

Correspondence

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Do 'numbers' count?

The article by Tomenson *et al*¹ raised some interesting questions. The study concluded that total somatic symptom score predicted health status and healthcare use. We would like to highlight that another important parameter that could have been included is the duration of the symptoms. The measures that were used in the trials studied were all different and assessed current or lifetime symptoms and not duration or severity of symptoms. This could have an impact on healthcare use. Other drawbacks relate to care pathways and age of participants. In low- and middle-income countries, where there are many coexisting healthcare systems, relying only on allopathic setups may be difficult. Hence, traditional health systems would be an important aspect that could have been taken into consideration. The mean age range in the studies included in Tomenson *et al*'s analysis was highly variable (18–75 years) and could result in both medically explained and unexplained symptoms or both existing in the same individual. Measuring bothersome somatic symptoms or those that interfered with functioning, which again varied across the different instruments, may alone not indicate severity. The intensity of symptoms can have a bearing on severity as has been demonstrated by Kroneke *et al*.² Another important component on health status and healthcare use would be the concept of abnormal illness behaviour.³ Abnormal illness behaviour could also determine significant healthcare use. Tomenson *et al* have made efforts to consider health anxiety as a variable, which could again influence health status. Thus, it is not only the number of somatic symptoms that account for health outcome but other variables mentioned above too. Future research should focus on both current and lifetime symptoms, number, duration and severity of symptoms, and abnormal illness behaviour to better understand health status and healthcare use.

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Authors' reply: We thank Desai & Chaturvedi for their interest in our paper. We agree that additional dimensions could be included as possible predictors of health status and healthcare use and that the latter would be influenced by the nature of local

healthcare facilities. It was impossible to include such additional measures in our study because we were restricted to those measures that had been used in the original studies.

Desai & Chaturvedi mention duration and severity of symptoms as possible predictors of outcome. Duration is important but may not predict number of subsequent doctor visits.¹ Severity is important and five of our studies used questionnaires (including the Patient Health Questionnaire-15) which assessed the degree of bothersomeness of each somatic symptom, a subjective measure of severity. The distinction between intensity and severity is complex, but one study noted that severity of pain did not explain the association between number of somatic symptoms and subsequent health status.²

The point raised by Desai & Chaturvedi regarding the co-occurrence of medically explained and unexplained symptoms is very important and forms one of the main points of the paper. Such co-occurrence of symptoms is common and constitutes one of the main difficulties of trying to make a diagnosis purely on the presence of medically unexplained symptoms. In the four sites where data were available, we found that the association of somatic symptoms with health status, after adjustment for confounders, was stronger for total somatic symptom score than for number of medically unexplained symptoms. We could not test this in relation to healthcare use but the association between number of somatic symptoms with healthcare use appears similar for medically explained and unexplained symptoms.³

Assessing abnormal illness behaviour is difficult in population-based studies using self-administered questionnaires, as most measures include items about how often the respondent visits doctors, which would overlap with our outcome measure of healthcare use. A better dimension might be a person's general tendency to visit doctors even for minor reasons; this is a predictor of healthcare use independent of number of bothersome somatic symptoms.⁴

The other dimension mentioned by Desai & Chaturvedi, health anxiety, is very important. In two studies a high number of somatic symptoms and pronounced health anxiety were both independent predictors of primary healthcare contacts (see Tomenson *et al*⁵). Two other studies have shown a complex interaction between these dimensions, with health anxiety being a predictor of subsequent healthcare use only in respondents without a high number of somatic symptoms or who also have serious medical illnesses.^{3,5}

This field of research suffers from lack of prospective studies. The correlates, or predictors, of healthcare use are somewhat different for past use and future use.^{5,6} One paper made the intriguing, but plausible, suggestion that frequent visits to the physician could increase health anxiety and precipitate more somatic symptoms rather than the other way round.⁶ Further prospective studies using well-validated questionnaires are needed.⁷

Declaration of interest

F.C. has been a member of the American Psychiatric Association DSM-5 work group on somatic distress disorders and is a member of the World Health Organization ICD-11 working group on the classification of somatic distress and dissociative disorders.

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Risk of dementia after anaesthesia and surgery: study design may affect reported outcome

Although not highlighted in their paper, the results of Chen *et al*¹ are fundamentally different from the preponderance of evidence that suggests a lack of association, as summarised in recent systematic reviews and a large case–control study.^{2–4} This is an important topic that is difficult to study in humans, and all observational studies in this area have substantial limitations. The authors point out some; we wish to amplify their identified limitation and to raise others.

The primary concern is that their matched cohort design, based on exposure history, is highly susceptible to confounds. Simply put, individuals who have conditions requiring surgery are fundamentally different from those who do not – as demonstrated by the finding that they were sicker and older. The ability to adjust analytically for such differences, even if the right covariates are chosen, is limited. Case–control methodologies, such as we utilised in a recent longitudinal population-based analysis using standardised diagnostic criteria which did not find an association between exposure to anaesthesia and Alzheimer's dementia,⁴ are less susceptible to such confounding (although such designs have their own problems). The use of large administrative data-sets can be very valuable given the ability to examine entire populations, but the lack of any consistent diagnostic criteria and the potential for incomplete or inaccurate coding makes it difficult to estimate the true population incidence of a condition such as Alzheimer's dementia. For example, there is the potential for substantial ascertainment bias, as those patients who need surgery likely have greater contact with the healthcare system, and are more likely to have the opportunity for an Alzheimer's dementia diagnosis.

Another design question is raised by the stated inclusion criteria for controls. For those who received anaesthesia, the date of their first anaesthesia exposure after 2004 is used as the index

date. The authors do not indicate what index date was used for controls, only that controls were selected from patients who did not receive anaesthesia during the study period. It is not clear whether individuals were excluded from the pool of potential controls if they had a diagnosis of dementia at any time prior to the end of the study period (31 December 2007) or whether these exclusion criteria were applied separately for each potential exposed/unexposed matched set based on an assigned index date. The results would be substantially biased if those with diagnoses of dementia at any time prior to 31 December 2007 were excluded from being potential controls.

Concerns regarding the impact of these and other methodological issues are heightened by the fact that if, as they speculate, anaesthesia and surgery is causative of Alzheimer's dementia, Chen *et al*'s results in many instances are simply not plausible. They report a uniformly positive association between anaesthesia and Alzheimer's dementia, regardless of the type, number of anaesthetics and cumulative anaesthesia duration. Those patients who received 'intravenous/intramuscular' anaesthesia, presumably mainly representing monitored anaesthesia care that most anaesthesiologists would not characterise as constituting a 'general anaesthetic', were just as likely to develop Alzheimer's dementia as those who were undergoing major surgical procedures. Those receiving regional anaesthesia, who in many cases have little central exposure to anaesthetic drugs, were even more likely to develop Alzheimer's dementia. It could be argued that the association is caused by the surgery, not the anaesthesia, but there are similar problems with the results here. More minor procedures, such as ophthalmological and dermatological surgery, were associated with risk, but major surgery such as cardiac and respiratory procedures were not. The most likely explanation for these implausible findings is a significant contribution of confounding factors.

More data on this important question are always welcome, and there are significant limitations of all human observational studies in this area. However, the introduction of Chen *et al*'s paper states that the purpose of the study is 'to determine whether the risk of neurodegenerative dementia increases after anaesthesia and surgery' (which to us implies causation), and we suggest that this purpose has not been fulfilled.

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Authors' reply: For each individual in the anaesthesia group we selected four or five age- and gender-matched control patients randomly who had not received anaesthesia since 1995, in which year the Taiwan National Health Insurance Research Database