GUIDELINES FOR IMMIGRANT HEALTH

Appendix 15: Iron-deficiency anemia: evidence review for newly arriving immigrants and refugees

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ABSTRACT

Background: Iron-deficiency anemia is the most common nutritional disorder in the world. Subgroups of immigrants and refugees have higher prevalence of iron-deficiency anemia than the Canadian-born population has. Growing children and women of reproductive age are at highest risk for iron deficiency and related morbidity. We conducted an evidence review to identify actions to be taken by primary care practitioners to prevent morbidity from iron-deficiency anemia among newly arriving immigrants and refugees.

Methods: We systematically assessed evidence on the screening and treatment of iron-deficiency anemia including benefits and harms, applicability, clinical considerations, and implementation issues. The quality of the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Results: Prevalence of anemia is high in subgroups of newly arriving immigrants and refugees (women >15% and children >20%). Screening and treating iron-deficiency anemia in children can improve cognitive development to a modest degree. Screening and treating female patients of reproductive age can improve hemoglobin and function (work productivity). Iron-deficiency anemia in children is often a combination of inadequate diet, low iron stores at birth, and frequent infections leading to anorexia and poor food intake. High parity, malaria, and hemoglobinopathies increase the risk of anemia.

Interpretation: Immigrant and refugee children and women of reproductive age are vulnerable to iron-deficiency anemia. Key interventions to detect, treat and prevent reoccurrences include measuring hemoglobin levels and recommending iron supplements and other dietary modifications. A culturally responsive nutrition assessment and counseling, when available, can identify specific nutritional issues and support appropriate diet modifications.

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Box 1: Recommendations on iron-deficiency anemia from the Canadian Collaboration for Immigrant and Refugee Health

Children:

Screen for iron-deficiency anemia in children aged one to four years (with hemoglobin) to improve cognitive development. If children's iron levels are deficient, recommend iron supplements.

Basis of recommendation

- **Balance of benefits and harms:** Treating children with iron-deficiency anemia improves cognitive development with standardized mean difference of 0.30: equivalent to a modest effect of 1.5–2 intelligence quotient points (number needed to treat [NNT] 7; 95% confidence interval [CI] 5–14). Immigrant and refugee children have a higher prevalence of iron-deficiency anemia (> 20%) than Canadian-born children (< 20%). Adverse effects from iron treatment are minimal. The NNT for immigrant and refugee children is expected to be similar because many of the studies were conducted in developing countries. Adverse effects from iron treatment are minimal.
- **Quality of evidence:** Moderate
- **Values and preferences:** The Guideline Committee attributed more value to ensuring optimal opportunities for immigrant children and potential reduction of education, literacy and wage disparities between immigrant and Canadian-born populations and less value to the discomfort of testing and treatment risk of diarrhea.

Women:

Screen for iron-deficiency anemia (with hemoglobin) in immigrant and refugee women of reproductive age to improve hemoglobin levels and work productivity. If iron levels are deficient, recommend iron supplements.

Basis of recommendation

- **Balance of benefits and harms:** Treating iron-deficiency anemia provides a net change in hemoglobin of 15 g/L (NNT 2; 95% CI 2–3), an increase in function and a net change in the productivity ratio (NNT 4; 95% CI 3–8). The prevalence of iron deficiency is higher in immigrant women (> 15%) than in Canadian-born women (< 15%). Harms are minimal and include diarrhea and personal costs of iron supplements.
- **Quality of evidence:** Moderate
- **Values and preferences:** The Guideline Committee attributed more value to improving health among women of child-bearing age and less value to uncertainty about whether asymptomatic immigrant and refugee women value the treatment outcomes.

The cases

Amina is a newly arriving Somali-speaking 19-year-old refugee. She spent three years with her extended family in a refugee camp. She presents for an employment-related Mantoux test.

Sabeen is a 40-year-old Syrian-born mother with two children (Ishtar, four years old, and Asu, two years old) who arrived in Vancouver two months ago. She presents to have Ishtar's immunizations updated so that he can attend school. After some discussion, she also accepts a preventive care examination for herself.

How would you approach these patients?

Introduction

Anemia is an important global health problem with consequences for human health and development.[1] Iron-deficiency anemia, the most common cause of anemia, is the most common nutritional disorder in the world.[2] Other nutritional deficiencies and causes of anemia (such as malaria and hemoglobinopathies) could coexist, depending on the patients' diets, living conditions and genetic predispositions.[1] We focus on iron-deficiency anemia, which can lead to poor pregnancy outcomes, impaired physical and cognitive development in children, and reduced work productivity in adults.[2]

Since 1980, most Canadian immigrants and refugees have originated from developing countries.[3] Newly arriving immigrants and refugees have two to three times the prevalence of anemia (16%–28%) compared with the Canadian-born population (2%–10%), excluding First Nations populations.[4-7] Growing children and female patients (adolescent girls and women) of reproductive age have higher iron demands and are at increased risk for iron deficiency.[1,2] No routine iron-deficiency screening or supplementation program is offered in Canada for immigrants and refugees either before or after their arrival. We reviewed the burden of iron-deficiency anemia in the immigrant and refugee population, searched for evidence that evaluated the effectiveness of screening and iron-supplement interventions, and identified challenges in implementation. We focused our review on young children and women of reproductive age who are not pregnant.

Methods

We used the 14-step method developed by the Canadian Collaboration for Immigrant and Refugee Health team.[8] We constructed a clinician summary table to highlight the population of interest, epidemiology, clinical

considerations and potential key clinical actions (Appendix 2). We then constructed a logic model to define the clinical preventive action, outcomes and key clinical questions.

Search strategy for systematic reviews, guidelines and population-specific literature

We designed a search strategy in consultation with a librarian scientist to identify relevant systematic reviews and guidelines from electronic databases (MEDLINE, CINAHL, EMBASE and Cochrane Database of Systematic Reviews) and websites including the National Guideline Clearinghouse (www.guideline.gov), Public Health Agency of Canada (www.phac-aspc.gc.ca), US Preventive Services Task Force (www.ahrq.gov/clinic/USpstfix.htm), Canadian Task Forces on Preventive Health Care (www.canadiantaskforce.ca) and the World Health Organization (www.who.int/en). The search was limited to English-language articles published from January 1996 to July 2007. Two reviewers screened eligible systematic reviews for their relevance to the key questions. We appraised eligible systematic reviews using the National Institute for Health and Clinical Evidence critical appraisal tool to assess systematicity (the review must apply a consistent and comprehensive approach), transparency, quality of methods and relevance, and we appraised relevant guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument. A reference systematic review was chosen for each outcome of clinical importance.

We conducted a second literature search for January 2007–September 2007, to assess whether the reference systematic reviews needed to be updated or supplemented with recent studies. Studies were included if the design was a randomized controlled trial, controlled clinical trial, or cohort study using a placebo or no treatment comparison and was relevant to the key question. The search update was based on the US Task Force's systematic review on iron-deficiency anemia,[9] which was the most up-to-date and comprehensive assessment of the effectiveness of screening for and treating iron-deficiency anemia. To focus our evidence review, we selected the most up-to-date and relevant evidence. The US Task Force review recommends routine screening for iron-deficiency anemia in asymptomatic pregnant women and children aged 6–12 months who are at increased risk of iron-deficiency anemia (which includes new immigrants). We chose to focus on evidence related to the prevalence of iron-deficiency anemia in immigrant and refugee populations, cognitive effect in growing children, and work productivity in women of reproductive age.

Using the same databases as the first search (January 1980–July 2007), we conducted a third literature search to identify studies on iron-deficiency anemia focusing on immigrants and refugees. Areas of focus included baseline risk or prevalence; risk of clinically important outcomes; genetic and cultural factors (e.g., preferences, values, knowledge); and compliance variation. An updating search, focusing on randomized controlled trials and systematic reviews during the period January 1, 2007 to January 1, 2010, was conducted to determine whether any recent publications would change the position of the recommendation.

Synthesis of evidence and values

We compiled the evidence from systematic reviews and pertinent clinical trials using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) summary of findings tables, which assess both relative and absolute effects of interventions. We also appraised quality of evidence for each outcome using the GRADE quality-assessment tool, which assesses study limitations, directness, precision, consistency, and publication bias across all studies (Box 2). In the review of clinical considerations, we report implementation issues. Finally, we identify gaps in the research evidence.

Results

The initial search found no systematic reviews or evidence-based guidelines on screening for iron-deficiency anemia among immigrants and refugees. The literature search that focused on the general population identified 535 titles with references to iron-deficiency anemia (Appendix 1). A total of 29 citations were selected for critical appraisal, and reviewers retained 9 key reviews as background evidence.[9-18] We identified relevant systematic reviews that would help assess the effectiveness of screening for and treating iron-deficiency anemia[10,13,18] and provided new and primary evidence to the published clinical trials.[19,20] Seventy-six citations were retrieved in the general search for articles related to screening for and treatment of iron-deficiency anemia among immigrants and refugees.

What is the burden of iron deficiency among immigrant and refugee populations?

The World Health Organization estimates the prevalence of iron-deficiency anemia among preschool children (the

subgroup of children with the highest prevalence of anemia) to range from 21% to 68% in six world regions (Table 1).[1] The prevalence of iron-deficiency anemia for women of reproductive age ranges from 18% to 48% (Table 1).[1] The World Health Organization (Figure 2) describes anemia in Canada as a mild public health problem and estimates prevalence rates of 7.8% in preschool children and 14.3% in women of reproductive age.[1]

Anemia and iron-deficiency anemia are often used

Table 1: Anemia prevalence and number of people affected among preschool-age children and nonpregnant women in each WHO region (adapted with permission from the World Health Organization).

	% (95% CI)			
	Preschool-age children*		Nonpregnant women†	
WHO region	Prevalence	No. affected, in millions	Prevalence	No. affected, in millions
Africa	67.6 (64.3–71.0)	83.5 (79.4–87.6)	47.5 (43.4–51.6)	69.9 (63.9–75.9)
Americas	29.3 (26.8–31.9)	23.1 (21.2–25.1)	17.8 (12.9–22.7)	39.0 (28.3–49.7)
Southeast Asia	65.5 (61.0–70.0)	115.3 (107.3–123.2)	45.7 (41.9–49.4)	182.0 (166.9–197.1)
Europe	21.7 (15.4–28.0)	11.1 (7.9–14.4)	19.0 (14.7–23.3)	40.8 (31.5–50.1)
Eastern Mediterranean	46.7 (42.2–51.2)	0.8 (0.4–1.1)	32.4 (29.2–35.6)	39.8 (35.8–43.8)
Western Pacific	23.1 (21.9–24.4)	27.4 (25.9–28.9)	21.5 (20.8–22.2)	97.0 (94.0–100.0)
Global	47.4 (45.7–49.1)	293.1 (282.8–303.5)	30.2 (28.7–31.6)	468.4 (446.2–490.6)

Note: CI = confidence interval.
*Preschool-age children (0.00–4.99 yr).
†Nonpregnant women (15.00–49.99 yr).

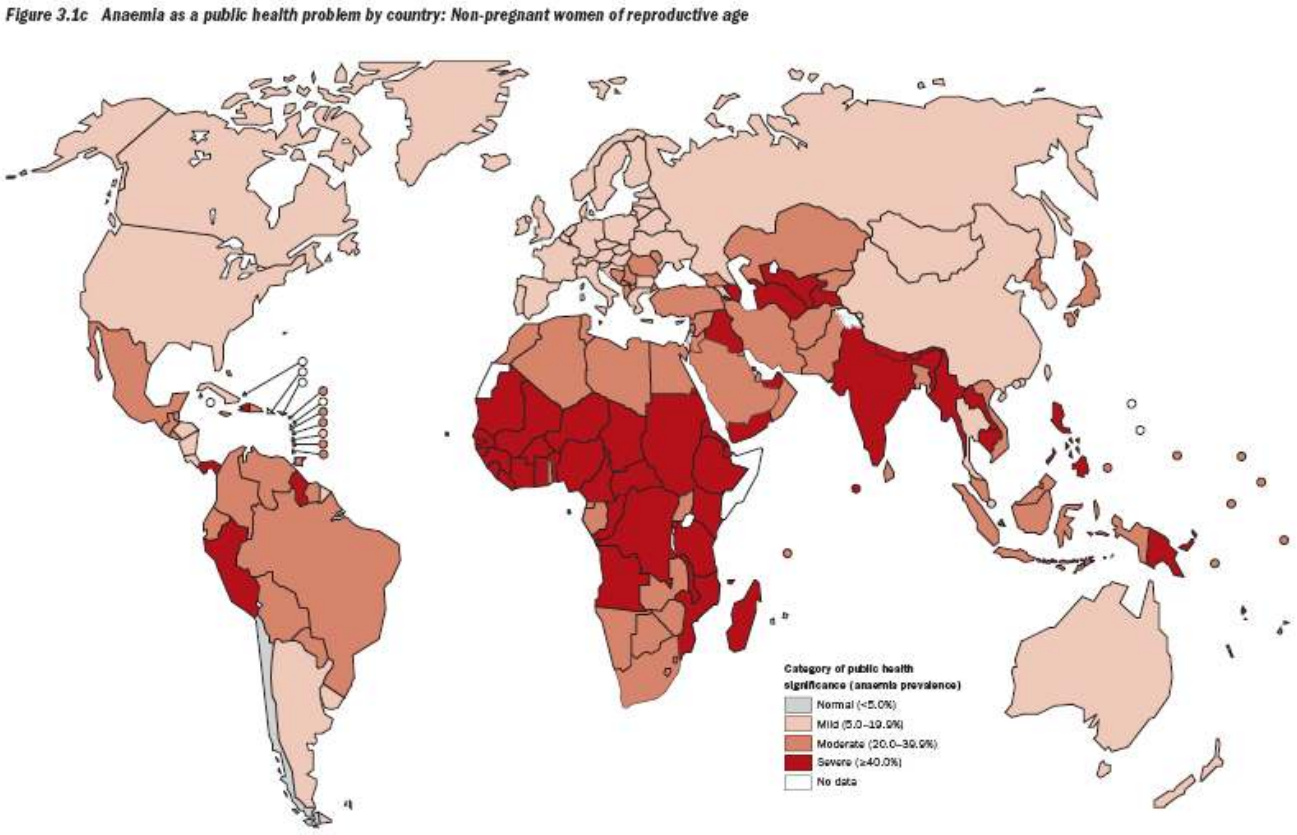

Figure 2: Anemia is a public health problem among nonpregnant women of reproductive age (reproduced with permission from the World Health Organization[1]).

synonymously, especially in prevalence studies where only the level of hemoglobin is reported without sufficient information to identify the causal factors underlying the anemia. It is now recognized that other nutritional disorders and other causes of anemia can coexist; however, etiologic data are limited. Data on the proportion of anemic people with moderate or severe iron-deficiency anemia are limited. Anemia occurs in young women in relation to heavy blood loss including menstrual bleeding. Among children, malaria, other infections (including hookworm and HIV), vitamin A and vitamin B_{12} deficiency, and genetic hemoglobinopathies are important causes.[21,22] Iron-deficiency anemia is not a cause of severe anemia in young children. Mild and moderate iron-deficiency anemia is associated with poor pregnancy outcomes,[2,23,24] impaired physical[18] and cognitive development in children,[10] and reduced work productivity in adults.[19,25,26]

We identified a series of prevalence studies mainly from the developing world that showed a high prevalence of iron deficiency in premigration refugees and moderate prevalence in postmigration populations.[6,27-29] While evidence evaluating the change in nutritional status during the settlement process is limited, the selection and availability of enriched grain products and other food in industrialized countries is likely to improve iron status over time. Three retrospective prevalence studies on African and Asian refugee children and women in the United States demonstrated a moderate (16%–28%) prevalence of anemia that is two to three times higher than the prevalence of anemia in industrial countries.[30-32] One Canadian study found that the prevalence of iron-deficiency anemia in immigrant women of reproductive age of East Indian origin was 16%.[6]

Overall, it is the poorest and the least educated that are disproportionately affected by iron deficiency.[1,33-35] The main risk factors for iron-deficiency anemia are low iron intake, poor absorption of iron related to diets high in phytate or phenolic compounds, and periods of life with high demand for iron.[1] Studies on newly arriving refugee children have identified exclusive breastfeeding after six months of age without the use of iron supplements or iron-rich complementary foods, use of cow's milk or nonfortified infant formula as weaning food, early and frequent consumption of tea, and relatively infrequent consumption of meat as potential risk factors.[36] Another important consideration is the presence of childhood illnesses associated with anemia.[2] Thus in some children, anemia could be caused by the combined effect of an iron-deficient diet and recent acute illness.[2] Another risk factor in children is obesity.[37,38] Traditional dietary patterns can also factor into iron absorption; for example, an elevated prevalence of iron deficiency was found in immigrant women of East Indian origin with diets high in dietary fibre, phytates and tannins.[6] Total iron intake is affected by access to iron enrichment in the country of origin.[39] Continued food insecurity after resettlement can be aggravated by language barriers and lack of familiarity with the Canadian food context.

Migrants from regions in the developing world with a high prevalence of hookworm and malaria,[40] high parity, and genetic predisposition for red blood cell disorders are at increased risk for anemia. Alpha- and beta-thalassemias are most common in Africa, the Mediterranean, India and Southeast Asia, while sickle cell anemia is most often found in people of African descent. Glucose-6-phosphate deficiency, which can lead to hemolysis in relation to oxidative injury from certain medications (i.e., nitrofurantoin, sulfamethoxazole), has a worldwide equatorial distribution.[30,31] In populations of African, Mediterranean or southeast Asian ancestry, mild anemia unresponsive to iron therapy can be due to thalassemia minor or the sickle cell trait.[2] Immigrant women can face iron-deficiency anemia risk related to parity. Many immigrants come from social structures where women often have several children close together after marriage, with an inadequate interval to replenish nutrition stores.[41]

Does screening for iron-deficiency anemia decrease morbidity?

Screening

Screening for iron-deficiency anemia in a clinical setting relies on hemoglobin, which has been found to be more accurate than clinical examination for diagnosing anemia.[1] Diagnostic measures used to confirm iron-deficiency anemia include hemoglobin or hematocrit response to iron administration, serum ferritin, free-erythrocyte protoporphyrin, transferrin saturation, or transferrin receptor or the ferritin:transferrin receptor ratio. Reported positive predictive value of hemoglobin

Table 2: Hemoglobin threshold by age group (adapted with permission from the World Health Organization).

Age group (yr)	Hemoglobin threshold (g/L)
0.5–4.99	110
5.00–11.99	115
12.00–14.99	120
≥ 15.0 (not pregnant)	120
Pregnant women	110
Men ≥ 15	130

concentration below 110 g/L alone for iron deficiency in children (12–35 mo) is 29% (95% CI 20%–38%), and the sensitivity is 30% (95% CI 20%–40%).[18] Hemoglobin below 107 g/L resulted in a positive predictive value of 38% (95% CI 24%–52%) but lowered the sensitivity to 15% (95% CI 7%–22%).[32] The World Health Organization's cut-off values for serum hemoglobin levels are presented in Table 2.[1]

Evidence to evaluate whether screening for general nutritional deficiency improves health outcomes is insufficient. Effectiveness of nutrition screening tools in identifying iron deficiency is controversial. Validated screening tools that identify nutritional risk in diverse and vulnerable populations, including immigrants and refugees, are unavailable. In Canada, a nutrition screening tool called NutriStep (Nutrition Screening Tool for Every Preschooler) is a reliable and valid tool for assessing the level of nutrition risk in preschoolers three to five years of age.[42,43] The NutriStep tool, however, is available only in French and English and has not been tested with recently arrived immigrants who could have differing diet and cultural understandings.

Relative benefits and harms of treatment

Iron-deficiency anemia can be addressed through primary prevention by ensuring adequate iron intake[1,2] or through secondary prevention by detecting the condition and treating it with iron supplements or diet education.[44]

Table 3: Summary of findings for iron supplements to treat iron deficiency in children

Patient or population: children with iron deficiency
Setting: international locations (developed and developing countries), participants identified within communities or schools.
Intervention: iron supplements

Comparison: children without iron deficiency

Sources: Sachdev H, Gera T, Nestel P. Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. *Public Health Nutr* 2005;8:117-32.

Gera T, Sachdev HP. Effect of iron supplementation on incidence of infectious illness in children: systematic review. *BMJ* 2002;325:1142.

Sachdev H, Gera T, Nestel P. Effect of iron supplementation on physical growth in children: systematic review of randomized controlled trials. *Public Health Nutr* 2006;9:904-20.

Outcomes	Absolute effect		Relative effect (95% CI)	No. of participants (studies)	GRADE quality of evidence	Comments (95% CI)
	Risk for control group	Difference with iron supplements (95% CI)				
Mental development Scale 0–100 (follow-up median 3 mo)	No data	SMD: 0.30 (0.15–0.46)		2827 (27)	Moderate	NNT 7 (5–14)†
Weight for height (follow-up 3–6 mo)	No data	SMD: 0.21 (0.09–0.52)		1246 (7)	High	
Infectious illnesses	1430 per 1000	29 more per 1000 (1344 more to 1515 more per 1000)	Incidence rate ratio 1.02 (0.96–1.08)	5650 (29)	Moderate‡	
Diarrhea events per child years	1160 per 1000	128 more per 1000 (1044 more to 1299 more per 1000)§	Incidence rate ratio 1.02 (0.96–1.08)	3379 (29)	High	

Note: CI = confidence interval; GRADE = Grading of Recommendations Assessment, Development and Evaluation; NNT = number needed to treat; SMD = standard mean difference.

†This is a modest effect, equivalent to 1.5–2.0 intelligence quotient points. In younger children (aged ≤ 27 mo), no effect of iron supplementation on mental development was detected.
‡Consistency in infectious illnesses: heterogeneity Q = 78.29, df = 28, $p < .0001$.
§Intervention and control group numbers are the number of events per child years (observation/exposure time).

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Cognitive development in children

Effectiveness estimates were compiled to summarize both absolute and relative effects for each outcome (Table 3).[10,13,18] Sachdev and colleagues[18] focused on how iron supplements affect physical growth in children.

Seven trials focused on changes in weight-for-height between the placebo and iron-treatment groups. All seven studies were from developing countries including those in Asia, Africa and Mexico. The pooled mean estimate of the standardized mean difference (SMD) in change in weight-for-height between the iron-treatment group and the control group was not statistically significant (SMD = 0.21; 95% CI –0.09 to 0.52; p = .170). Sachdev and colleagues[10] also conducted a meta-analysis combining 17 trials of iron supplements in infants or in children up to 12 years of age. Most of these trials were conducted in developing countries (10 of 17).

Overall, the SMD in mental development scores was 0.30 (95% CI 0.15–0.46, p < .001). This difference is equivalent to 1.5–2.0 points on a scale of 100. Separate analyses for mental development tests and motor development found no statistically significant difference.[10] It is important to note that, in the subgroup analyses, improvement in mental development scores was attributed mainly to five trials in children aged seven years and older and the effect was only intermediate for children between two and five years of age. The authors also highlighted the fact that they could not confidently differentiate the therapeutic from the preventive effects of iron supplements. They also emphasized their assumption that all cases of anemia were due to iron deficiency; however, only 10 studies determined the iron status of the children. The authors commented on the differential effect of iron supplements on children older than seven years and those younger than 27 months of age. Another review commented on the fact that this difference could be caused by better study designs, increased sensitivity of the instruments, and transitory effects of iron deficiency on these tests.[45]

Common adverse effects associated with iron supplements include dose-related reversible gastrointestinal symptoms[9] and unintentional overdose. In another meta-analysis of placebo-controlled trials of iron supplements focusing on infants and children (n = 7892) diarrhea increased by 11%, which corresponds to one episode per 20 children per year (95% CI 1.01–1.23; p = .04).[13] No increased risk of infection was found (1.02; 95% CI 0.96–1.08).[13]

Animal studies show that iron deficiency adversely affects neurotransmitter systems and can be reversed by supplementation.[46] This evidence suggests that the limited improvement in Bayley development scores could reflect irreversible effects of iron deficiency on a rapidly developing nervous system.[10] This evidence has led to a focus on screening tests for young infants[18] and was part of our rationale for focusing on young children, although we note that older children could also benefit from detection and treatment of iron deficiency (Table 3).

Work productivity in women of reproductive age

Evidence on the cognitive side-effects of iron supplements in iron-deficient women shows conflicting results for those who are not pregnant. A randomized controlled trial by Murray-Kolb and Beard[20] found increases in hemoglobin levels corresponded to better scores on attention and memory tasks in young women; however, this study failed to compare cognitive effects between the treatment and control group and was thus excluded from our analysis.

We identified three randomized controlled trials studying the effect of iron supplements on work productivity.[19,25,26] These trials, conducted in China, Indonesia and Sri Lanka, all reported increases in work productivity with iron supplements but used different work productivity outcomes, making it impossible to combine results. Table 4 presents the summary of findings for the study from China, which we chose as the best-quality study for women of child-bearing age who are not pregnant.[19] Because of the complexity of measuring work productivity and the significance in only one of the two primary measures, we rated the quality of this evidence as low.

Clinical considerations

Are immigrants screened for anemia?

All immigrants arriving in Canada undergo the Citizenship and Immigration Canada Immigration Medical Examination. The purpose of this examination is to protect the health and safety of Canadians and to reduce or prevent excessive demands on the Canadian health and social system. Screening tests for anemia, including iron-deficiency anemia, are not routinely included in the medical examination.

What considerations should be taken into account when screening and treating?

Poverty, circumstances, culture, custom, and education can affect the choice and availability of iron-rich foods. Accessibility to iron-enriched foods and supplementation programs in the country of origin can also affect total iron intake.[39] Early in the settlement process, families

Table 4: Summary of findings comparing iron supplements to placebo for women of reproductive age

Patient or population: women of reproductive age (19–44)
Setting: China, factory workers (cotton mill)
Intervention: oral iron supplements
Comparison: placebo

Source: Li R, Chen X, Yan H, et al. Functional consequences of iron supplementation in iron-deficient female cotton mill workers in Beijing, China. *Am J Clin Nutr* 1994;59:908-13.

Outcomes	Absolute effect		Relative effect (95% CI)	No. of participants (studies)	GRADE quality of evidence	Comments (95% CI)
	Risk for control group	Difference with oral iron supplements (95% CI)				
Hemoglobin g/L	Hemoglobin g/L in control group was 115 g/L (baseline)	Mean change (increase) in hemoglobin g/L in intervention groups was 15 g/L (higher) (10.53–19.47 higher)		80 (1)	Moderate†	$p < .001$ NNT 2 (2–3)
Energy expenditure at work, kj/d (follow-up: mean 12 wk)	Energy expenditure at work (baseline); kj/d in control group was 4162 kj/d (baseline)	Mean change (decrease) in the energy expenditure at work, kj/d in the intervention group was 538 kj/d (lower) (862.34–213.66 lower)		80 (1)	Moderate†	$p < .001$
PE, yuan/MJ (follow-up: mean 12 wk)	Mean PE (yuan/d); baseline in control groups was 1.86 yuan/MJ (baseline)	Mean productivity (yuan/MJ), change (increase) in the intevention groups was 0.33 yuan/MJ higher (0.18–0.46 higher)		80 (1)	Low†	$p < .001$ NNT 4 (3–8)

Note: CI = confidence interval; GRADE = Grading of Recommendations Assessment, Development and Evaluation; NNT = number needed to treat; PE = productivity efficiency.

sometimes experience food insecurity. Many refugees and some immigrants have ingested iron-insufficient diets for an extended period and do not recognize symptoms of iron deficiency.[47] Language barriers and poor access to health education further limit health literacy.[48]

A complex interaction of systemic, cultural, and individual factors contribute to iron deficiency. Thus interventions to improve iron status and prevent reoccurrence should include dietary modification supported by nutrition education. Reduction of iron-binding foods and addition of sources of vitamin C can improve iron status.[49] Culturally appropriate nutritional assessment and counselling by a registered dietitian, when available, can identify specific nutrition problems and support appropriate change.[9] In the absence of individual counselling, community nutrition programs can help clients improve their intake of iron-rich foods.

Only 2%–5% of adult men and postmenopausal women have anemia.[22,50] In healthy men, the prevalence of iron deficiency is very low.[51,52] No current guidelines recommend routine screening for iron-deficiency anemia in men or postmenopausal women. There could be other reasons to screen for anemia in men and older women (history of poor intake, blood loss, chronic disease, cancer, malaria or parasitic infection),[1] but this review does not consider evidence for these subgroups.

What are potential implementation issues?

Implementation issues include the challenge of conducting diet counselling across cultural and linguistic differences, the acceptance of blood testing, and the

adherence to iron supplementation.[52-54] Mild iron deficiency has not been clearly linked to adverse clinical outcomes, and thus we highlight the importance of patients' participation in making decisions about treatment: ensuring adherence to iron supplementation is one of the challenges of effective treatment of iron-deficiency anemia. Gastrointestinal adverse effects and changes in stool colour and three-times-a-day dosing have been shown to affect adherence rates.[9] Accessibility issues include language barriers, lower levels of education, follow-up availability, level of ongoing support and access to supplements.

Recommendations from other groups

The US Task Force recommends screening for iron-deficiency anemia in children 6–12 months of age and pregnant women who are at risk for iron deficiency.[9] The US Centers for Disease Control and Prevention recommend routine screening for all children and women of reproductive age, citing the linked risks of iron-deficiency anemia in pregnancy affecting both women and infants.[2] The World Health Organization highlights the multifactorial nature of anemia and recommends screening for at-risk women and children.[55]

The cases revisited

Amina's complete blood count shows a hemoglobin level of 94 g/L, with low mean corpuscular volume (MCV). Her Mantoux test result is negative. Iron-deficiency anemia is the most likely primary cause of her anemia, and a ferritin test demonstrates low iron stores. With the help of an interpreter, she is advised to take iron supplements with a good source of vitamin C, for example, orange juice. She is referred for culturally appropriate nutritional counselling to prevent recurrence.

Sabeen's two children are found to have mild iron deficiency (hemoglobin 90–110 g/L). Iron-rich diets are discussed and iron supplementation is offered. Sabeen, who has had limited access to preventive care, has a hemoglobin level of 62 g/L with iron deficiency confirmed on ferritin testing and good response to iron supplements. Sabeen is also advised to store iron supplements safely out of reach of children to prevent accidental overdose in her children.

Conclusion and research needs

Immigrants and refugees coming from regions with limited iron fortification of foods, higher rates of infectious disease and higher parity are at risk for iron deficiency. Preschool children and women of reproductive age are most vulnerable for related morbidity. We identified these subgroups for hemoglobin screening, as this is where we estimated the highest prevalence of iron-deficiency anemia and the best evidence for effectiveness in reducing related morbidity. Surveillance data on iron deficiency would help evaluate the prevalence and effectiveness of interventions among subpopulations of immigrants. Data on elderly immigrant populations are underrepresented in the literature. We suggest clinicians consider blood screening approaches, although we also recognize that diet education and low-dose iron supplementation is an alternative approach to prevention in vulnerable groups.[2,9] More qualitative studies are needed to characterize patient preferences and concerns regarding diet and supplementation. Further research is also needed to assess education and counselling programs to promote nutrition for new immigrants and refugees.

Key points

- Immigrants and refugees coming from regions with limited access to iron-rich foods, higher rates of infectious disease, and higher parity are at risk for iron deficiency.
- To improve their cognitive development, growing children aged one to four years should be screened for iron deficiency by means of hemoglobin.
- To improve hemoglobin levels and work productivity, immigrant and refugee women of reproductive age should be screened by means of hemoglobin.

Box 2: Grading of Recommendations Assessment, Development and Evaluation Working Group grades of evidence (www.gradeworkinggroup.org)

High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and could change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

REFERENCES

1. World Health Organization. *Worldwide prevalence of anaemia 1993–2005*. Geneva (Switzerland): The Organization; 2008. Available: http://whqlibdoc.who.int/publications/2008/9789241596657_eng.pdf (accessed 2008 Sept. 10).
2. Recommendations to prevent and control iron deficiency in the United States. *MMWR Recomm Rep* 1998;47:1-29.
3. Gushulak BD, Williams LS. National immigration health policy: existing policy, changing needs and future directions. *Can J Public Health* 2004;95:127-9.
4. Hayes EB, Talbot SB, Matheson ES, et al. Health status of pediatric refugees in Portland, Me. *Arch Pediatr Adolesc Med* 1998;152:564-8.
5. Geltman PL, Radin M, Zhang Z, et al. Growth status and related medical conditions among refugee children in Massachusetts, 1995–1998. *Am J Public Health* 2001;91:1800-5.
6. Bindra GS, Gibson RS. Iron status of predominantly lacto-ovo vegetarian East Indian immigrants to Canada: a model approach. *Am J Clin Nutr* 1986;44:643-52.
7. Rice JE, Skull SA, Pearce C, et al. Screening for intestinal parasites in recently arrived children from East Africa. *J Paediatr Child Health* 2003;39:456-9.
8. Tugwell P, Pottie, Welch V, et al. Evaluation of evidence-based literature and formation of recommendations for the Clinical Preventive Guidelines for Immigrants and Refugees in Canada. *CMAJ* 2010. DOI:10.1503/cmaj.090289.
9. U.S. Preventive Services Task Force. *Screening for iron deficiency anemia — including iron supplementation for children and pregnant women: recommendation statement.* Rockville (MD): Agency for Healthcare Research and Quality; 2006. Available: www.ahrq.gov/clinic/uspstf06/ironsc/ironrs.htm (accessed 2008 Jun. 30).
10. Sachdev H, Gera T, Nestel P. Effect of iron supplementation on mental and motor development in children: systematic review of randomised controlled trials. *Public Health Nutr* 2005;8:117-32.
11. Dodd J, Dare MR, Middleton P. Treatment for women with postpartum iron deficiency anaemia. *Cochrane Database Syst Rev* 2007;18:CD004222.
12. Fishman SM, Christian P, West KP. The role of vitamins in the prevention and control of anaemia. *Public Health Nutr* 2000;3:125-50.
13. Gera T, Sachdev HP. Effect of iron supplementation on incidence of infectious illness in children: systematic review. *BMJ* 2002;325:1-10.
14. Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2006;4:CD004905.
15. Pena-Rosas JP, Viteri FE. Effects of routine oral iron supplementation with or without folic acid for women during pregnancy. *Cochrane Database Syst Rev* 2007;3:CD004736.
16. Reveiz GL, Cuervo LG. Treatments for iron-deficiency anaemia in pregnancy. *Cochrane Database Syst Rev* 2007;1:CD003094.
17. Sloan NL, Jordan E, Winikoff B. Effects of iron supplementation on maternal hematologic status in pregnancy. *Am J Public Health* 2002;92:288-93.
18. Sachdev H, Gera T, Nestel P. Effect of iron supplementation on physical growth in children: systematic review of randomized controlled trials. *Public Health Nutr* 2006;9:904-20.
19. Li R, Chen X, Yan H, et al. Functional consequences of iron supplementation in iron-deficient female cotton mill workers in Beijing, China. *Am J Clin Nutr* 1994;59:908-13.
20. Murray-Kolb LE, Beard JL. Iron treatment normalizes cognitive functioning in young women. *Am J Clin Nutr* 2007;85:778-87.
21. Calis JCJ, Phiri KS, Faragher EB, et al. Severe anemia in Malawian children. *N Engl J Med* 2008;358:888-99.
22. Goddard AF, McIntyre AS, Scott BB. Guidelines for the management of iron deficiency anaemia. *Gut* 2000;46:iv1-iv5.
23. Scholl TO, Hediger ML. Anemia and iron-deficiency anemia: compilation of data on pregnancy outcome. *Am J Clin Nutr* 1994;59:492S-500S.
24. Rasmussen K. Is there a causal relationship between iron deficiency or iron-deficiency anemia and weight at birth, length of gestation and perinatal mortality? *J Nutr* 2001;131:590S-601S.
25. Basta SS, Soekirman, Karyadi D, et al. Iron deficiency anemia and the productivity of adult males in Indonesia. *Am J Clin Nutr* 1979;32:916-25.
26. Edgerton VR, Gardner GW, Ohira Y, et al. Iron-deficiency anaemia and its effect on worker productivity and activity patterns. *BMJ* 1979;2:1546-9.
27. Mekki N, Galan P, Rossignol C, et al. Iron status in presumably healthy children 10 months, 2 years and 4 years of age. *Arch Fr Pediatr* 1989;46:481-5.
28. Seal AJ, Creeke PI, Mirghani Z, et al. Iron and vitamin A deficiency in long-term African refugees. *J Nutr* 2005;135:808-13.
29. Dickson N, Morison I. Iron deficiency in infants of Cambodian refugees. *N Z Med J* 1992;105:83-4.
30. Hurley R. Chronic illness in immigrants: anemia and red blood cell disorders. In: Walker P, Barnett E, editors. *Immigrant medicine*. Philadelphia (PA): Saunders Elsevier; 2007.
31. Lorey F. Asian immigration and public health in California: thalassemia in newborns in California. *J Pediatr Hematol Oncol* 2000;22:564-6.
32. White KC. Anemia is a poor predictor of iron deficiency among toddlers in the United States: for heme the bell tolls. *Pediatrics* 2005;115:315-20.
33. Sargent JD, Stukel TA, Dalton MA, et al. Iron deficiency in Massachusetts communities: socioeconomic and demographic risk factors among children. *Am J Public Health* 1996;86:544-50.
34. Soekarjo DD, De Pee S, Bloem M, et al. Socio-economic status and puberty are the main factors determining anaemia in adolescent girls and boys in East Java, Indonesia. *Eur J Clin Nutr* 2001;55:932-9.
35. Bodnar LM, Cogswell ME, Scanlon KS. Low income postpartum women are at risk of iron deficiency. *J Nutr* 2002;132:2298-302.
36. Hassan K, Sullivan KM, Yip R, et al. Factors associated with anemia in refugee children. *J Nutr* 1997;127:2194-8.
37. Brotanek JM, Gosz J, Weitzman M, et al. Iron deficiency in early childhood in the United States: risk factors and racial/ethnic disparities. *Pediatrics* 2007;120:568-75.
38. Sutcliffe TL, Khambalia A, Westergard S, et al. Iron depletion is associated with bottle feeding in the second and third years of life. *Arch Pediatr Adolesc Med* 2006;160:1114-20.
39. Menon P, Ruel MT, Loechl CU, et al. Micronutrient sprinkles reduce anemia among 9- to 2-mo-old children when delivered through an Integrated Health and Nutrition Program in rural Haiti. *J Nutr* 2007;137:1023-30.

40. López-Vélez R, Huerga H, Turrientes MC. Infectious disease in immigrants from the perspective of a tropical medicine referral unit. *Am J Trop Med Hyg* 2003;69:115-21.

41. Kilbride J, Baker TG, Parapia LA, et al. Anaemia during pregnancy as a risk factor for iron-deficiency anaemia in infancy: a case-control study in Jordan. *Int J Epidemiol* 1999;28:461-8.

42. Rysdale L. Evaluation of a nutrition education component nested in the NutriSTEP project. *Can J Diet Pract Res* 2008;69:38-42.

43. Randall Simpson JA. Nutrition screening tool for every preschooler (NutriSTEP): validation and test-retest reliability of a parent-administered questionnaire assessing nutrition risk of preschoolers. *Eur J Clin Nutr* 2008;62:770-80.

44. Feightner JW. Prevention of iron deficiency anemia in infants. In: *Canadian Task Force on the Periodic Health Examination. Canadian guide to clinical preventive health care*. Ottawa (ON): Health Canada; 1994. p. 244-55.

45. Nokes C, van den Boshch C, Bundy DAP. *The effects of iron deficiency and anaemia on mental and motor performance, education achievement and behaviour in children: An annotated bibliography, Report of the International Nutritional Anemia Consultative Group (INACG)*. Washington (DC): International Nutritional Anemia Consultative Group; 1998.

46. Symes AL, Missala K, Sourkes TL. Iron and riboflavin dependent metabolism of a monoamine in the rat in vivo. *Science* 1971;174:153-5.

47. Galloway R, Dusch E, Elder L. Women's perceptions of iron deficiency and anemia prevention and control in eight developing countries. *Soc Sci Med* 2002;55:529-44.

48. Nutbeam D. Health literacy as a public health goal: a challenge for contemporary health education and communication strategies into the 21st century. *Health Promot Int* 2000;15:259-67.

49. Gibson SA. Iron intake and iron status of preschool children: associations with breakfast cereals, vitamin C and meat. *Public Health Nutr* 1999;2:521-8.

50. Calvey HD, Castleden CM. Gastrointestinal investigations for anaemia in the elderly: a prospective study. *Age Ageing* 1987;16:399-404.

51. MartiCarvajal AJ, Sola I. Treatment for anemia in people with AIDS. *Cochrane Database Syst Rev* 2007;1:CD004776.

52. Anderson J, Kirkham RS. Constructing nation: the gendering and racialization of the Canadian health care system. In: Strong-Boag V, Grace S, Eisenberg A, Anderson J, editors. *Painting the maple: essays on race, gender and the constructions of Canada*. Vancouver (BC): UBC Press, 1998. p. 242-61.

53. Kelaher M, William G, Manderson L. Towards evidence-based health promotion and service provision for new migrants to Australia. *Ethn Health* 1999;4:305-13.

54. Stewart M, Anderson J, Beiser M, et al. *Weaving together social support and health in a multicultural context*. Edmonton (AB): Social Support Research Program; 2003.

55. World Health Organization. *Iron deficiency anaemia: assessment, prevention and control*. Geneva (Switzerland): The Organization; 2001. Available: www.who.int/nutrition/publications/micronutrients/anaemia_iron_deficiency/WHO_NHD_01.3/en/index.html (accessed 2009 Nov. 1)

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Clinical preventive guidelines for newly arrived immigrants and refugees

This document provides the review details for the CMAJ CCIRH Iron-Deficiency Anemia paper. The series was developed by the Canadian Collaboration for Immigrant and Refugee Health and published at www.cmaj.ca.

Appendix 1: Figure 1

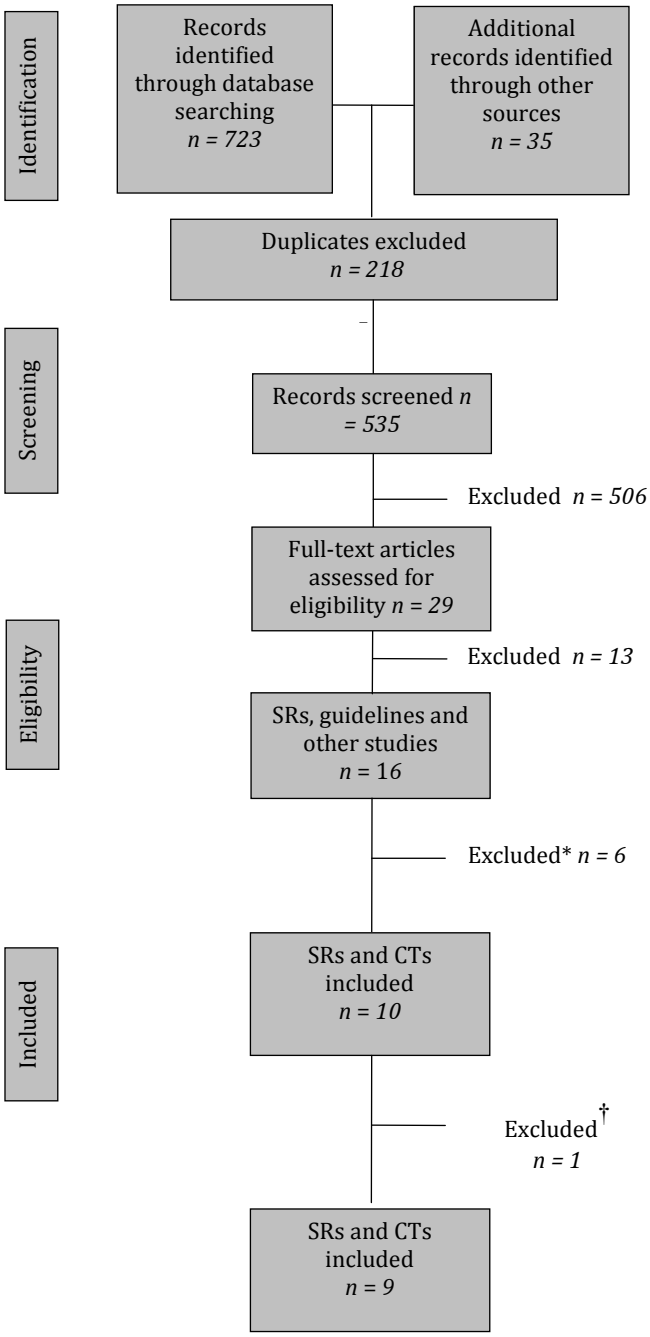

Figure 1: Literature search for systematic reviews and guidelines on iron-deficiency anemia.
Note: CT = clinical trial, SR = systematic review. * Excluded because of lack of relevance, poor quality or outdated findings. †Excluded because review was withdrawn by Cochrane.

Appendix 2: Iron-Deficiency Anemia Evidence Based Clinician Summary Table

Children

Screen for iron deficiency in children aged one to four years (with hemoglobin to improve cognitive development. If children's iron levels are deficient, recommend iron supplements.

Women

Screen for iron-deficiency anemia (with hemoglobin) in immigrant and refugee women of reproductive age to improve hemoglobin levels and work productively. If iron levels are deficient, recommend iron supplements.

Prevalence: Newly arriving immigrant and refugee children and women have a higher prevalence of anaemia (15%-28%) compared with the Canadian-born population (2%-10%), excluding First Nations populations. Iron-deficiency anemia, the most common cause of anemia, is the most common nutritional disorder in the world.

Burden: Overall, it is the poorest and the least educated that are disproportionately affected by iron deficiency. Iron-deficiency anemia can lead to poor pregnancy outcomes, impaired physical and cognitive development in children, and reduced function in adults.

Access to Care: Accessibility issues include language barriers, lower levels of education, follow-up availability, level of ongoing support, and access to supplements.

Gastrointestinal side effects and changes in stool colour and three times a day dosing have been shown to affect adherence rates.

Key Risk Factors for Iron-Deficiency Anemia: Key risk factors are exclusive breast feeding after six months of age without iron supplementation or the use of iron-rich complementary foods, use of cow's milk or non-fortified infant formula as weaning food, early frequent consumption of tea and relatively infrequent consumption of meat. Anemia could also be due to the combined effect of ingestion of an iron-deficient diet and other childhood illnesses. Immigrant women are at increased risk for iron deficiency related to iron-deficit diets and high parity.

Screening Test: Hemoglobin is a reliable test to diagnose anemia. Diagnostic measures used to confirm iron-deficiency anemia include hemoglobin response to iron administration, serum ferritin, free-erythrocyte protoporphyrin, transferrin saturation, or transferrin receptor or the ferritin:transferrin receptor ratio.

Treatment: Iron-deficiency anemia can be effectively addressed through primary prevention by ensuring adequate iron intake or through secondary prevention through detection and treatment with iron supplementation or diet education.

Special Considerations:

- Poverty, circumstances, culture, custom and education can affect the choice and availability of iron-rich foods. Many refugees and some immigrants have ingested iron-insufficient diets for an extended period and do not recognize symptoms of iron deficiency.
- Culturally appropriate nutritional assessment and counselling by a registered dietician, when available, can identify specific nutrition problems and support appropriate change.

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