type of one-to-one randomisation that does not favour either treatment group and the chance of patient crossover from the standard-of-care group to the intervention group.

Given that the results of the KEYNOTE-40 trial support those of the Checkmate 141 trial, two studies now suggest the superiority of PD-1-directed antibody therapy over standard of care in head-and-neck squamous cell carcinoma at a particularly vulnerable timepoint (ie, 3–6 months after cisplatin failure). The Article also reveals promising data for the overall survival and quality of life of the patients, given the lower toxicity of the checkpoint inhibitors compared with chemotherapeutic agents. Fewer patients appear to have side-effects in the checkpoint group (155 [63%] of 246, 33 [13%] of which were grade 3, 4, or 5) than in the standard-of-care group (196 [84%] of 234, 85 [36%] of which were grade 3, 4, or 5). Future analyses will have to re-evaluate this side-effect pattern in more detail in the long term.

The Article will be important for the further de-velopment of checkpoint therapeutic strategies in squamous cell carcinoma of the head and neck because the paper not only describes the study in detail but also compares patient subgroups with the CheckMate 141 study.[1] Differences and similarities are depicted in a point-to-point manner that is educative.

Another important factor is the definition of predictive biomarkers that might help to distinguish responders from non-responders. The study analyses the prognostic predictive value of PD-L1 expression on cells of the lymphocytic infiltrate in the primary cancer versus expression on primary cancer cells. Other biomarkers still need to be evaluated in future studies. Several ideas point to the markers needed for implementation of precision medicine and prediction of resistance to therapy.[5–7]

Cohen and colleagues' study might prove to be an argument to alter guideline-based treatment of patients with head-and-neck squamous cell carcinoma and implement PD-1-targeting antibodies in standard care in the setting of second-line treatment failure.

The publication of the first data from the KEYNOTE 48 study,[8] presented during ESMO 2018, represents another major study having the potential to alter treatment guidelines as it shows the superiority of pembrolizumab over the EXTREME regimen, which could shift the use of PD-1 antibodies to standard care of patients with head-and-neck squamous cell carcinoma already in the setting of first-line treatment failure.

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I declare no competing interests

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Framing an agenda for children thriving in the SDG era: a WHO–UNICEF–*Lancet* Commission on Child Health and Wellbeing

The Millennium Development Goal (MDG) era witnessed an unprecedented drop in mortality among children younger than 5 years and in undernutrition across all regions. However, the poorest children remain 1·9 times more likely than others to die before reaching the age of 5 years.[1] If these child mortality trends persist, the Sustainable Development Goal (SDG) child mortality targets (reducing neonatal mortality to at least as low as

12 per 1000 livebirths and under-5 mortality to at least as low as 25 per 1000 livebirths in all countries by 2030) will not be met in 47 countries, 34 of which are in sub-Saharan Africa. Additionally, undernutrition is prevalent in some regions, with an estimated 151 million children affected by stunting worldwide.[2] This situation is further complicated by burgeoning overnutrition together with vitamin and mineral deficiency in early childhood and their links to adult non-communicable diseases. Reversing current trajectories requires not only applying lessons learned from the MDG era but also addressing all the determinants of child health and wellbeing that will impact whether today's children achieve their maximum potential in every situation. Indeed, evidence shows that about 50% of the reduction in child mortality in low-income and middle-income countries (LMICs) between 1990 and 2010 was due to indirect influences beyond the health sector.[3] The focus on the health of children must expand beyond mortality to include healthy growth, development, and wellbeing.[4]

A multisectoral approach that addresses all the determinants (social, economic, cultural, political, environmental, and commercial) of child health and wellbeing resonates with the SDGs' promotion of an integrated approach to global social and economic development.[5] There is increasing recognition, for example, of the importance of early life determinants (stimulation, socialisation, and a stable, clean environment) on child social and economic potential over the life course. The 2016 *Lancet* early child development Series reported that 250 million children (43%) younger

than 5 years in LMICs are at risk of not reaching their developmental potential,[6] with widespread consequent impacts. Further, WHO estimates that 27% of all child deaths now arise from environmental causes[7] and almost 90% of the world's children do not breathe clean air. Clean water and sanitation remain beyond the reach of billions of people, and conflict and insecurity affect the domestic stability of and access to health care, good nutrition, and early child education for many children globally. Coordinated action across multiple sectors is required for all children to be able to develop their maximum potential in every country and community. All nations aspire to see their children develop and flourish as a human right and as the basis for a strong economy. In this context, there is a need for guidance and agreement on maximising child health and wellbeing in the SDG era.

In response to this need, and after reviews of several global child health approaches and policies,[8,9] WHO and UNICEF have initiated a *Lancet* Commission on Child Health and Wellbeing, with support from the Bill & Melinda Gates Foundation. The Commission's findings will be published as a report in *The Lancet*, expected in 2019. The Commissioners are drawn from every geographical region and from disciplines including maternal and child health, nursing, nutrition, epidemiology, human rights, education, environmental and political science, economics, anthropology, and social science.

The Commissioners met in Dakar, Senegal, in February, 2018, to reflect on the state of the world's children and agreed on a process of elaborating a cross-sectoral agenda on child wellbeing that reflects realities in the SDG era. Consensus emerged around the need to address influences during the first two decades of life, with "child" denoting those aged 0–18 years. Five working groups have been established with experts from many disciplines and global regions to collectively address the following areas.

A group on leadership and governance will address how to secure commitment and accountability at all levels of government, as well as among donors, international organisations, non-governmental organisations, faith-based organisations, and corporations. A second group will use a systems lens for multisectoral action, and examine how to bring together diverse systems across different sectors to maximise the health and wellbeing outcomes for children in the first 18 years of life, and how to increase accountability for enabling child health

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and wellbeing across all platforms and levels. A group on financing and economics will consider challenges around microeconomic modelling for financing and focus on identifying the new partnerships, investment policies, and priorities that will increase the chances of more children thriving by 2030. Equity focused data and information for action and accountability that build capacities for accountability and agency will be addressed by a fourth group. Finally, a fifth group will explore family, household, and community approaches to health and wellbeing, and will identify priorities for governments and districts in different settings and how to support the most marginalised communities to build resilience and tackle the drivers of their disadvantage.

This Commission will take a whole of government approach, addressing health and development beyond mortality, and will encapsulate children's perspectives and visions. Of course, context is key. The problems facing Nigeria, Nicaragua, and the Netherlands are different. But there are commonalities. The Commission will focus on the "how to" as opposed to the "what", the process rather than content. This approach will go beyond a focus on national and ministry decision making. Districts and communities are where multisectoral approaches work best. And community engagement is critical to success; we intend to capture the views, hopes, and dreams of children and young people. At the same time, country ownership and political leadership are necessary. Our Commission will be mindful to align with country level planning processes that address realities on the ground. The methods and findings of the Commission will be inclusive, participatory, and incorporate the perspectives of adolescents and other constituencies, as appropriate.

The Commission's report will not only examine the successes and lessons learned from previous efforts but will also strive to balance optimism with acknowledged harsh realities. Solutions for child health and wellbeing will be viewed through the lens of protection, promotion, prevention, and treatment. We want to build the case for a coordinated response from government, business, and civil society that acknowledges the interdependent nature of the challenge to sustainably improve children's lives in different settings. And we shall suggest monitoring indicators that nations can use to assess progress between now and 2030.

Investment in our children is the first step towards cultivating a healthy, productive society, and should be central to any government's policy and in line with the statutes of the Convention on the Rights of the Child. We are confident that the experience and passion of our Commissioners for this topic can benefit generations of children to come.

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Health-emergency disaster risk management and research ethics

Health-emergency disaster risk management (health-EDRM) aims to reduce the health risks and vulnerability associated with emergencies and disasters,[1–3] such as natural disasters, infectious disease epidemics, complex emergencies, technology failure, or global population movement. Medical care and health responses in emergency contexts often rely on best-fit interventions rather than best practices to protect communities in suboptimally functioning systems and complex

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contexts.[4,5] Unlike health emergency actions that are focused on the response, the health-EDRM approach emphasises emergency preparedness and disaster risk reduction and can take account of the limitations of the response-focused research landscape.[4,6] A greater emphasis on prevention can provide opportunities for research infrastructure building in normal times to support any emergency-related research attempts.

The ecology of the global emergency research system involves a range of stakeholders including, but not limited to, families, caregivers, local governments or authorities, funders, research institutions, journals and publishers, and users of the relevant research results. Although research stakeholders have a responsibility to protect the interests of communities involved in research, achieving this is rarely straightforward in emergencies. Research can be simultaneously subject to different, sometimes competing, requirements and expectations. Issues such as decision making about research participation, determination of duties and roles at the research interface, treatment and public health, management of expectations on the front line, and participant protection from stigmatisation, discrimination, and exclusion are questions hotly debated in the bioethics community.[5,7]