

**Response to commentary on “Public care during childhood and biomedical risk factors in middle-age: the 1970 birth cohort study” by Hilary K Brown entitled “Biomarkers for mortality among individuals with a history of out-of-home care: Implications for study design and conceptualizations of risk”**

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We thank Dr. Brown for her careful reading of our manuscript<sup>1</sup> and her thoughtfully composed commentary.<sup>2</sup> Within the space constraints of this piece it is not possible to delve into all the points raised; instead, we focus on what we regard as the salient issues in understanding the economic, social, and health consequences, if any, of exposure to public care in childhood and adolescence.

As in any sphere of epidemiology, the validity of the data is crucial. As we outlined in our original manuscript, and as reiterated by Dr. Brown, parents reported the care status of study members. Although this was captured serially across childhood and is presumably preferable to the study members' own reporting, the concern is nonetheless raised about bias due to social desirability, amongst other sources. We are unaware of any work comparing parent-reported care status against a presumed gold standard such as state records in countries with advanced systems of electronic registers. In preliminary findings from a systematic review of care and mortality studies, however, the elevated mortality risk in adults who, as children, experienced care, was of very similar magnitude across cohorts using these two approaches to exposure assessment.<sup>3</sup> This suggests predictive validity.

While certainly lacking important accompanying information on type, duration, and reason for care – again, points we raised in our manuscript – our prospectively gathered care data are certainly no weaker than in two of the studies cited by Dr. Brown which provide more positive results than our own. In one of these,<sup>4</sup> participants recalled foster care status many decades after the experience – 14% of the sample were over 65 years of age – raising concerns about accuracy, while in the other,<sup>5</sup> the same care data as our own were utilised alongside an array of self-reported outcomes. In both studies there was little overlap with our outcomes, rendering direct comparison problematic.

In existing studies of care and mortality risk, participants are typically censored around middle-age before chronic illness become manifest. Comparison across different causes of mortality are therefore rare – we are unaware of any studies with cardiovascular disease events, for instance –

and when they do exist, the event classifications are unconventional: ‘illness’, ‘chronic disorder’, ‘risky behaviour’, and ‘substance abuse, accidents, and suicide’. Given that the magnitude of association between ‘unnatural’ deaths – presumably, largely completed suicides, which would be hypothesised as being most closely tied to care – is typically markedly higher than for those apparent for total mortality<sup>6</sup> would imply that effects for chronic disease are modest. As such, it might be anticipated that the relation between care and the biomedical factors linked to vascular disease, the focus of our research letter, and another study,<sup>7</sup> would also be weak. It is also the case that other psychosocial characteristics captured pre-adulthood, such as cognitive function (IQ), psychological distress, and poverty, tend towards the same observation of shallow gradient in relation to biomarkers.

Of the various life course models advanced as a framework for understanding disease processes, Dr. Brown focuses on accumulation of risk. We think there is in fact growing evidence to suggest that childhood care may offer a very rare example in epidemiology of sensitive or critical periods, such that exposure outside a specific time frame has a diminished or zero impact on risk. This is seen in the few studies that have explored timing of entry to care and its relationship with total mortality in adulthood whereby those who entered care later appear to experience higher mortality rates than those who did so earlier in the life course.<sup>6</sup> While this may be due to older children being more cognisant of their very difficult circumstances and vulnerabilities, it may simply be that they have the greatest risk because they had been exposed to disadvantage for a more prolonged period having continued to reside with their family of origin.

Lastly, while observational studies suggest there may be emerging links between care and total mortality, completed suicide, socioeconomic circumstances, health behaviours, and mental health, we disagree with Dr. Brown that this evidence base is sufficiently substantial to permit policy change. Findings in social epidemiology should be subject to the same level of scrutiny and doubt deployed elsewhere. In cardiovascular medicine, for instance, control of blood pressure, serum cholesterol, and diabetes in randomised controlled trials has been shown to cause reductions in cardiovascular event rates, while links between cigarette smoking and respiratory cancers are irrefutable owing to the substantial weight of observational evidence despite very few experiments in the general population.<sup>8</sup> Until more well-designed observational studies, natural experiments, and trials occur in the care field, and their findings are shown to be robust, we think the current evidence based is too weak to steer policy.

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