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
first for iron-deficiency anaemia: a Numbers Needed to
doi:10.1093/qjmed/hcl143

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 pre-
senting with iron-deficiency anaemia and, more
importantly, to compare patient outcomes follow-
ing 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 Weaver1 assert that recent publications
suggesting that the medieval Black Death could be
responsible for the origin 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 assump-
tions 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
smallpox3 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

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The greatest recorded historical epidemic. For now, multiple lines of research continue to raise more questions than answers about the world’s relationship between the Black Death and the CCR5-Δ32 allele seems at best premature. In time, the posited connection between plague and the HIV-resistant allele may indeed turn out to be a red herring. For now, multiple lines of research continue to raise more questions than answers about the world’s greatest recorded historical epidemic.

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References

doi:10.1093/qjmed/hcl145

Response

Sir,

Dr. Bossak alleges that ‘it is unclear who is supposed to have made these assumptions’—that the Black Death provoked a genetic shift that bestowed greater resistance to HIV for Europeans, and in particular those from northern Europe—we think our references leave no doubt as to who supports this thesis (references 1–5, 7–10 from the original article).

Dr. Bossak asserts: ‘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’. We do not make any such positive claim; rather, we have questioned those who have assumed that Black Death mortalities followed a north–south cline matching that of the geographical distribution of CCR5-Δ32 in present-day descendants. By turning to historical research (references 15, 17, 27, 28, 29, 31, 32, 34 and particularly 16 from the original article, which relies on >40,000 death records across Europe) we show that the Black Death mortalities as well as plague mortalities through the early modern period more likely reflect the opposite cline, with the highest mortalities most often recorded in the Mediterranean and little or no evidence of plague in the highlands of Scotland or the northern parts of Scandinavia and especially Finland.

Dr. Bossak also raises questions about using genotype evidence from present-day descendants to study characteristics of historical and pre-historical populations, as though we were the pioneers in such research and methodology. Unfortunately, we cannot make any such grandiose claims. With regard to the question of CCR5 distributions and the Black Death, we have pointed out the limitations of this particular genotype evidence (original article, referenced above, p. 501). Those who developed these methods, however, are aware of the problems of subsequent migration. Indeed, several decades ago, scientists such as Luigi Cavalli-Sforza used such evidence and method to establish new findings about global migration and long-term transcontinental integration and communication of races and societies in pre–historical times. More recently, his students and others have devised genetic methods for distinguishing the effects of recent immigration among populations.

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References

doi:10.1093/qjmed/hcl147