Adverse childhood experiences (ACEs) can affect development in ways that disrupt the formation of human capital and contribute to later-life morbidity and mortality. Theories of development predict that the timing of adversity will affect its outcomes. However, empirical evidence for timing-specific effects remains scant. In this issue of JAMA Network Open, Andersen reports an analysis of population-register data from Denmark that suggests timing-specific associations of household dysfunction ACEs with young people’s successful transition to adulthood. Andersen’s study linked data from several Danish registers to compose records tracking children born between 1987 and 1995 and their families from the child’s birth until they reached age 19 years. The analysis tested how exposure to household dysfunction ACEs during ages 0 to 2, 3 to 5, 6 to 12, and 13 to 17 years were associated with disruptions in children’s transition to adulthood. Children’s ACE exposure was measured from records of parental unemployment, incarceration, psychiatric diagnoses, and divorce as well as children’s placement in foster care. Disruption to the transition to adulthood was measured from records of education, employment, criminal charges, and psychiatric diagnoses. Andersen’s analysis compared siblings in the same family who experienced household dysfunction ACEs at different stages of development, eg, when a younger sibling’s early-childhood exposure was simultaneously their older sibling’s middle-childhood exposure. Using this sibling comparison design, Andersen identified a dose-response association between accumulation of ACEs and increased likelihood of experiencing disruption to the transition to adulthood. Adversity exposures during adolescence (ages 13-17 years) had larger magnitude risk associations compared with adversities that occurred earlier in development. Effect sizes for adolescent exposures were nearly 2-fold those for exposures in middle childhood and more than 3-fold those for exposures earlier in life. The findings of stronger associations for exposures during adolescence contrast with the popular narrative of the first 1000 days as a unique window of opportunity to promote positive development. They are also at odds with theoretical estimates from models of dynamic skill formation, which suggest that investments during early childhood should have higher returns than investments later in life. Andersen’s results resonate with emerging research streams in both neuroscience and the social sciences to suggest that benefits of interventions in adolescence may be underappreciated.

The US Centers for Disease Control and Prevention ACE Pyramid proposes that childhood adversity affects future health through pathways of disrupted neurodevelopment, leading to social and cognitive impairment and the adoption of health risk behaviors. One reason for an early-childhood focus in intervention efforts is the concentration of critical periods in neurodevelopment in the first years of life. However, as Andersen notes, this same logic may also encourage focus on adolescence. New science suggests that adolescence is a second critical period in neurodevelopment, characterized by experience-dependent plasticity affecting higher-order cognitive functions, including memory and self-control. Robust development of these higher-order cognitive functions is essential for a successful transition to adulthood and for health and well-being across adult life. If household dysfunction during adolescence interferes with this development, consequences for the transition to adulthood and beyond may be substantial.

Setting aside specific neurodevelopmental vulnerability, adolescence may also be thought of as a critical period in children’s human capital development. During adolescence, heightened social sensitivity and increased sensation seeking coincide with tracking into differentiated academic curricula and the first option to drop out of school. Even small disruptions in academic performance can severely reduce access to postsecondary education and future economic opportunities. One
example is the observation that changes in family economic circumstances have relatively larger associations with children's educational attainment when they occur during adolescence than when they occur earlier in childhood. Importantly, interventions that specifically target the developmental vulnerabilities of adolescents can help them stay in school.

Two features of Andersen's analysis build confidence in the conclusions of the article and outline important directions for future research. First, Andersen's study used administrative records that prospectively recorded the ACE exposures of an entire nation's population of children across a series of birth cohorts. These data are less subject to bias that can arise if individuals with high levels of ACE exposure or those with more severe challenges during the transition to adulthood are less likely to participate in research. They are also not subject to the biases that can arise from selective recall of ACEs in retrospective studies or selective underreporting of ACEs in prospective studies. In addition, register data may provide greater precision in recording the specific timing of exposures, such as parental unemployment. Furthermore, because of their size and scope, register data make analyses like Andersen's sibling comparisons possible. Many nations have registers like Denmark's. Andersen's analysis illustrates the potential of these administrative databases to inform understanding of how adversity shapes child development.

Second, Andersen used the register data to compare siblings who shared the same ACE exposures but experienced them at different stages in development. This design blocks confounding from all other exposures shared by siblings in the family, including characteristics of parents, neighborhoods, and the 50% of genetic variation shared by siblings. Such confounding is likely substantial. Figure 2B in the study by Anderson shows the contrast between the sibling comparison design and a traditional analysis that compares children in different families. Effect sizes from the sibling comparison design are far from trivial, but they are much smaller. Future ACE studies must do more to address the threat of residual confounding by risks shared within families.

Important questions remain. The register data analyzed by Andersen captured household dysfunction dimensions of ACEs but not abuse or neglect. It is possible those exposures differ from household dysfunction in the association between developmental timing and long-term consequences. Andersen studied children growing up in Denmark, a country with generous social welfare policies. In this context, household dysfunction may not result in the same degree of material deprivation as in, for example, the United States. Therefore, Andersen's results highlight the importance of social and emotional consequences of household dysfunction and potential value of interventions that do more than ameliorate material disadvantage. At the same time, the direct implications of Andersen's findings for program and policy design are less clear in settings where household dysfunction may more often result in physical insults to child development.

Within the context of Denmark and other countries with generous social welfare policies, Andersen's results have policy implications. First, policies that have the same cost and same effectiveness regardless of the age of the child—such as interventions targeted at parents via unemployment benefits, family services, or support for mental disorders—should consider prioritizing parents of adolescent children. Second, adolescents themselves might be the primary target for programs and policies. Unlike newborn children, adolescents can interact directly with program officers. Some adolescent programs might be less expensive and more effective than comparable parental programs: children could be more malleable than their parents, and the time and effort would be focused directly on the child, rather than influencing them indirectly via their parents. Both policy avenues would improve the cost-benefit analysis of money spent on public programs, the first having higher returns but similar costs and the second cutting costs directly.

Prevention of ACEs for children of all ages is a public health priority. Effective design of programs and policies to prevent ACEs and to buffer children from the consequences of ACEs when they do occur depends on research studies like that by Andersen. Her findings contribute to evidence that programs and policies that stabilize and strengthen families well beyond the first years of a child's life have potential to generate lasting benefits. Furthermore, her innovative application
of big data to study the timing of ACEs reveals new evidence for adolescence as a critical period in child development.

REFERENCES
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