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Racial and economic disparities in transplant outcomes: the not-so-hidden morbidities

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The Institute of Medicine (IOM) notes that equity is fundamental to the quality of health care (1). In this issue Thamanna and colleagues (2) present us with an important and challenging paper. They undertake careful analyses to document racial/ethnic inequities in liver transplant outcomes. As with any empirical analysis, the optimal conclusion relates both to the methods and to the underlying conceptual frame. This paper reports differences in outcomes and shows that several variables may attenuate the magnitude of such differences. How best should we understand this important contribution?

The article (2) addresses disparate outcomes. Its focus is not potential differences in the actual provision of medical care. It does explore other covariates in its very careful analysis of survival (graft survival and all-cause mortality) in pediatric and young adult liver transplant recipients in one center in Georgia, US. For reasons of sample size and clarity, the study team utilized 3 broad categories for race: Black, White, and Other, using retrospective chart analyses. The study's primary finding that white children have better outcomes than black children or children from other races is an all too familiar and yet still deeply disturbing observation. Those findings are not surprising: as the authors point out, in the US, infant mortality rates, mortality rates across the life span, and global life expectancy are all significantly lower for blacks as compared with whites. The World Health Organization (WHO) defines disparities as “differences in health which are not only unnecessary and avoidable but, in addition, are considered unfair and unjust.” (3). The IOM's 2003 Unequal Treatment Report defines health care disparities more narrowly as “racial or ethnic differences in the quality of healthcare that are not due to access-related factors or clinical needs, preferences, and appropriateness of intervention.” (4). Therefore, while the IOM focuses on the provision of the same level of health care to everyone, the WHO goes one step further and suggests that the health care system is charged not only with the provision of an adequate level of care to everyone, but also with alleviating remediable health differences. Disparities in health care may cause or exacerbate disparities in health. This manuscript is unable to characterize clearly the presence or absence of disparities in the way care is delivered to different patients, and so it is limited in its capacity to clearly identify the causes of outcome differences.

Clinicians and policy-makers increasingly are coming to understand the extent to which pediatric and adult outcomes reflect the cumulative insults and benefits of the encounters and exposures experienced during the life time. The life course perspective, as this view has come to be known, holds that health insults in the prenatal and childhood period can alter

life trajectories. Such insults may be varied and include medical, social, environmental factors as well as psychological and sociological ones. The life course perspective supports the idea that the failure to optimize health, or health care, in early life can have profound consequences (5–10). This perspective, also cited by the paper's authors, leads us towards the broader framing of disparities that is championed by the WHO. If inequitable exposure to social disadvantage or racial discrimination, or even genetic disadvantage, leads to poorer outcomes, then equal care may not be equitable care.

When interpreting outcome differences in more fine detail, it may be useful to think through potential early causes for differences as informed by the literature (11). We list here a dozen that may be relevant in the current context. These are not mutually exclusive and we could readily have added to this list: 1) Genetics; 2) Premorbid life course; 3) Biology of Specific Liver Disease; 4) Treatment received for this Liver Disease before the transplant was known to be necessary; 5) Treatment received for the End Stage Liver Disease before transplant was planned; 6) Pre-transplant care while on transplant list; 7) Source and “quality” of graft; 8) Transplant care quality; 9) Post transplant care quality; 10) Patient adherence; 11) Environmental factors or exposures (including as a consequence of SES or race) and 12) existing co-morbidities. Treatment differences may occur at any clinical site. True causal modeling would require far more data than was available in the current study. (12–14)

However, the authors did examine several important covariates, such as those grouped under the generic title of “socio-economic status” (SES), including income, insurance status, and place of residence. As expected, the authors found that SES variables attenuate the observed magnitude of the racial differences. As illustrated in the Figure, the meaning of this latter finding is unclear, as controlling for SES factors that relate to race may represent statistical over-adjustment, depending upon the underlying causal model. Many SES variables are closely allied with race, making interpretation of their distinction challenging. In addition, as the authors acknowledge, they were not able to measure many relevant SES variables. Insurance status is unquestionably important (15) and was measured in this study. But, for example, parent (especially maternal) education (16,17) and mental health (18) are also important variables, and those were not measured.

The authors are on uncertain grounds in their examination of the potential effects of nonadherence to the medical regimen on the observed differences in outcomes. We advise readers not to interpret the reported results to mean that blacks are less adherent to their liver transplantation regimen than whites, as the present study's methods are not capable of a valid examination of the relationship between race and adherence. The authors found that whites are less likely to have a note in their medical chart that mentions nonadherence. But the low reliability of physicians' assessment of adherence has been documented in many settings of care, including the pediatric liver transplant setting. (19) It is particularly unreliable in the context of the present study: an equally plausible interpretation of their findings is that differential reports of nonadherence themselves represent a disparity – that physicians are more likely to record nonadherence among black patients than for white ones. The authors attempted to mitigate such concerns with an analysis that looked for an out-of-range blood level in a small subsample of patients. There are two significant problems with their approach. First, they only did so with a small subsample. Since the availability of a recorded level is likely to be associated with adherence (less adherent patients would be less likely to have a level recorded in the first place), a selection bias is almost certain – the sample used for sub-analysis is not a true representation of the study population as a whole. Second, the authors seem to suggest that their sub-analysis establishes that clinicians' notes about nonadherence are accurate because those notes are “corroborated” by the existence of out-of-range blood levels in many of those cases. But those are not independent measures of the same construct. In our view a more likely explanation of the correlation between the two

is that physicians who see an out-of-range level (which may be related to a variety of causes, of which nonadherence is only one) are likely to assume that the patient is nonadherent, whether or not this is true.

In addition, the study's results hint that the chart entry did not, in fact, reflect true adherence at all. In table 4, the authors report that chart indicators of nonadherence were somewhat (not significantly) *lower* in *deceased* patients (38.2% had nonadherence mentioned in the chart) compared with survivors (42.5% had nonadherence mentioned). To accept that result would mean that one would have to believe that either poor adherence is not associated with poor transplant outcomes (which would make this analysis irrelevant for the purposes of this manuscript), or that adherence is improved when patients' outcomes are worse (a highly unlikely assumption).

We therefore believe that the statement that “black participants show the highest proportion of non-adherence” is not supported by the findings in this study. A more accurate characterization may be: “Doctors in this study were more likely to suspect nonadherence in patients belonging to a minority group”. But even that conclusion may not be well justified given the lack of statistical adjustment for such things as SES in this analysis. Regardless, we note that the fact that so many patients had chart notes documenting a suspicion of nonadherence ought to stimulate activities to enhance the capacities of families to adhere to these challenging regimens.

This important study documents racial disparities in pediatric liver transplant outcomes. The higher graft failure and mortality rates among black children are both alarming and unacceptable. Although this study's findings may not be surprising, they are a reminder of the need for research to uncover racial/ethnic disparities in pediatric health and health care as these disparities can have large repercussions for health status across the life course. The study's primary finding is sufficient to represent an important call for the liver transplantation community to both monitor and reduce disparities. Quality improvement and other implementation research strategies may simultaneously generate improvement and knowledge that can help us to understand the causes of the observed disparities. To the extent that race, SES and other nonclinical factors may increase the challenges for medical management, resources for treating these at-risk children may need to be increased above the baseline considered appropriate for liver transplantation. Early targets for intervention may be enhanced services to support coordination of care and routine objective assessment of adherence to drug regimens (and intervention when needed). A transplant is a highly valuable and scarce resource; the goal of preserving this resource more than justifies the additional investment.

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**Figure.**

If Race/ethnicity is a predictor of socioeconomic status (SES), then even if both race and SES are independent predictors of outcomes, fully adjusting for SES may falsely reduce the estimate of the magnitude of race as a predictor of outcomes.