samples, for all the routine measurement procedures for which such a correction is intended.[2–4]

Commutability has been defined in metrological terms in several ISO documents and the following working definition was suggested in a recent editorial: 'the equivalance of the mathematical relationships between the results of different measurement procedures for a reference material and for representative samples from healthy and diseased individuals'.[4]

Commutable EQAS materials with target values assigned by a reference method are required to obtain the trueness bias for a given routine method. When non-commutable materials are used, the observed bias may include contributions from trueness bias as well as from non-commutability. Because it is not possible to determine the sources of the total observed bias from EQAS results alone, an incorrect assessment of trueness bias can result when materials of unknown commutability status are used as EQAS samples. It has been reported in numerous investigations that a substantial and variable fraction of typical EQAS materials are not commutable with native clinical samples for many routine measurement procedures, including commonly used measurement procedures for serum creatinine.[2,3,5]

Clinical laboratories and EQAS providers are cautioned to avoid the use of correction factors based on EQAS results to adjust serum creatinine values from routine measurement procedures to agree with an IDMS reference method, unless the EQAS samples have been validated for commutability with native clinical samples for each routine measurement procedure of interest. If commutability is not validated for the EQAS samples, there is significant risk that a correction factor based on EQAS results may be incorrect, potentially leading to even greater, rather than reduced, bias in the estimation of GFR.

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Disclaimer

The findings and conclusions presented in this letter are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, or those of Ortho Clinical Diagnostics.

References

1. MacGregor MS, Boag DE, Innes A. Chronic kidney disease: evolving strategies for detection and management of impaired renal function. *Q J Med* 2006; **99**:365–75.
2. Miller WG. Specimen materials, target values and commutability for external quality assessment (proficiency testing) schemes. *Clin Chim Acta* 2003; **327**:25–37.
3. Franzini C. Ceriotti F. Impact of reference materials on accuracy in clinical chemistry. *Clin Biochem* 1998; **31**:449–57.
4. Miller WG, Myers GL, Rej R. Why commutability matters. *Clin Chem* 2006; **52**:553–4.
5. Miller WG, Myers GL, Ashwood ER, Killeen AA, Wang E, Thienpont LM, Siekmann L. Creatinine measurement: State of the Art in Accuracy and Inter-Laboratory Harmonization. *Arch Pathol Lab Med* 2005; **129**:297–304.

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Colonoscopy first for iron-deficiency anaemia

Sir,

I read the article 'Colonoscopy first for iron-deficiency anaemia' with interest.[1] Surgeons doing endoscopic investigations for iron-deficiency anaemia often seem to have a blind spot when it comes to diagnosing coeliac disease, a very common cause of iron deficiency. Endoscopic small bowel biopsy should be done routinely in all cases, as recommended by the BSG guidelines, yet this is often not done.

The fact that apparently no case of coeliac disease was diagnosed in a series of 2318 patients, and that coeliac disease is not even mentioned in this paper, suggests that small bowel biopsies were often not done, and consequently many of their patients who had coeliac disease are continuing to suffer with chronic ill-health, due to the lack of a proper diagnosis.

Judging by our figures in Bristol, in a series of 2318 patients with iron deficiency, about 200 might

be expected to have coeliac disease. I hope that the authors can confirm that some at least were diagnosed and given appropriate management.

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References

1. Stephens MR, Hopper AN, White SR, *et al.* Colonoscopy first for iron-deficiency anaemia: a Numbers Needed to Investigate approach. *Q J Med* 2006; **99**:389–95.

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Response

Sir,

We appreciate Dr Harvey's interest in our paper, and wholeheartedly agree that coeliac disease is an important cause of iron-deficiency anaemia; this diagnosis will have been considered and pursued where appropriate in the patients in our study. However, the purpose of our study was not to expound every presumed cause of iron-deficiency anaemia in our large series of patients. Such a report would not have added any new information to the existing literature on iron-deficiency anaemia. Rather, our purpose was to compare diagnostic yields for malignant disease from upper and lower gastrointestinal investigation among patients presenting with iron-deficiency anaemia and, more importantly, to compare patient outcomes following a diagnosis of upper or lower gastrointestinal malignancy as a cause for the anaemia.

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AIDS and the Black Death

Sir,

Cohn and Weaver[1] assert that recent publications suggesting that the medieval Black Death could be responsible for the origin of the CCR5-Δ32 allele[2–4] are mistaken. They say: 'scientists . . . have assumed that the north-south European geographical cline in the frequency of the CCR5-Δ32 allele among present-day descendents parallels the severity of the Black Death in 1348 . . .' and 'it is erroneous to assert that the plague mortalities exhibit a north–south cline; rather the opposite seems to be the case'. It is unclear who is supposed to have made these assumptions, or asserted this north–south cline. Published research indicates such assumptions to be unsubstantiated and counter to modern Black Death understanding.

Cohn and Weaver argue that if the Black Death were responsible for the spread of the CCR5-Δ32 allele, then present-day frequencies of the allele should correlate positively with recorded mortality during the Black Death. As Italy suffered greater mortality than Scandinavia during the time of the Black Death, yet but has a lower sampled CCR5-Δ32 allele frequency, the Black Death cannot be responsible. However, it is not clear that this argument is conclusive.

Firstly, it is not obvious whether we should expect high Black Death mortality to correlate with high levels of CCR5-Δ32 (because of the Black Death selectively killing those who lacked the allele) or low levels (because populations lacking the allele would be more at risk from the disease). In other words, how much the distribution has been shaped by selection, and how much it reflects pre-Black Death variation. As we do not know the frequency of the CCR5-Δ32 allele in European populations at the time of the Black Death, this question seems unanswerable.

Secondly, it is unclear to what extent the present-day distribution of the allele reflects that 700 years ago. It is general knowledge, for example, that immigration and population mixing over that time have been far more pronounced in southern and central Europe than in Scandinavia. Over time, migration would be expected to dilute selection effects from disease, once those diseases were no longer epidemic. 'Black Death' epidemics in Scandinavia continued well beyond the time at which they died out in southern Europe.[2] As Cohn and Weaver note, Finland did not experience the plague until 1440, almost 100 years after the disease entered southern Europe. This would tend to favour a higher level of CCR5-Δ32 allele in Scandinavia, as observed. Other diseases may also have affected this distribution, although modelling suggests that smallpox[5] could not have elevated CCR5-Δ32 allele frequencies to those witnessed in Europe today.[3]

Martinson *et al.*[6] found a cline of the indigenous population demonstrating detectable levels (>1.5%) of the CCR5-Δ32 allele, from central Asia through southern Europe and extending up to the Arctic