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## Clinical opinion

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# Associations and clinical significance in meta-analysis: when are the deductions too presumptive?

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**TITLE** Off hour presentation and outcomes in patients with acute myocardial infarction: systematic review and meta-analysis

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## SUMMARY

This meta-analysis of publications over an approximate ten-year period from 2002–12 looked at mortality after coronary presentations. A total of 487 reports were studied and 48 were assessed for the impact of nominal 'off hours' (night and weekends) presentation for catheter-based revascularisation for ST elevation myocardial infarction (STEMI). Smaller studies tended to show increased mortality off hours, larger samples little or no adverse effect. The net impact, using a random effect meta-analysis model, was a statistically significant 2–4% mortality excess. This was linked by the authors to an increase in hospital 'door to balloon' times.

Data on time to recognition and hospital presentation were not available but were said to be shorter off hours as seen in other publications. More adverse effects were seen off hours in non-North American centres and was associated with a reduced door to balloon time in North American registries.

The authors go on to suggest these observations have implications for the assessment of quality of care by hospitals (and staff) and should guide 'value based purchasing' on the basis of off hours performance. The limitations – lack of randomisation, inconsistent definition

of 'off hours', high heterogeneity, publication bias, overlapping patients – were all felt to be offset by the statistical power of analysis (more than one million patients from the 48 publications included). The authors considered that previous failed attempts to confirm the adverse off hours effect on mortality were due to a lack of statistical power.

## COMMENTARY

Most practitioners have accepted that adverse outcomes can follow out-of-hours or weekend management in communities or hospitals. This rightly attracts much political attention, yet where we do not understand the basic mechanisms; the causes of any adverse clinical effects are unlikely to be generalisable. Does this further analysis in STEMI add anything new?

The presumption that every intervention can be, or should be, performed in the same way, day or night, regardless of individual circumstances is a basic error. That biological variance can be explained via statistical association in a meta-analysis is also erroneous. Where numbers are this large, statistical significance can be guaranteed. Plausible explanations can be suggested (staff/facilities don't respond quickly or are not available), but they remain speculative.

This article shows where statistics can mask reality. Seeking out causative mechanisms is largely ignored in favour of presumptions, associations and relative risk ratios. Boldly suggesting health policy (or purchasing) on the basis of such analyses seems unwise and, given political interest in quick and simple explanations, dangerously misleading.

That night and day have biologically different effects on many human response mechanisms is well recognised after more than 100 years of established chronobiology.<sup>1</sup> To suggest that coronary reperfusion overrides all such variance seems counter-intuitive or simplistic. Night or day procedures are unlikely ever to be equivalent for patients or staff, no matter how available staff and facilities are.

The presumption of linearity between door to balloon time and subsequent mortality is also simplistic and has no evidence base. In particular functional recovery from occlusion is individual and not time-dependent, due to variable collateral blood flow. No attempt to study balloon opening or reperfusion versus outcome is made here, notwithstanding that individual anatomy is critical to the outcome and is routinely recorded in practice.

The extent of the putative 'off hours' effect found here is in real terms surprisingly small. Cost-effectiveness in a poorly resourced healthcare system of having staff literally waiting to perform invasive cardiac assessment is, of

course, problematic and profoundly influenced by errors of clinical judgment and wasted resources. Normal or near normal coronary studies in and out of hours are now routine and acceptable limits for this error (providing an expensive resource for reassurance but no benefit) creep ever upwards. Such errors are generally based on rushed/poor basic clinical assessment (no credible history, no context, no basic examination) and over-interpretation of non-specific or long-standing ECG changes. The costs of such unnecessary deployment of staff and resources out of hours are never measured but could easily cripple any healthcare system, public or insurance-based. In the latter, some individuals profit; in the former, everyone loses.

Inevitably, more work is needed in order to delineate less presumptive associations and to evaluate relevant individual elements. Confirmation of the biology of occlusion, day or night; detailed analysis of pre-hospital responses across weekends/nights; clarification of the medical quality of assessment; a cost-effectiveness analysis of the suggested re-deployment of resources/rearrangement of services would all be very useful consequences of this work.

Should anyone consider change in health policy? Clearly not on this basis and not until we carry out much more work with real patients in controlled observations rather than desktop statistics.

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