

Editorial Perspective: Adverse childhood events causally contribute to mental illness – we must act now and intervene early

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Introduction

Current thinking about psychiatric etiology is that genes predispose individuals for deleterious outcomes when exposed to environmental triggers. Adverse childhood experiences (ACEs; e.g. exposure to violence or neglect) are the earliest known triggers in a person's life and may lead to substantial health problems. Indeed, findings from two of the most comprehensive and influential reviews of ACEs as risk factors document that high ACE exposure increase risk for a long list of adverse health outcomes (Felitti et al., 1998; Hughes et al., 2017; see Table 1). Associations were modest for physical inactivity, overweight or obesity, and diabetes (ORs

<2); large for smoking, poor self-rated health, cancer, heart disease, and respiratory disease (ORs of 2–3), strong for sexual risk-taking, mental ill health, and problematic alcohol use (ORs of 3–6), and strongest for problematic drug use and interpersonal and self-directed violence (ORs >7). Interestingly, the results of both reviews are strikingly similar and are not affected by the passage of time, despite having been conducted approximately 20 years apart.

Given the pernicious sequelae of ACEs, policies and interventions are needed to mitigate downstream effects; however, funds for mental health care are scarce and public investment in reduction of ACEs and its consequences is more likely when causality can be shown. Thus, our objective is twofold: (1) synthesize research on potential causal links of ACEs and its deleterious consequences and (2) develop a roadmap for large-scale policy and intervention.

Table 1 Odd ratios for specific ACEs and corresponding specific outcomes

Outcome variable	Hughes et al. (2017) <i>N</i> = 253,719 O vs. 4 and > events	Felitti et al. (1998) <i>N</i> = 9,508 O vs. 4 and > events
Physical inactivity	1.3	1.3
Overweight or obesity	1.4	1.6
Diabetes	1.5	1.6
Cardiovascular disease	2.1	2.2
Heavy alcohol use	2.2	7.4 ^a
Cancer	2.3	1.9
Liver or digestive disease	2.8	n/a
Smoking	2.8	2.2
Respiratory disease	3.1	3.9
Multiple sexual partners	3.6	3.2 ^b
Anxiety	3.7	n/a
Early sexual initiation	3.7	n/a
Teenage pregnancy	4.2	n/a
Depression	4.4	4.6
Illicit drug use	5.6	4.7
Problematic alcohol use	5.8	7.4 ^a
Sexually transmitted disease	5.9	2.5
Violence victimization	7.5	n/a
Violence perpetration	8.1	n/a
Problematic drug use	10.2	10.3 ^c
Suicide attempt	37.5	12.2

n/a, no data were reported on this variable.

^aDefined as “considered oneself an alcoholic”.

^b50 or more intercourse partners.

^cEver injected drugs.

Definition of ACE

ACE is a broad umbrella term that describes the presence of severe negative environmental events that require significant emotional, cognitive, or neurobiological adaptation by an average child. ACEs may be chronic (e.g. prolonged separation from a caregiver) or involve single events. Common ACEs include parental incarceration, domestic violence, household mental illness/suicide, household alcohol and substance misuse, exposure to physical and sexual abuse, neighborhood violence, bullying, discrimination, and parental death.

Objective 1: Examine evidence of causality

Absolute “proof of causality” in science is difficult, cumbersome and expensive. A widely accepted approach to study causal mechanisms and to rule out alternative explanations is via logical criteria. Particularly influential have been Austin Bradford Hill's criteria (Hill, 1965) which are probabilistic and cumulative, and emphasize plausibility; no absolutes are claimed.

Our synthesis systematically used Hill's nine criteria to document evidence for the causality of ACE exposure and risk for adverse health outcomes. The

full results are placed in a Supplemental file due to their length (<https://daslab.psych.ubc.ca/publications/supplemental-materials/>) and a synthesis of these results is presented below, followed by the policy recommendations that emerge from them.

1. Strong *Linkage* has been documented and replicated between ACEs and a wide range of deleterious outcomes.
2. There is remarkable *Consistency* of linkages between ACEs and deleterious outcomes (see Table 1). Suicidal behavior tops every list and substance abuse ranks second. Risk for mental health outcomes is strong and physical and mental illnesses are also consistently predictable following ACE exposure.
3. Testing for *Specificity* is now considered of limited use because its logic is too narrow and even counterproductive; a swath of deleterious outcomes is demonstrated.
4. *Temporality* (i.e. the causal event must precede the outcome) is integral to ACE research by design and is well-documented across studies. That being said, it is important to acknowledge that many studies rely on retrospective assessments of ACEs, and the strongest evidence of temporality comes from prospective assessments. Moreover, given the long-term consequences of ACEs, research likely underestimates negative sequelae in late life.
5. *Gradient effects* (i.e. dose-response effects) are seen consistently, thus adding to a causal inference interpretation. However, this criterion fails to consider promising nonlinear models (i.e. threshold or curved models).
- 6 & 7. Biological *Plausibility* and *Coherence* were clustered together because of their overlap and are evident via strong (while still growing) neuroscience findings supporting the existence of multiple interacting mechanisms via mediational causation models (Lupien, McEwen, Gunnar, & Heim, 2009; McLaughlin et al., 2016). Research now looks at possible differential effects for neglect versus abuse, and accumulates evidence for the perniciousness of ACEs by showing systematic changes in age-specific brain development, and revealing the mechanisms of ACEs functioning as toxic stressors with measurable changes in biological processes, cognitive function, and emotion regulation.
8. Extensive animal *experimentation* supports causal models but human research is scarce because it is ethically problematic; available research supports early intervention/prevention and long-term benefits. Early intervention may even change underlying physiological dysregulation (McLaughlin et al., 2016). Missing, however, is longitudinal research on potential benefits lasting into adulthood.

9. A useful *Analogy* is tobacco use which, like ACE research, also fits within research paradigms on health. Smoking reduction has been partly successful and its usefulness for triggering social policy changes inspires hope for reduction of ACE sequelae.

Objective 2: Consider health care policy implications

This synthesis of research on ACE outcomes supports causal inferences for later adverse health outcomes and offers a solid and logical foundation for proposing urgently needed prevention. Goals of treatment and prevention are to minimize suffering of individuals and improve their health, prevent transgenerational transmission of risk, and reduce long-run costs to health care systems and society. Specifically, we propose to (a) initiate more preventive efforts now rather than waiting for even more evidence, (b) focus on parents and children, especially during pregnancy and the first two years of life, and (c) to push for multipronged, simultaneous prevention and treatment.

A distinction of primary, secondary, and tertiary prevention may be useful in structuring the following section which lays out the opportunities and pitfalls of our propositions.

Primary prevention

A great advantage of primary prevention is its potential to prevent initial disease onset and its ability to be offered to large groups without labeling “problem” populations or individuals. Primary prevention can be geared toward the entire population by targeting factors such as poverty, income inequality, and low education. Although these targets offer promise for reducing ACE exposure, they require stable funding and significant political will, and are lofty goals even in rich countries. Such targets are outside the daily activities of mental health professionals who, however, can be active in lobbying and provide the scientific justification for prevention as this editorial perspective is intended to support.

Alternative primary prevention approaches can target entire countries or states/provinces (e.g. through the school system) by teaching resiliency skills that mitigate risk for adverse health outcomes in youth or by providing courses in sex education and drug awareness that can decrease youths’ engagement in risky behaviors. Community services (e.g. parent training, parent drop-in centers, or widely accessible quality daycare) can also provide parent support and coping skills to manage their own stress and mental health concerns, which may decrease the prevalence of ACEs (Lundahl, Nimer, & Parsons, 2006). We believe that these efforts work because they teach problem solving skills to children

and parents that are transferable to diverse life challenges and because they offer support to parents who themselves often have trauma backgrounds and trouble with emotion regulation.

Many such programs can be delivered via face-to-face or virtual methods and have been tested for efficacy and cost-effectiveness (Skeen et al., 2019). However, the majority are geared toward risk reduction for substance abuse, which highlights the urgent need to expand the range of prevention targets. Excellent technical reports are available to judge efficacy and cost-effectiveness of existing prevention programs, from which three targets emerged as most promising: interpersonal skills, emotion regulation, and alcohol and drug education (Skeen et al., 2019).

Secondary prevention

Secondary prevention requires screening and identification of at risk groups, which unfortunately can lead to discrimination or can benefit some population subgroups more than others. A valuable focus of secondary prevention is the support and training of parents to minimize abuse and neglect. A particularly well-received program is the Nurse-Family Partnership (NFP), which is designed for young, first-time mothers, and their children who are coping with socio-economic disadvantage. This intervention starts early in pregnancy and continues until children reach their second birthday. An intensive home-visiting program is provided by public health nurses that focuses on children's mental health and development and reduces childhood injuries while also improving mothers' lives.

Another approach to secondary prevention is to address long-term outcomes for children who develop behavior problems as a result of ACE. Whereas existing primary prevention programs have predominantly targeted school-age children, there is a relative dearth of evidence-based secondary prevention for children below school age. Particularly promising results have been shown for treatment of oppositional defiance and conduct disorders. For example, a recent systematic review concluded that intervention reduced subsequent criminal activity. Three programs were identified as most effective: Class-Room Centered intervention, Good Behavior Game, and Fast Track (Waddell, Schwartz, Andres, Barican, & Yung, 2018).

Tertiary prevention

Prevention is "tertiary" when individuals already affected by a disease (e.g. depression) are treated to restore health. With respect to psychiatric sequelae of ACE, effective tertiary prevention requires affordable access to high-quality psychotherapy and/or psychopharmacological intervention, in particular for the treatment of trauma (Post Traumatic Stress

Disorder) or other sequelae of ACE (e.g. depression, anxiety, substance use, and low self-esteem). The literature often makes reference to "trauma-informed therapy" but this concept cannot be categorically ascribed to only one particular therapeutic approach; it reflects well-trained clinicians who integrate the known ACEs when selecting treatment targets and approaches for a client. Trauma-focused cognitive-behavioral therapy is a clearly structured approach with good empirical support (Ramirez de Arellano et al., 2014). Nevertheless, access to affordable, high-quality treatment providers presents a challenge, particularly for those individuals most at need and with limited financial resources. Ideally, individuals with a history of ACEs should be referred to psychotherapy before they become parents to minimize transgenerational effects of ACEs.

The "win-win" of multiple interwoven benefits of prevention

Some blurring between the subtypes of prevention appears inevitable (and desirable!). For example, extended follow-up into teenage years and adulthood reveals that successful treatment of the child with high ACEs morphs into secondary prevention of adulthood behavior problems and psychiatric diagnoses. This may in turn serve as primary prevention for the next generation by minimizing their risk of exposure to ACEs (Waddell et al., 2018). Thus, successful treatment of childhood behavior problems can have far-reaching benefits.

Caveats for investment in and implementation of prevention programs

There are at least three, interconnected, critical caveats to consider when making social policy change and investing in prevention: (a) political, (b) timing, and (c) social considerations.

Political considerations. The multi-pronged treatment and prevention efforts we propose need strong political and budgetary support. It is widely recognized that new programs have to be added to annual budgets and politicians may principally be keen to support constructive long-term changes but are under pressure from the electorate to show cost-effectiveness swiftly.

Tertiary prevention (i.e. treatment) is beneficial for quality of life of the affected individual, but at a global level it might be perceived as less cost-beneficial because the client is older, problems are deep-seated, physiological stress responses are "programmed," and adults in treatment might already have children of their own. In secondary prevention, there are many gaps in the literature, particularly promising however, is treatment of peri-natal depression in mothers, which can reduce psychiatric

problems in children and adolescence. The reader will notice that this target overlaps with that for the Nurse-Family Partnership program described above.

Lastly, there need not be an either-or competition between primary prevention via advertising or school programs and targeted, community-based secondary programs; both can run parallel, meet unique needs and are complementary.

Usually, for prevention funding to be sustained by politicians, some successes need to be shown by the time of a next election campaign. This, in turn, creates enormous pressure for health professionals, policy-makers, and elected politicians, and it highlights the importance of selecting programs that have clearly documentable short-term and long-term benefits.

Critical timing of prevention efforts. Research makes a strong case that prevention programs are maximally effective when they contain all of the following elements: (a) target pregnancy and the initial years of life, (b) benefit all known deleterious outcomes, and (c) are studied over such a lengthy follow-up period that age-specific deleterious outcomes have a chance to actually show.

As mentioned earlier, timing is critical to prevent transgenerational damage. Given the long-term impact of synaptic pruning processes, prevention ideally targets children younger than two years of age, after which damage to stress response systems is more difficult to undo.

In many jurisdictions, people are encouraged to adopt children currently in foster care. Given that children growing up in extremely adverse environments may end up in an orphanage or foster care, adoption stabilizes the child and prevents further disruption, offers greater emotional security, and engenders a sense of belongingness. Adoption is also more economical than foster care and is most beneficial when the child is very young and attachment problems are lessened. Given, however, that adoption is relatively rare, the next best alternative is to invest in stable, loving foster care to avoid that children have to move from one foster home to another.

Social factors. Children are at risk for adversity during childhood regardless of age, sex, race, or family background. Yet implementation of secondary prevention requires awareness and sensitivity that some subgroups are already disproportionately disadvantaged and/or stigmatized for a number of reasons, including race or mental illness history. Screening for “at-risk” must be followed-through with intervention or support. Ignoring the high needs of such populations in a well-meant attempt at stigma-avoidance raises the peril of intergenerational continuation of the very adversity that triggered the initial disadvantage.

There is also evidence that perpetrators of abuse and/or neglect may respond with anger, retaliation,

or defensiveness when they are identified as alleged abusers. This possibility can thwart disclosure of ACEs and reduce access to treatment for both victims and perpetrators. Such consideration is especially critical when the child is the victim who cannot avoid the perpetrator.

Conclusion

There is substantial evidence to support causal pathways between ACE exposure and disease development. Based on this evidence, we posit that multi-pronged prevention and treatment are urgently needed now and likely cost-efficient. To avoid the known fading of benefits from one-shot prevention efforts, we urge policy makers to establish annual-repeat budget envelopes for prevention, possibly via allocation of a fixed percentage of health care and social benefits budgets.

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