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IN REPLY: Much of the literature about evidence-based medicine (EBM) has focused on the science of generating evidence, or the technical process of critically appraising and interpreting evidence for individual patients. In our article¹ we opted to discuss EBM as a social activity with inherent potential for multiple manifestations. To describe EBM as a social activity is to emphasise how its definition, interpretation and application, and the ethical implications of those factors, are dependent on societal values and priorities — be they explicit or implicit.

Debate about what EBM means, or should mean, in the context of Australian policy and practice does not degrade or negate the clearly ethical practice of consulting the best available research when making clinical or policy decisions. We challenge the view of Parker et al that by identifying and discussing how the concepts or language associated with EBM could be misused or misappropriated we will somehow reduce the motivation of health professionals to find and apply the best treatments. Indeed, our proposition is quite the opposite.

Few of today's readers of the *MJA* will be unfamiliar with the benefits of systematic reviews of the best available research in their clinical area, and few are likely to be dissuaded of that view by our article.

Our exploration of the relationship between ethics and EBM does not "misinterpret" EBM, but, rather, purposefully describes scenarios or social consequences about which there may be ethical concerns. If we can articulate clearly what we do *not* want EBM to mean, and describe the processes and consequences that we would consider unethical, it can only strengthen the development of an ethical and acceptable notion of what we *do* want from evidence-based policy and practice.

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Serum alanine aminotransferase levels and the detection of hepatitis C virus (HCV) in chronic HCV infections

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TO THE EDITOR: Chronic hepatitis C virus (HCV) infection affects almost 200 000 Australians.¹ It is monitored clinically by serial liver function tests (LFTs) and HCV RNA detection by polymerase chain reaction (PCR). HCV RNA is a marker of chronic infection and levels reflect response to antiviral therapy. However, testing for the presence of HCV RNA is expensive and, under the current Medicare Benefits Schedule, is not available to people with HCV antibodies and abnormal LFTs unless they are undergoing antiviral therapy.

Using an in-house PCR assay, it has been shown that abnormal LFTs largely predict the presence of HCV RNA.² We aimed to confirm this finding using a more reproducible PCR assay (Roche Amplicor HCV test) and to further investigate the relationship between LFTs and HCV RNA.

We studied 323 HCV antibody-positive patients seen at the Fairfield Infectious Diseases Hospital, Melbourne, between May 1995 and September 1996. The Victorian Infectious Diseases Reference Laboratory performed all PCR assays and LFTs on these patients. Approval for the use of de-identified data was obtained from the Ethics Committee of the Royal Melbourne Hospital Research Foundation. Normal serum alanine aminotransferase (ALT) levels from at least two tests over a period of at least six months were considered to demonstrate normal liver function. In order to determine improved predictors of the presence of HCV RNA, the proportion of patients who were HCV RNA-positive and had an initially normal ALT level and the proportion with a normal ALT level persisting over six months were examined for each 10-IU/mL subdivision within the normal ALT range (0–50 IU/mL).

Of the 323 patients, 88% were aged between 20 and 49 years and 68% were men. At initial testing, 251 (78%) were HCV RNA-positive by PCR, 206 (64%) had an abnormal ALT result and 183 (57%) had both a positive PCR result and an abnormal ALT level. An abnormal ALT level predicted the detection of HCV RNA in 89% (183/206) of patients and in 82% (14/17) if an abnormal ALT result was found within six months of an initial normal result.

Of the 117 patients with a normal initial ALT level, only 49 (42%) had a negative PCR result. However, an initial ALT level of ≤ 20 IU/mL was more likely to be associated with a negative PCR result than an initial normal ALT level > 20 IU/mL (78% v 23%, respectively; $P < 0.001$). The probability of a negative PCR result was highest if the initial ALT level was ≤ 20 IU/mL and remained normal for at least six months (see Box).

We concluded that, while an abnormal ALT level in a patient with HCV antibody generally predicted the presence of HCV RNA, the absence of HCV RNA was best predicted by an initially low ALT level that remained within the normal range for at least six months.

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Proportion of patients with normal initial serum ALT level and persistently normal ALT level who were positive for HCV RNA by PCR, divided into 10-IU/mL subdivisions of the normal ALT range

Initial ALT range (IU/mL)	Number (%) PCR positive, all patients	Number (%) PCR positive, patients with persistently normal ALT over six months
≤ 10	2/11 (18%)	2/3 (67%)
11–20	7/29 (24%)	0/11 (0)
21–30	18/30 (60%)	11/12 (92%)
31–40	23/27 (85%)	8/8 (100%)
41–50	18/20 (90%)	2/2 (100%)

ALT = Alanine aminotransferase. HCV = Hepatitis C virus. PCR = Polymerase chain reaction.