

glucose tests daily to be eligible, and were advised to test levels at least seven times a day; pregnant women with diabetes typically perform seven to ten tests per day. Furthermore, a cost-benefit analysis from this study needs to justify use of CGM during pregnancy compared with self-monitoring alone.

Use of CGM alone does not alter insulin delivery; therefore, patient interventions are needed to reduce hypoglycaemia (despite nocturnal alarms or alerts) and hyperglycaemia. We believe that the use of integrated systems (pumps with CGM), in which insulin delivery is stopped automatically at or before a low sensor glucose level, reduces hypoglycaemia, especially overnight.<sup>11,12</sup> Because hypoglycaemia, particularly at night, is a substantial concern in this high-risk population in whom the aim is to maintain lower HbA<sub>1c</sub> and fasting glucose,<sup>6</sup> future studies need to evaluate the now approved hybrid closed-loop system<sup>13</sup> during pregnancies associated with type 1 diabetes, as well as new artificial pancreas systems that might reach the market.

\*Satish K Garg, Sarit Polsky

The Barbara Davis Center for Diabetes, University of Colorado Denver, Aurora, CO 80045, USA  
satish.garg@ucdenver.edu

SKG has received advisory board consulting fees from Medtronic, Roche, Merck, Lexicon, Novo Nordisk, Sanofi, Mannkind, Johnson & Johnson, T1D Exchange (JAEB Center), and Eli Lilly, and has received grant funding from Eli Lilly, Novo Nordisk, Merck, Lexicon, Mannkind, Medtronic, Dario, T1D Exchange, DexCom, and Sanofi; these consulting fees and research grants are for insulin treatment, diabetes device use, and other therapies for type 1 diabetes and are all paid to the University of Colorado Denver. SP has received research funding from DexCom for diabetes device use in patients with diabetes paid to the University of Colorado Denver.

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## The price of blood is measured in iron

Volunteer blood donors give about 500 mL of whole blood, approximately 10% of their total blood volume. After removal of plasma during processing, each mL of packed red blood cells contains 1 mg of iron. Thus, 200–250 mg iron are removed from the donor at each donation depending on their haematocrit. Since average iron stores are only 250 mg in women and 1000 mg in men, repeated donation produces iron deficiency in many donors.<sup>1</sup> Iron deficiency induced by blood donation has potential for untoward effects, including impaired neurocognitive development in teenagers or in the fetus of a donor who becomes pregnant.<sup>2</sup> Additionally,

physicians might initiate unnecessary evaluations for gastrointestinal bleeding in male donors with iron deficiency.

There are two ways in which a blood donor can mitigate development of iron deficiency: take iron pills or lengthen their inter-donation interval. Although full recovery of iron stores following donation takes over 6 months for the average donor and over 90 days for an average donor taking a daily iron supplement,<sup>3,4</sup> minimum inter-donation intervals range from 8 weeks to 16 weeks in different countries.

In this context, the findings of the INTERVAL study<sup>5</sup> presented in *The Lancet* are of great importance. The



Published Online  
September 20, 2017  
[http://dx.doi.org/10.1016/S0140-6736\(17\)32156-6](http://dx.doi.org/10.1016/S0140-6736(17)32156-6)  
See [Articles](#) page 2360



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investigators recruited 45 263 whole-blood donors between 2012 and 2014 from 25 centres across England and randomly assigned 22 466 men to 12-week (UK standard) versus 10-week versus 8-week inter-donation intervals, and 22 797 women to 16-week (UK standard) versus 14-week versus 12-week intervals. The primary outcome of blood units collected was increased with shorter compared with longer inter-donation intervals, as might be expected. Perhaps more important were the secondary safety outcomes. In men, at 2 years, mean haemoglobin was 143.1 g/L in the shorter inter-donation interval group versus 146.4 g/L in the longer inter-donation interval group ( $p < 0.0001$ ) and mean ferritin was 25.7  $\mu\text{g/L}$  versus 36.3  $\mu\text{g/L}$  ( $p < 0.0001$ ). Although overall quality of life, cognitive function, and physical activity did not appear to be adversely affected, participants in the shorter inter-donation interval group reported more symptoms possibly related to iron deficiency, including feeling faint, tiredness, breathlessness, dizziness, and restless legs (all  $p < 0.0001$  for men).

Strengths of this study include its randomised trial design, large study population, multicentre scope, and close adherence to the intervention by most participants. Additionally, the study included measurement of both biochemical (haemoglobin and ferritin) and subjective (symptomatology and quality of life) secondary safety outcomes. However, INTERVAL did have the weakness of potentially reduced generalisability inherent to many randomised trials. The proportion of donors participating among those approached was less than 50%, and enrolled donors lived closer to donation centres and had higher previous donation frequency than all UK donors. The findings are therefore strictly applicable to the UK and extrapolation to other countries should be done with caution.

What implications can be drawn from the study? First, over a 2-year period many donors can increase their donation frequency without a measurable effect on overall quality of life. As the authors conclude, the study suggests that for short-term periods blood collection agencies can safely use shorter donation intervals (8 weeks in men or 12 weeks in women) to meet shortages in periods of high demand. However, increased donation frequency comes with the cost of iron deficiency and related anaemia: about 25% of men and women at the most frequent inter-donation

interval had iron deficiency and a third had at least one deferral for low haemoglobin.

Second, when blood supply is adequate or in surplus—as is the case currently in the USA<sup>6</sup>—longer intervals or iron supplementation should be used to prevent iron deficiency and associated symptoms.<sup>7</sup> Some blood centres have already introduced ferritin screening and lengthened the inter-donation interval for donors found to have low ferritin concentrations.<sup>8</sup> Given the advances in automated laboratory testing, information technology, and the high compliance of blood donors, individualised approaches for prevention of iron deficiency could be feasible, as has been done in Denmark.<sup>9</sup> Teenage blood donors might be particularly susceptible to the negative consequences of iron deficiency and should be treated with increased care.<sup>10,11</sup>

The authors are to be commended for this groundbreaking study. Blood donors already provide the life-saving resource of blood through their altruistic donations and should not be asked to pay the additional price of iron deficiency. Blood centres now have the necessary tools to monitor their donors and adjust inter-donation intervals or provide iron supplementation.

Alan E Mast, \*Edward L Murphy

Blood Research Institute, BloodCenter of Wisconsin, Milwaukee, WI, USA (AEM); Department of Pathology and Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, WI, USA (AEM); Department of Laboratory Medicine and Department of Epidemiology/Biostatistics, University of California, San Francisco, San Francisco, CA 94143, USA (ELM); and Blood Systems Research Institute, San Francisco, CA, USA (ELM) [murphy@ucsf.edu](mailto:murphy@ucsf.edu)

AEM reports grants from Novo Nordisk and honoraria from Siemens, outside the area of work discussed here. ELM declares no competing interests.

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## Estimating abortion safety: advancements and challenges



In *The Lancet*, Bela Ganatra and colleagues<sup>1</sup> present an innovative and important analysis of global abortion safety, in which they attempt to move beyond the binary understanding (safe or unsafe) of abortion safety. As the availability of misoprostol increases, and abortion telemedicine services reach more women worldwide, fewer women are undergoing abortions with invasive or outdated methods and more women are having abortions outside of formal health-care systems.<sup>2</sup> These changes prompt a need for rethinking how we view and measure abortion safety. Therefore, the study by Ganatra and colleagues is very timely.

The approach used in the study, although it had limitations, offers a more nuanced gradation of safety: abortions were classified as safe or unsafe, and unsafe abortions were further divided into less-safe and least-safe categories. This three-tiered classification focused on two technical aspects of the abortion process (abortion provider and method) and is said by the authors to be aligned with the conceptual definition of unsafe abortion used by WHO. However, the safety classification did not consider abortion outcomes, as was recommended by Sedgh and colleagues.<sup>3</sup> Outcomes were instead considered by examining the association between abortion safety and case fatality rates.

An editorial<sup>4</sup> on how to operationalise and interpret the WHO definition of unsafe abortion states that, rather than a binary measure, abortion safety should be characterised along a risk continuum, which is affected by contextual factors, such as abortion laws and presence of stigma. The model and analysis used by Ganatra and colleagues did, to some extent, take the social and legal context into account. The authors divided factors affecting abortion safety into five conceptual domains: abortion service delivery environment; legal context of abortion; financial access to services; abortion stigma; and development. However, the model predictors used

cannot be said to completely represent these domains because of the unavailability of predictor data. For example, although gender inequality might be the best available proxy for stigma, measures of gender inequality and data on the abortion process (provider type and abortion method) cannot capture all scenarios. Abortion stigma has a substantial impact on access to both safe abortion and post-abortion care. Young women who seek abortion (including from trained providers using evidence-based methods) sometimes turn to unsafe methods to manage bleeding and delay seeking care for complications because of costs and fear of stigma, exposure, and legal repercussions.<sup>5</sup> Not accounting for these types of outcomes results in an incomplete picture. Efforts are needed to measure and quantify abortion stigma to understand its implications for safety and quality of care.

Another issue, recognised by the authors, is the poor association between drug registration and availability. Registration of mifepristone and misoprostol provides no assurance of the drugs being available or of high quality.<sup>6</sup> The emergence of telemedicine services and

Published Online  
September 27, 2017  
[http://dx.doi.org/10.1016/S0140-6736\(17\)32135-9](http://dx.doi.org/10.1016/S0140-6736(17)32135-9)  
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