

# COVID-19, children and non-communicable diseases: translating evidence into action

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The world faces an existential, once in a lifetime pandemic due to a novel coronavirus (SARS-CoV-2) which has to date infected over 25 million people across the world, with nearly 850 000 deaths.<sup>1</sup> The disease, labelled COVID-19 by the WHO, has now spread to almost all the countries of the world and crippled the global economy. While high-income countries have been able to tap into their resources and reserves, for many low-income and middle-income countries, rising unemployment, population lock downs and closure of businesses have inflicted crippling damage on fragile economies, with rising inequalities and worsening poverty.

While early reports of the infection<sup>2,3</sup> suggested that the infection may be generally mild in children with COVID-19, with general case fatality rate less than 1%, there are increasing reports of complications among children and adolescents.<sup>4</sup> In addition, a recent series of cases with multisystem inflammatory response merits reconsideration of these risks.<sup>5</sup> There are also clear signals of predictors for adverse outcomes from COVID-19 infections. The disease has disproportionately taken a toll among the elderly population in long-term care facilities, with many dying without even being tested for COVID-19 infection.<sup>6</sup> There is clear evidence of excess mortality in subgroups, especially those with comorbidities, most commonly related to non-communicable diseases (NCDs), such as diabetes, hypertension, obesity, heart disease and cancer.<sup>7</sup> The same appears to be true among paediatric COVID-19 infections. A systematic review analysed a total of 7780 paediatric COVID-19 positive cases globally, and found that patients with information on

underlying conditions (n=655) included the following comorbidities: immunosuppression (30.5%), respiratory conditions (20%) and cardiovascular disease (14%).<sup>8</sup> A recent report from the UK of 651 hospitalised children with COVID-19 from 260 hospitals identified comorbidities in 42% (276/651) of cases.<sup>9</sup> Comorbidities most commonly associated with critical care admission on univariable analysis were prematurity (50% (15/30), critical care admissions vs 18% (30/165) of standard care admissions; p=0.001), respiratory comorbidities (10% (12/115) vs 4% (21/491); p=0.019), cardiac comorbidities (11% (13/115) vs 5% (25/493); p=0.018) and obesity (6% (7/115) vs 2% (10/487); p=0.028), although none reached significance on multivariable analysis.<sup>9</sup>

This nexus between a communicable disease and NCDs is one of the first demonstrations at scale of the multiplicative risks of these conditions. While much of the current outbreak-related information is from settings in China, Europe and North America where undernutrition rates are low, the association of excess risk of mortality with obesity is now well known. Expression of ACE2 (the functional receptor for SARS-CoV-2) is upregulated in adipocytes of obese patients and patients with diabetes, which turns adipose tissue into a potential target and viral reservoir and could explain the role of obesity and diabetes are potential comorbidities for COVID-19 infections.<sup>10</sup> The pulmonary lipofibroblasts located in the alveolar interstitium are also closely related to classical adipocytes and could differentiate into myofibroblasts causing pulmonary fibrosis and significantly exacerbating the pulmonary damage caused by SARS-CoV-2 infection.<sup>10</sup> The association of obesity and complications among paediatric admissions is further underscored by a study of 48 children with COVID-19 admitted to 46 participating paediatric intensive care units in the USA where obesity was notable as a comorbidity, particularly in older children (20.5% of children 6 years or older were obese).<sup>11</sup>

So how do we respond? The recognition that NCDs are a massive contributor to COVID-19 mortality and severe illness across all age groups should be a wake-up call to accelerate the implementation of preventive strategies for NCDs. Many of the known NCDs such as obesity, diabetes, hypertension and cardiovascular diseases have their origins in childhood or related to epigenetic influences and stressors in early life.<sup>12</sup> Optimising maternal nutrition and exclusive breast feeding is one of the best investments to reduce the risk of fetal growth retardation and optimising growth in early infancy, known risk factors for the development of NCDs.<sup>13</sup> Given the sudden rise in poverty and the threat to global food security, focusing on the health and nutrition of pregnant and lactating women and attention to breastfeeding support measures in early infancy should be prioritised in our COVID-19 response.

School age and adolescence offers additional window of opportunity to modify NCD risk factor behaviour. Reddy *et al*<sup>14</sup> have recently highlighted the 31% increased risk of severe COVID-19 among patients with a history of smoking. A national online survey of 4351 adolescents and youths in May 2020 in the USA<sup>15</sup> revealed that COVID-19 diagnosis was five times more likely among ever-users of e-cigarettes only (95% CI: 1.82 to 13.96), seven times more likely among ever-dual users (95% CI: 1.98 to 24.55) and 6.8 times more likely among past 30-day dual users (95% CI: 2.40 to 19.55). A survey of 1054 Canadian adolescents comparing behaviours before and after social distancing practices also suggests that while the percentage of users decreased, frequency of alcohol and cannabis use increased.<sup>16</sup> Promoting healthy behaviours and reducing risks is an essential part of universal health coverage and must be reinforced as part of COVID-19 mitigation strategies. Strategies for reducing dietary risk factors for obesity are most successful when begun early and when healthy foods must be available and affordable to all.<sup>17</sup> In the COVID-19 crisis and response period, given the common enforced restriction on physical activity and access to playgrounds as well as disproportionate intake of unhealthy, fast foods, these preventive strategies become even more important. The pandemic will likely result in exacerbation of mental health crises, including anxiety, depression and chronic stress. Young people and adults alike are at risk for short-term and long-term mental health sequelae, and preventive strategies must be further underscored.<sup>18</sup>

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In addition to prevention strategies, it is important to ensure that the needs of children and adolescents with existing NCDs such as type 1 diabetes mellitus, asthma and other chronic disorders are met. This will mean adapting and strengthening health systems at all levels to maintain supply chains and access to essential medicines for all living with NCDs, including children, and creating safe opportunities for ambulatory care. Routine care for existing conditions and immunisations including human papillomavirus must also not be overlooked in the setting of pandemics. Task sharing or task shifting in rural settings at this time of limited mobility through community health workers employing adequate personal protection could ensure continuity of integrated COVID-19 screening and health services including NCDs for people living in resource-poor settings. These principles are the fundamental pillars of the approaches recommended by the Lancet Non-Communicable Disease and Injuries Commission for the Poorest Billion for reaching those in greatest need and are especially applicable to the current pandemic.<sup>19</sup>

Women and children are among the most susceptible to pandemics and COVID-19 is no exception. While the face of NCDs is visible in those severely ill and dying with the infection, we make a fervent plea not to ignore the opportunity for preventive strategies and risk mitigation. Prevention and control of NCDs should become effective tools to prevent drastic consequences of future pandemics and should be an integral part of the WHO's plans to serve three billion additional people in various contexts.<sup>20</sup> These investments, if made during the adolescent period, would bring a triple dividend of protection and health benefits during adolescence, across the life course and into the next generation<sup>21</sup>

COVID-19 has unearthed the inequities in our society and access to health-care like no other. This association of increased risk of hospitalisation and excess mortality and adverse outcomes is reflective of the disproportionate clustering of such risks among the poor and marginalised populations, often ethnic minorities.<sup>22</sup> The clustering of NCDs in these marginalised population subsets is the underbelly of society in many instances and also perpetuates the vicious cycle of disease, poverty and premature mortality.

With legitimate concerns that mitigation strategies and COVID-19 response may push an additional 42–66 million children into extreme poverty,<sup>23</sup> responding to this crisis must have a poverty and equity focus. Many of these poorest children also have a disproportionate burden of NCD risks, and uncovering that reality could well be the silver lining in COVID-19's dark clouds.

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**Contributors** The lead author ZAB and coauthors contributed to drafting and approved the final version of manuscript for submission.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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**To cite** Bhutta ZA, Hauerslev M, Farmer M, *et al.* *Arch Dis Child* Epub ahead of print: [please include Day Month Year]. doi:10.1136/archdischild-2020-319923

Received 11 June 2020

Revised 31 August 2020

Accepted 18 September 2020

*Arch Dis Child* 2020;0:1–2.

doi:10.1136/archdischild-2020-319923

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