

Extremely premature infants, scarcity and the COVID-19 pandemic

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Scarcity is Nature's creative provenance, the wellspring of human conflict and subsequent adaptation. Deficiencies of food, shelter and basic safety are primary, but secondary privations real or imagined (material comforts, money, power and sex), are often perceived insufficient by humankind and drive history's discord.¹ The COVID-19 pandemic spotlights scarcity and resource allocation, and we hope rational scrutiny of value in healthcare (benefits accrued/resources consumed). Physicians are more aware of this historic opportunity to thoughtfully study value considerations as objective metrics that can facilitate reasoned analysis, innovation and justice.²

Considerable time, equipment and energy have been diverted to subdue COVID-19, and for generally sound reasons. But concerns of resultant deficiencies providing basic health services, for example cardiovascular, prenatal and preventive care, are worrisome. Because >80% of COVID-19 deaths are in senior citizens, legitimate questions arise regarding scarcity and quality-of-life-years.³ We can anticipate medical specialties and interest groups to claim the primacy of their target population should any care-rationing loom. Neonatology should not be immune to scrutiny; we have an opportunity to improve our ability to serve whole families best.

The care of extremely premature infants born <26 weeks highlights multifaceted interplay between scarcity, value and justice. To be clear, COVID-19 has not created this dynamic. It is misleading if obstetricians, neonatologists and/or ethicists blur legitimate extreme prematurity issues of suboptimal health outcomes, resource consumption and authentic shared decision-making with care-rationing, and for five reasons we briefly highlight.

First, the enormous cost of premature infant care in the United States has recently been elucidated with impressive summary graphics.⁴ These data highlight the challenges of population health management and prioritising value. Example, our healthcare organisation

has co-developed a paediatric accountable care initiative in response to third-party payers' increasing requirement for value measurements. A fixed dollar payment is provided for the total care of a group of children, thus necessitating careful consideration of sustained benefits vs. resource consumption. It is not a policy framework we accept as optimal, but it is the 'new normal' condition we must comply with. Example—if we accrue \$650,000 (550,000 euros) in expenses caring for a 24-week infant,⁴ we must apportion resources with other needs—primary care, behavioural health and specialty care. How do we allocate wisely and consider the interplay of value and justice? Who ultimately decides?

Second, Table 1 concisely summarises the recent neurodevelopmental outcomes literature. Not only is the neurodevelopmental impairment (NDI) rate disturbingly high after extreme prematurity survival, it is largely not improving in diverse settings. Scrutiny of the Table 1 manuscripts demonstrates that centres with near-universal NICU care of extremely premature infants do have higher survival rates, but do not demonstrate the most favourable morbidity rates, nor superior NDI outcomes. The most-cited manuscript to support aggressive NICU care proves that point—higher resuscitation rates of 22- to 24-week infants correlate with greater survival, but the morbidity rates and long-term NDI outcomes from these NICUs are not uniform quality benchmarks.⁵ Furthermore, 'trial-of-life' arguments are not supported by the Table 1 references, that is deaths of extremely premature infants are often not in the first few days of life. A recent large European collaboration documented that one-quarter of the deaths were after 3 months of age (Franz, Table 1).

Third, we are not aware of a single report from higher income countries of a premature infant denied a ventilator because of COVID-19 scarcity issues. Some authors have suggested this is happening by confusing shared decision-making regarding

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TABLE 1 Summary of recent, international neurodevelopmental follow-up studies of extremely premature infants

Author, Journal, Year	Report type	Population	Locale	Principal findings
Joseph, <i>Pediatrics</i> , 2016	10 year neurocognitive and academic evaluation, births 2002–2004	23–27 weeks GA	ELGAN Study, USA	>50% exhibited moderate-to-severe neurocognitive and academic deficits, with the most extensive impairments at 23–24 weeks GA
Serenius, <i>JAMA Pediatrics</i> , 2016	NDI rates compared at 2.5 and 6.5 years in the same cohort, births 2004–2007	22–26 weeks GA	Swedish EXPRESS group	36% free of NDI. 47% remained in the same NDI category at 6.5 years, 21% moved to a better, 32% to a worse category. 96%, 79%, and 63% of 22-, 23- and 24-week infants either died or had moderate-to-severe NDI.
Younge, <i>N England J Med</i> , 2017	Survival and NDI comparing three epochs, births 2000–2003, 2004–2007, 2008–2011	22–24 weeks GA	Neonatal Research Network, USA	Survival without NDI improved from 16% in Epoch 1 to 20% in Epoch 3. <1% and 1% of 22-week infants survived without NDI in Epochs 1 and 3. 7% and 13% of 23-week infants survived without NDI in Epochs 1 and 3
Cheong, <i>Pediatrics</i> , 2017	IQ, academic achievement, neurosensory assessment comparison births 1991–92 vs. 1997 vs. 2005	<28 weeks GA	Victoria, Australia	Major neurosensory impairment rates have not improved across 3 eras, academic performance deteriorated in the latest cohort.
Linsell, <i>Arch Dis Child FNN</i> , 2018	Long term, prospective, population-based, cohort study, births 1995	<26 weeks GA	United Kingdom and Ireland	No evidence of improvement in impaired cognitive function in premature infants through 19 years of age.
Synnes, <i>Arch Dis Child FNN</i> 2017	21 month corrected age neurologic assessment, births 2009 to 2011	<29 weeks GA	Canadian Neonatal Network	63%, 62% and 52% of surviving 23-, 24- and 25-week infants had NDI
Twilhaar, <i>JAMA Pediatrics</i> , 2018	Meta-analysis and meta-regression of cognitive outcome reports, births 1990–2008	<32 weeks GA or <1500 g BWT	All publications, all languages in North America and Europe	13 point mean overall IQ deficit shown in premature infants compared to term infants. No evidence of improvement over time in this significant cognitive impairment
Brydges, <i>Dev Med Child Neurology</i> , 2018	Meta-analysis of cognitive outcome reports	<32 weeks	All publications in English	Significantly lower IQ, executive functioning, and processing speed in premature infants compared to full-term infants, and worsens with lower GA and BWT.
Adams-Chapman, <i>Pediatrics</i> , 2018	Full spectrum neurologic evaluation, births 2011–2015	<= 27 weeks GA	Neonatal Research Network, USA	Rate of NDI (BSID III < 85) did not improve over time period (34% vs. 31%).
Spittle, <i>Pediatrics</i> , 2018	Motor impairment comparison, births 1991–1992 vs. 1997 vs. 2005	<28 weeks GA < 1000 g BWT	Victoria, Australia	Increasing motor impairment rate across the 3 eras, 23% to 26% to 37%
Burnett, <i>Pediatrics</i> , 2018	Executive functioning comparison, births 1991–1992 vs. 1997 vs. 2005	<28 weeks GA < 1000 g	Victoria, Australia	Worse executive function scores in premature infants compared to controls in all 3 eras, most notable in the latest cohort
Nakanishi, <i>J Perinat</i> , 2018	Full spectrum neurologic evaluation trend, births 2003–2012	22–24 weeks GA	Japan	No improvement in cognitive impairment rates over ten years in surviving 22- to 24-week infants (35%–40%), and an increase noted in CP over the most recent 5 years
Inoue, <i>Pediatrics</i> , 2018	Full spectrum neurologic evaluation trend, births 2003–2012	<= 500 g BWT	Japan	No improvement in neurodevelopmental outcomes over 10 years. 60% of survivors were neurologically impaired.

(Continues)

TABLE 1 (Continued)

Author, Journal, Year	Report type	Population	Locale	Principal findings
Ding, <i>Acta Paediatrica</i> , 2018	Meta-analysis of survival and neurodevelopmental outcomes, births 2005–2016	22–25 weeks GA	All English language publications with a minimum 4–10 years follow-up	Moderate-to-severe NDI in survivors was 42%, 41%, 32%, and 23% at 22, 23, 24 and 25 weeks
Hirschberger, <i>Pediatric Neurology</i> , 2018 See related Joseph report above	10 year comprehensive neurodevelopmental burden assessment of infants, births 2002–2004	23–27 weeks	ELGAN Study, USA	52% of 23- to 24-week survivors had at least one significant neurologic impairment (low IQ/EF score, CP, autism, seizures), 26% had two or more deficits
Myrhaug, <i>Pediatrics</i> , 2019	Meta-analysis of survival and neurologic impairment, births 2000–2017	22–27 weeks GA	All publications in English, German, French or a Scandinavian language	Moderate-to-severe NDI in survivors was 60%, 50%, 40% and 30% at 22, 23, 24 and 25 weeks. Risk of NDI was not reduced for children born in the most recent years
Rysavy, <i>J Pediatrics</i> , 2019	Survival and NDI, births 2006–2011	22–26 weeks GA	Neonatal Research Network, USA	Survival without moderate-to-severe NDI was 9%, 16%, 31%, 45% and 59% at 22, 23, 24, 25 and 26 weeks
Brumbaugh, <i>JAMA Pediatrics</i> , 2019	Survival and NDI, births 2008–2016	<400 g BWT	Neonatal Research Network, USA	Only 23 of 90 actively treated infants survived, 19 were evaluated, 14/19 (74%) had moderate-to-severe NDI
Watkins, <i>J Pediatrics</i> , 2019	Survival and NDI, births 2006–2015	22–25 weeks GA	University of Iowa, USA	Centre that advocates near-universal NICU care <25 weeks: 27% of surviving evaluated infants had moderate-to-severe NDI. 36% of surviving 22- to 23-week infants had moderate-to-severe NDI. No improvement over time noted
O'Reilly, <i>Pediatrics</i> , 2020	Comprehensive neuropsychological evaluation at 19 years, births 1995	<26 weeks GA	United Kingdom and Ireland	45% of survivors had major full scale IQ impairments at 19 years of age, a rate 15 times higher than term controls
Franz, <i>JAMA Pediatrics</i> , 2020	Survival and NDI, births 2011–2014	400–999 g BWT	European collaboration	44% of actively managed infants either died or had NDI. 36% of survivors had significant cognitive impairment

Note: Search strategy employed Ovid Medline, PubMed, the Cochrane Library, and Google Scholar.

Abbreviations: BSID III, Bayley Scales of Infant and Toddler Development, Third Edition; BWT, birth weight; CP, cerebral palsy; EF, executive functioning; ELGAN, extremely low gestational age newborn; EXPRESS, Extremely Preterm Infants Study in Sweden; g, grams; GA, gestational age; IQ, intelligence quotient; NDI, neurodevelopmental impairment; NICU, neonatal intensive care unit; NRN, Neonatal Research Network; USA, United States of America.

extreme prematurity care with COVID-19 adult-medicine triage discussions.⁶ In reality, pregnant women choose palliative comfort care for legitimate reasons unrelated to COVID-19, specifically the overwhelming majority of infants born 22–25 weeks either die in the NICU or suffer moderate-to-severe NDI and other chronic health issues (Table 1 references). Families of diverse cultural circumstances do not uniformly desire to accept these risks, thus respected medical organisations unequivocally endorse shared decision-making and informed choice regarding palliative vs. NICU care.⁷

Fourth, intrinsic worth of children with disabilities, or capacity to enjoy existence, are not the sole issues for every family facing extreme prematurity. Authentic informed choice amidst considerable family uncertainty and risk (maternal morbidities, caesarean sections, variable income, future children, NDI and inadequate social support) underscores the fundamental right families deserve—compassionate

dialogue, honest evidence review and avoidance of hierarchical coercion.⁸

Fifth, we are concerned with the premise implied by aggressive NICU care and 'trial-of-life' proponents: whatever happens in the hospital, it will be a 'good' outcome for the family, infant, providers and society. This is simply not the multiform, lived experience of many families nor providers, it risks coercion of vulnerable women, and is inconsistent with population health, justice and value pluralism.^{7–9} Advocates of NICU care for all extremely premature infants focus upon disagreements they have with physicians who do not agree with their constructs. But the true misalignment is with pregnant women and families of diverse circumstance who do not share their beliefs nor desires.^{9,10}

The authentic choice of palliative vs. NICU care springs from admixtures of disparate cultures, compassionate dialogue during shared decision-making, the sobering Table 1 references and the

authenticity of value pluralism. This historically evident principle illustrates human values have always been diverse, not necessarily irrational but often incommensurable, and at times irresolvable absent of hierarchy or force. Our point is that COVID-19 and adult-medicine triage controversies are not creating scarcity or new ethical issues in neonatology; palliative vs. NICU care decisions rest upon other legitimate considerations.

Medicine is often described as a deontological enterprise (duty-based), but often without clear reasoning or references. Today's medical-industrial complex suggests the opposite of deontology as the guiding principle. Conflicts of interest related to extreme prematurity advocacy (and palliative care) abound, for example census-based salaries, research projects and career paths related to NICU care, and religious/cultural beliefs of physicians variant from families.⁹ Virtuous neonatology exemplifies evidence-based care, culturally realistic and pragmatic ethical constructs that reflect humility, a circumspect view of technology's seductions and scientism's zeal, and keen awareness of scarcity's ubiquitous genesis of privation, adaptation and creativity.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this manuscript.

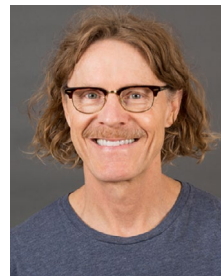
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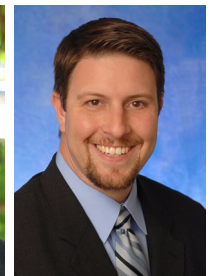
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