, or in combination with maize flour, only twelve had consistent, nationally representative anaemia data suggesting that increased surveillance efforts are important for most countries. As more anaemia surveys are conducted using consistent methodology, the association between flour fortification and anaemia prevalence will be better elucidated, and stronger support for the effectiveness of flour fortification may be achieved.

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None of the authors has any conflicts of interest to declare.

The authors' contributions are as follows: J. S. B., K. S. W. and H. P. designed the study; J. S. B. and K. S. W. conducted the study; J. S. B. analysed the data; J. S. B., K. S. W. and H. P. wrote the manuscript; J. S. B. had primary responsibility for the final content of the manuscript. All authors read and approved the final manuscript.

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