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replacement therapy that has prolonged survival in infants with the disease.⁹ In animal models of spinal muscular atrophy and autopsies of patients with severe phenotypes, almost every organ and tissue is affected.¹⁰ Consistent with our experience with treating patients with Pompe disease, impaired function of peripheral tissues and organs might result in substantial comorbidities in infants with spinal muscular atrophy later in life, particularly among those who receive only CNS-directed treatment.¹¹ Screening of newborn babies and early treatment are effective but might nevertheless result in systemic phenotypes. Systemic treatments might best mitigate systemic manifestations, but off-target effects accrued over a lifetime of treatment can potentially be limiting to normal development and function. Expert consensus must be reached on surveillance testing for organ pathology that might not be clinically symptomatic or detected by routine clinical testing, to understand the true extent and clinical implications of treatment-modified phenotypes.

A pressing need exists to establish centralised international databases for real-world longitudinal monitoring of long-term drug efficacy and toxicities. Systematic efforts are needed to monitor systemic and treatment-modified phenotypes, identify treatment responders and non-responders, and define appropriate therapeutic windows and cell targets for repletion therapies. Ultimately, the goal is to find the optimum therapeutic regimens to treat the entirety of Pompe disease and spinal muscular atrophy pathology.

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Human papillomavirus vaccination for young survivors of cancer



Human papillomavirus (HPV) vaccine can prevent six types of cancers and has a strong safety profile. However, only 55% of US adolescents (ie, aged 13–15 years) are up to date on HPV vaccination.¹ This proportion is well below the Healthy People 2030 goal of 80% and coverage for other adolescent vaccines of almost 90%.¹ HPV vaccination rates

also decreased notably during the COVID-19 pandemic, a problem that was probably amplified for survivors of cancer. Low uptake of HPV vaccine is an especially pressing problem for adolescent and young adult (AYA) survivors of cancer, whose risk of a new cancer diagnosis is 3–10 times higher than the general population.²

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A study by Wendy Landier and colleagues in *The Lancet Child & Adolescent Health*³ shows that HPV vaccine is most likely effective for AYA survivors of cancer. In this single-arm, non-inferiority trial in the USA, survivors of cancer who were aged 9–26 years received three doses of quadrivalent or nonavalent HPV vaccine over 6 months. The study noted that antibody response against HPV types 16 and 18 in survivors of cancer was non-inferior to estimates for the general population in other studies. Indeed, survivors of cancer appeared to mount an even more vigorous immune response than did the general population in 15 of 16 subgroup analyses. Although it is not yet known what level of immune response confers protection against HPV-related cancers, immunobridging studies such as this are a standard tool for understanding how a vaccine will perform where a full trial might not be feasible.

Unfortunately, uptake of HPV vaccine appears to be lower among AYA survivors of cancer than among the general population. In a US study of 982 AYA survivors of cancer, uptake of HPV vaccine was lower than were national estimates for adolescents in the general population (ie, 24% vs 41%).⁴ The deficit existed for all subgroups in stratified analyses by sex and age. An earlier study by the same research group noted no difference in uptake of HPV vaccine between 230 US female AYA survivors of cancer when compared with 70 age-matched controls with no previous history of cancer.⁵ Other studies also suggest low uptake of HPV vaccine among AYA survivors of cancer, but many either did not include comparison with healthy AYAs or examined intentions rather than behaviour. Cross-sectional studies of just AYA survivors of cancer have reported that male and younger (9–12 years compared with 13–17 years) respondents are less likely to receive HPV vaccine than are other AYA survivors of cancer.⁴

The Increasing Vaccination Model⁶ offers insights into effective approaches for promoting vaccine uptake, and is used by WHO and the US Centers for Disease Control and Prevention. The model's first proposition is that what people think and feel motivates vaccination. As with vaccine confidence in general, AYA survivors of cancer and their families have safety concerns that might undermine the uptake of HPV vaccine.⁷ Families might also see the threat of cancer as more pressing than prevention of other diseases later in life. A surprising finding is that efforts to change what people think and

feel outside of clinical settings, such as through risk communication and confidence-boosting campaigns, are not reliably effective in increasing uptake.⁶

The model's second proposition is that social processes, including social norms and recommendations, motivate vaccination. AYA survivors of cancer face challenges such as absence of recommendations from primary care providers⁴ and ineffective communication when providers recommend the vaccine.⁷ Many caregivers also have not themselves received HPV vaccination, making the norm less salient. Efforts to leverage social processes are promising, especially through increasing the frequency and quality of provider recommendations.⁸ Opportunities include making HPV vaccination for AYA survivors of cancer a social norm, such as through advocacy by vaccinated AYA survivors of cancer,⁹ and encouraging more frequent and higher quality provider recommendations between ages 9 years and 12 years.⁹

The model's third proposition is that direct behaviour change increases vaccine uptake. The general idea is to help people to act on their willingness to vaccinate without trying to change what they think or feel or their social environment. Direct behaviour change interventions are the most reliably effective in increasing vaccine uptake. First, in-person reminders or reminders sent to patients via email or text message are relatively low cost and reliably effective at increasing uptake when coordinated centrally. Qualitative research suggests that AYA survivors of cancer would welcome reminders to complete the series of HPV vaccines, especially when accompanied by visual media.⁷ Second, ensuring easy access to vaccination is another reliably effective intervention. AYA survivors of cancer whose parents believe that they have inadequate health-care insurance coverage are less likely to receive HPV vaccine compared with parents who believe that they have adequate insurance coverage.⁴ For example, all US insurance plans already provide first dollar coverage for vaccination, and it is free to uninsured children through the Vaccines for Children programme. It is important to ensure that families know of these resources. Finally, automatic appointments, school-located vaccination, and cash incentives are also effective interventions that might be especially applicable to AYA survivors of cancer.

Low uptake of HPV vaccine among AYA survivors of cancer is worrisome given their high cancer risk

and national recommendations for vaccination before age 13 years.² Risk of HPV exposure accelerates during adolescence, and the vaccines also generate the highest immune response when delivered at a young age. For these reasons, HPV vaccine is most effective when given at young ages, making vaccination of AYA survivors of cancer important. Clinicians and families might defer preventive services, including HPV vaccination, during cancer treatment. Additionally, many survivors of cancer are not fully reconnected to primary care once their treatment ends.¹⁰ Substantial opportunities exist for ensuring high uptake of HPV vaccine among AYA survivors of cancer. Improving engagement between cancer care and primary care teams is an important first step.

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School violence: where are the interventions?

Globally, 1 billion children experience some form of physical, sexual, or emotional violence each year.¹ Most of these children live in low-income and middle-income countries, and much of this violence occurs in and around schools.² For the 90% of children who are enrolled in primary school, violence might be even more common in school than at home.² About 60% of children aged 6–10 years report recent physical and emotional violence from peers at school,² and 46–95% of primary school students experience corporal punishment from teachers, including in countries with legal prohibitions.³ According to a UNESCO report, sexual violence and harassment are also common, experienced by more than 10% of students in 96 countries. But some groups are at an even higher risk. In Uganda, for example, 20% of primary school girls aged 11–14 years with disabilities, but 10% of primary school girls of the same age without disabilities, reported sexual violence, mainly from peers but also from teachers.⁴

Young people who experience physical, sexual, or emotional violence are more likely to experience

further violence, and to perpetrate it. Violence is associated with a range of adverse health and social outcomes, including increased risk of poor mental health, substance use, chronic inflammation, poor educational outcomes, and worse future employment prospects. Teachers' use and tolerance of violence at school is likely to reinforce girls' and boys' use of violence in peer interactions and intimate partnerships, owing to social learning about how to navigate



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For more on **bystander programmes** see <https://www.campbellcollaboration.org/better-evidence/bystander-programs-sexual-assault-adolescents-college-students.html>
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