The biopsychosocial sequel of childhood adversity from a developmental life-course perspective – from understanding to caring

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……..
Dean of the Medical Faculty

Prof. Dr. Primo Schär

To the little girl from a township in Cape-Town –
who broke my heart and gave me meaning

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Abstract

Background: Childhood adversities belong to the most important risk factors for adverse functional outcomes in adulthood, comprising risk across biological, psychological and social domains. This long-term bio-psycho-social sequel of adversity spans from major medical diseases, diseases of aging and premature mortality, to internalizing and externalizing psychopathology, to social outcomes including delinquency, poor educational outcomes, early parenthood, and low social support. In the last two decades, a huge publication effort around the long-term sequel of childhood adversities emerged and many studies replicated the obvious finding that cumulated childhood adversities have long-lasting and deleterious effects throughout an individual's life-course.

Aims: This cumulated dissertation adds to this heterogeneous body of research by looking at the biopsychosocial sequel of adversity from different theoretical perspectives. The research presented in this thesis investigates the prevalence, incidence, distribution and cumulation of adversities and subsequent trauma exposures in an attempt to provide understanding of adversity to shape individuals' subsequent trajectories.

Method: The studies presented in this thesis are based on different methodological approaches. First, we aggregated findings from the broad literature on the association between childhood adversity and telomere length as presented in a theory-driven review. Second and third, we used data from the large-scale U.S. population-based Health and Retirement Study (HRS) to analyze the cumulation and patterning of childhood adversity and adulthood trauma in older adults.

Results: These studies show, first, the heterogeneity in findings of associations between adversities and telomere length in part through heterogenous assessments of adversities. Second, the compounding of stressors in that childhood adversities increase the risk for subsequent adulthood trauma and that beyond the association of cumulative scores there is a patterning of specifics. And third, that the incidence of specific exposures is embedded within the life-course and related to age, period or cohorts, which is important to consider disentangling fact from artefact.

Discussion: From a theoretical standpoint, advancements in the conceptualization of stress and resilience will help to integrate stress responses and resilience processes, and research on risk and protective mechanisms. Improved and higher-resoluting measures of clearer concepts and heuristics will help to foster understanding of the adverse nature of certain types of exposures and will help to uncover different exposure-related mechanisms that mediate the association between childhood adversities and long-term bio-psycho-social outcomes. And in this way reduce the heterogeneity in findings related to imprecise measures of overlapping concepts. New approaches towards analysis, in particular theory-driven, person-oriented

modelling approaches, hold promise to improve our understanding of the cumulation of specific types of adversities within a developmental perspective as well as the subsequent divergent trajectories. Targeting mechanisms, mediators, and moderators that convey risks following childhood adversity will not only provide further understanding of said trajectories, but also highlight opportunities for prevention, intervention and caring efforts.

Conclusion: Targeting childhood adversity at its roots is ethically imperative, a major public health concern, and an issue of social justice. When targeting adversity, a kilo of prevention might be worth a ton of intervention, but still the earlier the intervention the better. Both are preferrable to the costs of starting intervention decades later or doing neither. Understanding the bio-psycho-social sequel of childhood adversity – an interdisciplinary sequel by definition – is crucial to target these prevention and intervention efforts. Research tackling this sequel however has to keep up with the complexity and interdisciplinary nature of the problem it tries to address. There is more to be done, as safe childhoods confer lifelong benefits.

Zusammenfassung

Hintergrund: Belastende Kindheitserfahrungen gehören zu den wichtigsten Risikofaktoren für eine niedrige soziale Teilhabe im Erwachsenenalter und umfassen Risiken für biologische, psychologische und soziale Bereichen. Diese langfristigen bio-psycho-sozialen Folgen von Belastungen reichen von schwerwiegenden medizinischen Krankheiten, Krankheiten des Alterns und vorzeitiger Sterblichkeit, hin zu internalisierender und externalisierender Psychopathologie, als auch zu sozialen Folgen wie Delinquenz, niedriger Bildung, früher Elternschaft und geringer sozialer Unterstützung. In den letzten zwei Jahrzehnten gab es eine enorme Publikationsanstrengung rund um die langfristigen Folgen von Belastungen in der Kindheit und viele Studien replizierten den offensichtlichen Befund, dass eine Anhäufung an Belastung in der Kindheit das Risiko für langanhaltende und schädliche Auswirkungen über den gesamten Lebensverlauf mit sich bringt.

Ziele: Diese kumulierte Dissertation trägt zu diesem heterogenen Forschungskorpus bei, indem sie die biopsychosoziale Folge von Belastungen in der Kindheit aus verschiedenen theoretischen Perspektiven betrachtet. Die in dieser Arbeit vorgestellte Forschung untersucht die Prävalenz, Inzidenz, Verteilung und Kumulation von Belastungen in einem Versuch ein Verständnis für diese Widrigkeiten zu schaffen, um deren Folgeverläufe von Individuen zu beeinflussen.

Methode: Die in dieser Arbeit vorgestellten Studien beruhen auf unterschiedlichen methodischen Ansätzen. Erstens haben wir Erkenntnisse aus der breiten Literatur über den Zusammenhang zwischen Belastungen in der Kindheit und der Telomerlänge zusammengefasst, und in einer theoriegeleiteten Übersichtsarbeit dargestellt. Zweitens und drittens haben wir Daten aus der groß angelegten bevölkerungsbasierten US-amerikanischen Health and Retirement Study (HRS) verwendet, um die Kumulation und Verteilung von Widrigkeiten in der Kindheit und Traumata im Erwachsenenalter bei älteren Erwachsenen zu analysieren.

Ergebnisse: Diese Studien zeigen, erstens, die Heterogenität in den Ergebnissen der Assoziationen zwischen Belastungen und Telomerlänge, zum Teil durch eine heterogene Erfassung dieser Widrigkeiten. Zweitens die Kumulation von Stressoren, indem Widrigkeiten in der Kindheit das Risiko für spätere Traumata im Erwachsenenalter erhöhen. Jenseits der Assoziation von kumulativer Belastung, finden sich spezifische Kombinationen von belastenden Erlebnissen. Und drittens, dass die Inzidenz spezifischer Belastungen in den Lebensverlauf eingebettet ist und mit Alter, Zeitraum oder Kohorten zusammenhängt.

Diskussion: Aus theoretischer Sicht werden Fortschritte in der Konzeptualisierung von Stress und Resilienz dazu beitragen, Stressreaktionen und Resilienz-Prozesse sowie die Forschung zu Risiko- und Schutzmechanismen miteinander und ineinander zu integrieren. Verbesserte

und höher auflösende Maße für klarere Konzepte und Heuristiken werden dazu beitragen, das Verständnis für die belastende Natur bestimmter Arten von Erfahrungen zu fördern und verschiedene expositions-bezogene Mechanismen aufzudecken, die den Zusammenhang zwischen Widrigkeiten in der Kindheit und langfristigen bio-psycho-sozialen Ergebnissen vermitteln. Neue Analyseansätze, insbesondere theoriegeleitete personenorientierte statistische Modellierungsansätze, sind vielversprechend, um unser Verständnis der Kumulation von Spezifika innerhalb einer Entwicklungsperspektive sowie der darauffolgenden divergierenden Verläufe im Zeitverlauf besser zu verstehen. Das Erforschen von Mechanismen, Mediatoren und Moderatoren, die Risiken nach Widrigkeiten in der Kindheit vermitteln, wird zu einem weiteren Verständnis der unterschiedlichen Wege die Belastungen folgen führen und dabei helfen, Präventions-, Interventions- und Betreuungsbemühungen gezielt einzusetzen.

Fazit: Belastungen in der Kindheit an der Wurzel zu bekämpfen ist nichts weniger als ein ethischer Imperativ, sollte ein wichtiges Anliegen der öffentlichen Gesundheitsvorsorge und Förderung sein und ist eine Frage der sozialen Gerechtigkeit. Bei der Bekämpfung von Belastungen in der Kindheit, kann ein Kilo Prävention eine Tonne Intervention wert sein – je früher, desto besser – wobei beides immer noch viel kosteneffizienter ist im Vergleich zu den Kosten, die entstehen, wenn man erst Jahrzehnte später mit der Intervention beginnt, oder weder präventiv noch intervenierend tätig wird. Das Verständnis der bio-psycho-sozialen Folgeerscheinungen kindlicher Widrigkeiten - als interdisziplinäre Folgeerscheinungen per Definition - ist von entscheidender Bedeutung, um diese Präventions- und Interventionsbemühungen auszurichten. Die Forschung, die sich mit dieser Folgeerscheinung befasst, muss jedoch mit der Komplexität und Interdisziplinarität des Problems, das sie anzugehen versucht, Schritt halten. Es gibt noch mehr zu tun, denn sichere Kindheiten gehen mit lebenslangen Vorteilen einher.

Chapter 1: General Introduction

Childhood adversities, including maltreatment and interpersonal traumatic experiences, are highly prevalent and related to various types of adverse bio-psycho-social outcomes. Various large-scale studies and meta-analyses report strong associations between adversities in childhood and a broad range of both mental disorders and somatic diseases (Anda et al., 2006; Bellis et al., 2019; Brown et al., 2009; Copeland et al., 2018; Dube et al., 2001; Felitti et al., 1998; Gilbert et al., 2009; Kessler et al., 2010; Widom et al., 2012). After decades of research, the relationship between these kinds of adversities and their long-term outcomes is still only partially understood. Understanding the multifinality in outcomes as well as the diversity in trajectories and mechanisms is crucial to prevent the long-term sequel of adversity by targeting prevention and intervention efforts, and by informing social policy making.

1.1 Childhood adversities

1.1.1 A working definition

Childhood adversities comprise a broad array of harmful exposures on a child or adolescents' development, however there is still a considerable debate about what should be considered as 'childhood adversity'. Current working models define childhood adversity as an "exposure during childhood or adolescence to environmental circumstances that are likely to require significant psychological, social, or neurobiological adaptation by an average child and that represent a deviation from the expectable environment" (McLaughlin, 2016, p. 363). Such forms of deviations in experiences generally take two forms: an absence of expected positive input (i.e. neglect and deprivation), and the presence of unexpected negative inputs (i.e. abuse, violence and trauma) (Humphreys & Zeanah, 2015; McLaughlin, 2016; McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). Therefore, in this thesis 'childhood adversity' refers to a broad and overarching construct that includes all forms of violence, maltreatment, abuse, neglect, and trauma during childhood and adolescence.

1.1.2 Prevalence rates of childhood adversities

Childhood adversity is highly prevalent in community-based and population-based samples world-wide (Copeland et al., 2007; Green et al., 2010; Hussey et al., 2006; Kessler et al., 2017; Kessler et al., 2010). About 50-70% of children in North America are exposed to some kind of Childhood Adversities, with multiple adversities being quite common among those affected (Bellis et al., 2019; Copeland et al., 2007; Felitti et al., 1998; Green et al., 2010; Hussey et al., 2006). Estimates of European samples are slightly lower with a current meta-analysis finding an aggregated prevalence of 42% of children and adolescents being exposed to childhood adversities across studies (Bellis et al., 2019). Current German population-based estimates of childhood maltreatment report 31% having been exposed to at least one form of abuse or neglect, with two-thirds of those having experienced multiple forms (Witt et al., 2017). Hence,

childhood adversity is highly prevalent even in population-based samples, but exact prevalence rates are difficult to achieve due to the heterogeneity in concepts and measures of what constitutes adversity. Compared to the general population, those at the margins of our societies are at higher risk to be exposed to multiple forms of adversities – for example racial minorities, those living in poverty, or out-home-placed children and adolescents within the foster and residential care system (Hughes & Tucker, 2018; Kim & Drake, 2018; Lanier et al., 2014; McEwen & McEwen, 2017). Out-of-home placed children and adolescents and those leaving care are at a particularly high risk to be exposed to adversity with three-quarters reporting some type of adversity and trauma, and most of these reporting multiple forms (Fischer et al., 2016; Garcia et al., 2017; Jaritz et al., 2008; Woods et al., 2013). In light of these high exposure rates in the community and the cumulative adversity of those at the margins of our societies, it is important to understand the sequel of childhood adversities across bio-psycho-social domains to adequately target prevention and intervention efforts to those most in need.

1.2 The long-term sequel of childhood adversities

1.2.1 The biological sequel

Numerous studies found childhood adversities to be associated with poor pediatric health, major and chronic diseases, diseases of aging, cardio-metabolic diseases, and with premature mortality (Baldwin & Danese, 2019; Bellis et al., 2019; Clemens et al., 2018; Gilbert et al., 2015; Jakubowski et al., 2018; Johnson et al., 2020; Oh et al., 2018; Riedl et al., 2019). Major interdisciplinary lines of research link early adverse exposures with subsequent health consequences leading to new disciplines emerging and gaining importance like psycho-neuro-endocrinology, psycho-neuro-immunology (Heim, 2020; Kuhlman et al., 2017; Nusslock & Miller, 2016) and research around redox-(dys)regulation and mitochondrial health (Picard & McEwen, 2018b; Ridout, Khan, et al., 2018). These processes accelerate aging, which has been proposed as a promising pathway explaining the link between chronic stressors and poor health; specifically, telomere maintenances contribute and interact in disease risk, aging and protection (Blackburn et al., 2015; Epel et al., 2004; Epel & Lithgow, 2014; Shalev, 2012). Focusing on specific systems mediating these long-term outcomes, four promising biological mechanisms emerge in the literature:

Telomere maintenance is a possible pathway explaining the link between childhood adversity and poor health (Belsky & Shalev, 2016; Blackburn et al., 2015; Shalev, 2012). Telomeres are repeated non-coded Deoxyribonucleic acid (DNA) sequences (TTAGGG nucleotide tandem repeats) at the end of chromosomes, protecting the coded sequences (Blackburn, 1991). Telomeres shorten during cell division caused by an incomplete replication of the chromosome ends and when being critically short, cells become genomically instable and malfunction in cell-specific ways (Lindqvist et al., 2015). Telomeres appear to shorten with age, which makes

telomere length (TL) an interesting marker of biological aging (Aubert & Lansdorp, 2008; Blackburn, 2005; Cawthon et al., 2003; Takubo et al., 2010). Several meta-analyses show negative associations between stress, adversity, early life adversity, childhood trauma, childhood psychosocial stressors and telomere length with aggregated effect sizes ranging from small to small-to-medium magnitudes and large heterogeneity in associations (Epel & Prather, 2018; Hanssen et al., 2017; Li et al., 2017; Pepper et al., 2018; Ridout, Levandowski, et al., 2018). In moderator analyses, studies attribute this heterogeneity to differences in the following three constructs: developmental timing of adversities and comorbidities (Ridout, Levandowski, et al., 2018), the heterogenous features of childhood trauma itself (Li et al., 2017) and categorical versus continuous measures of stressors (Hanssen et al., 2017).

Hypothalamic–pituitary–adrenocortical (HPA) axis reactivity and regulation, along with other endocrinological processes, mediate the relationship between adversity and ill-health via the system's broad impact on gene expression and neurodevelopment (Kamin & Kertes, 2017; Koss & Gunnar, 2018; Zänkert et al., 2019). The HPA-axis is by activated by acute stressors causing the release of corticotropin-releasing hormone (CRH) in the hypothalamus, followed by the release of adrenocorticotropic hormone (ACTH) in the anterior pituitary. ACTH then initiates the synthesis and release of cortisol and dehydroepiandrosterone (DHEA) in the adrenals (Kamin & Kertes, 2017). Chronically high cortisol is known to promote psychiatric illness in part through neurotoxic effects (Kamin & Kertes, 2017; Maninger et al., 2009; Stalder & Kirschbaum, 2012; Vyas et al., 2002), whereas DHEA is supposed to have neuroprotective effects potentially related to its inhibitory effects on cortisol, and its support of neurogenesis, and antioxidant and anti-inflammatory effects (Kamin & Kertes, 2017; Maninger et al., 2009; Russo et al., 2012). Cortisol and DHEA are increasingly measured in hair samples as a non-invasive measure of chronic long-term stress (Koss & Gunnar, 2018; Stalder et al., 2017; Vives et al., 2015).

Inflammatory processes as part of the innate immune response are another promising pathway linking childhood adversity with long-term adverse health outcomes (Danese & Baldwin, 2017b; Slavich, 2020). Inflammatory processes, in particular the release of cytokines, are part of the immune systems' innate response to anticipated threat, physical trauma, and infection, and in this way are highly adaptive responses that secure our protection, survival and well-being (Danese & Baldwin, 2017a; O'Donovan et al., 2013; Slavich, 2020). However, a prolonged and chronic overactivation of this system is damaging and is proposed to be one of the most important physiological pathways linking childhood adversities with psychopathology and disease (Danese & Baldwin, 2017b; Furman et al., 2019). Recent findings from meta-analyses and large-scale studies show associations between early life adversity and markers of inflammation in minors and adults (Baumeister et al., 2016; Kuhlman et al., 2020; Lacey et al., 2020; Lin et al., 2016).

Oxidative stress and redox dysregulation are another major area of research, and of particular interest in explaining the link between early stressors and poor health (Picard et al., 2014; Picard & McEwen, 2018a; Picard & McEwen, 2018b; Ridout et al., 2016; Ridout, Khan, et al., 2018). Oxidative stress closely interacts with HPA functioning and inflammatory processes in mental disorders (Kim et al., 2016; Miller & Sadeh, 2014; Steullet et al., 2017). In adolescents increased oxidative stress is found after childhood adversity (Horn et al., 2019; Mansur et al., 2017). Interestingly, redox dysregulation as a consequence of early adversity seems to persist during adolescence (do Prado et al., 2016) and adulthood (Boeck et al., 2016; Tyrka et al., 2015; Tyrka et al., 2016).

Taken together, the biological sequel of childhood adversities includes a heightened risk for morbidity and premature mortality. Different systems, mechanisms, and interactions – in particular telomere maintenance, HPA-functioning, inflammatory processes, and oxidative stress – mediate the relationships between childhood adversity and poor health. This interplay and interaction of biological systems underlines the need for multi-system approaches when considering the impacts of childhood adversity.

1.2.2 The psychological sequel

Childhood adversities often result in long-lasting psychological sequel and increase the risk for internalizing and externalizing psychopathology (Bellis et al., 2019; Carr et al., 2013; McCrory et al., 2017; McLaughlin, 2016; McLaughlin, Colich, et al., 2020). For example, exposure has been shown to increase risk for various psychological outcomes such as drug abuse and alcohol misuse (Anda et al., 2010; Anda et al., 2006; Dube et al., 2001; Felitti et al., 1998; Green et al., 2010; Heim & Binder, 2012; Horwitz et al., 2001; Kessler et al., 2010; Widom et al., 2007). Individuals with internalizing psychopathology (e.g., depression, anxiety disorder) that were maltreated show an earlier age of onset of symptoms as well as greater severity, more comorbid diagnoses, an increased risk for suicide, and generally poorer treatment outcomes than non-maltreated individuals (Heim & Binder, 2012; Heim et al., 2008; Heim et al., 2010; Teicher & Samson, 2013; Widom et al., 2007). In addition to findings around internalizing psychopathology, research showed abuse and exposure to violence being related to subsequent violence and aggression, and early adversity being related to externalizing behavioral problems, substance dependences, and conduct disorder (Dodge et al., 1990; Dodge et al., 1995; Enoch, 2011; Humphreys & Zeanah, 2015; Widom, 1989a). Important mechanisms within the psychological domain explaining the association between adversity – in particular early trauma – and psychopathology include problems with emotion processing (e.g. heightened emotional reactivity with poor regulation capabilities) and social information processing (e.g. enhanced threat detection and hostile attribution bias) (McLaughlin, Colich, et al., 2020). Hence, the psychological sequel following adversity includes a broad range of

mental health problems and important mechanisms that might be targeted by psychosocial as well as therapeutic interventions.

1.2.3 The social sequel

Beyond their influence on biological and psychological outcomes, childhood adversities increase the risk for adverse social outcomes across multiple domains (Copeland et al., 2018; Currie & Spatz Widom, 2010). First, childhood adversity and trauma were shown to be associated with aggressive and delinquent behavior (Buffington et al., 2010; Duke et al., 2010; Maschi et al., 2008; Steiner et al., 2011). Second, low educational outcomes driven by less school engagement are found in those with adversities (Bethell et al., 2014; Jimenez et al., 2016; Pan et al., 2020; Sheridan & McLaughlin, 2016). Third, childhood adversities are related to teenage pregnancies and early unplanned parenthood, thus contributing risk for intergenerational transmission of risk onto the next generation as well as perpetuating financial difficulties (Anda et al., 2002; Hillis et al., 2004). Fourth, childhood adversity was shown to be related to lower social support, fewer people within social networks, lower support from parents in particular, and later relationship disruptions (Copeland et al., 2018; Horan & Widom, 2015). Taken together a broad range of adverse social outcomes are associated with childhood adversities, which is particularly concerning as stable social support is considered a very, if not the most, important protective factor buffering stressors across domains.

1.2.4 The bio-psycho-social sequel

As introduced above, childhood adversities are related to broad and diverse adverse bio-psycho-social outcomes ranging from lower educational achievements to premature mortality. The bio-psycho-social outcomes are not independent of each other, rather they are clustered within individuals, intertwined and interrelated with one another, and at times share common causes or outcomes. The cumulation of adversities and trauma in particular is associated with higher risk for multiple poor outcomes across domains. Those at the margins of our societies are at particular heightened risk for these adverse outcomes as they often accumulate adversities in the context of a lack of resources. These findings are concerning and leave us with the question of how childhood adversity can serve as a risk factor for such a broad range and diversity of outcomes later in life?

1.3 A diversity in theoretical concepts and perspectives

As broad as the literature about adversity and its sequel is, as diverse and heterogenous are the concepts, theories and meta-theories trying to explain them. Different theoretical approaches arose from different disciplines – for example from developmental psychology, clinical psychiatry, gerontology, sociology, evolution sciences and interventional research. Major interdisciplinary lines of research tried to integrate these diverse, and at times, fragmented bodies of literature into meta-theoretical approaches as for example stress and

ageing research. Hereinunder, we draw from these ideas and lines of theorizing to explore different perspectives from which one might approach the biopsychosocial sequel of childhood adversities. This overview has selected only a portion of existing viewpoints out of a vast body of literature in order to provide new perspectives on the existing heterogenous body of literature in which the work presented in this thesis is theoretically embedded.

1.3.1 The developmental (psycho-)pathological perspectives – multifinality, equifinality and divergent trajectories, from facts to knowledge

One perspective – possibly the most important – to understand the long-term sequel of adversity comes from developmental psychopathology. This framework is not only implemented more and more into our understanding of psychopathology, but it was and is fundamental to the formulation of the concept of resilience (Cicchetti & Toth, 2009; Rutter & Sroufe, 2000). Developmental psychopathology, as an interdisciplinary field and perspective, has the goal to investigate the interplay of bio-psycho-social aspects by studying normal functioning and pathology over development, with a specific focus on processes underlying adaption or maladaption, continuity, and change in patterns (Cicchetti & Toth, 2005, 2009; Rutter & Sroufe, 2000). Two important concepts in the field are multifinality and equifinality (Cicchetti & Rogosch, 1996), which are derived from general systems theory (Boulding, 1956). Equifinality refers to the idea that, “in an open system […] the same end state may be reached from a variety of different initial conditions through different processes” (Cicchetti & Rogosch, 1996, p.597). Multifinality “states that the effect on functioning of any one component's value may vary in different systems. […]. Stated differently, a particular adverse event should not necessarily be seen as leading to the same psychopathological or non-psychopathological outcome in every individual” (Cicchetti & Rogosch, 1996, p.598). In this sense, individuals might start on the exact same pathway, and - in relation to their following choices- will endure very diverging patterns of adaption or maladaption (Cicchetti & Rogosch, 1996).

Developmental psychopathological perspectives show the need of a “pathways approach to causal processes that recognizes both direct and indirect effects, and which accepts that a single risk factor may have diverse consequences [multifinality] and that a single disorder outcome may arise by a variety of routes [equifinality]“ (Rutter & Sroufe, 2000, p.287). The developmental psychopathological framework has resulted from its receptivity and respect for previous knowledge and theory together with its willingness to challenge existing beliefs. In this way it moves beyond previous disciplinary boundaries and lays fertile ground for moving beyond simplistic descriptive approaches towards progression of the field (Cicchetti & Toth, 2009). In this perspective, important theories such as attachment theory as formulated by Bowlby and later specified by Ainsworth (Bowlby, 2005; Bretherton, 1992), social learning theory (Bandura & McClelland, 1977) and other important developmental perspectives are integrated into the developmental psychopathological framework. As Cicchetti and Toth (2009,

p. 17) state, “one of developmental psychopathology’s potential contributions lies in the heuristic power it holds for translating facts into knowledge, understanding, and practical application” (Cicchetti & Toth, 2009, p. 17). Therefore, a developmental (psycho-)pathological perspective may further foster our understanding of the long-term sequel of adversity.

1.3.2 The life-course perspectives – from accelerated aging to cumulative inequality

The life-course perspectives as framed in research offers another important heuristic to understand the biopsychosocial sequel of adversity, drawing from sociological perspectives and social psychology (Elder Jr, 1994), life-course epidemiology (Kuh et al., 2003; Lynch & Smith, 2005), and from evolutionary-developmental theories (Belsky et al., 1991). The study of aging as a lifelong process started with an early focus on specific diseases, and how they increase the risk for disability and mortality in the field of geronto-sciences (Moffitt et al., 2016). Newer research however linked childhood risks to disease and mortality, with resulting paradigm of the developmental origins of health and disease (DOHaD) (Barker, 2007). Recent and current research is trying to fill the gap in between childhood risks and later diseases and focusses on trajectories of risk and resilience and the pace of aging as a predictor of disease (Moffitt et al., 2016). More recently, evolutionary-developmental scholars conceptually linked two lines of theoretical approaches DOHad paradigms with evolutionary-based theories (as evolutionary life-history perspectives) (Belsky, 2019; Belsky & Shalev, 2016; Ellis & Del Giudice, 2019). This integration of paradigms both underlines accelerated aging but also a trade-off between growth and reproduction in early life with survival or reproduction in later life (Belsky, 2019; Belsky & Shalev, 2016; Ellis & Del Giudice, 2019). In this sense children are “active agents in their own development, engaging in a process of predictive adaptive response” (Belsky & Shalev, 2016, p.1373). Children might make developmental commitments towards reproduction early in life in a trade-off with later disease over and beyond simple “adversity-induced wear and tear on the developing individual” (Belsky, 2019, p. 244).

Next to such perspectives, multiple scholars in the sociological field argue that disparities and inequalities over a life-course can be theoretically conceptualized from a cumulative advantage and disadvantages approach (Ferraro & Shippee, 2009; O'Rand, 1996; O'Rand & Hamil-Luker, 2005; Willson et al., 2007). These approaches underscore the “dynamic interplay of individual life trajectories and structural and contextual factors that have affected inequality in the past” (O'Rand, 1996, p.236). Drawing from these concepts, cumulative inequality theory states that “social systems generate inequality, which is manifested over the lifespan via demographic and developmental processes, and that personal trajectories are shaped by the accumulation of risk, available resources, perceived trajectories, and human agency” (Ferraro & Shippee, 2009, p. 334). Beyond an individual’s lifespan, cumulative inequality might be converted into a multigenerational family life course framework (Ferraro & Shippee, 2009; Gilligan et al., 2018). This theory tries to integrate different

disciplinary approaches to the overall study of aging, which includes biological systems, in particular immunology, as well as epidemiological findings, and therefore offers a guiding theory and heuristic for interdisciplinary collaboration (Ferraro et al., 2016; Ferraro et al., 2009; Schafer et al., 2011). Taken together as research frameworks, the life-course perspective and the conceptual integration of development and aging offer various point of views and opportunities to integrate the broad literature of the biopsychosocial sequel of adversity.

1.3.3 The stress perspectives – from wear and tear, stress processes and toxic stress

Stress research is a very informative paradigm and heuristic to understand the long-term effect of adversity on later health. Since its earliest mentioning, the concept of stress is followed by a controversy about what constitutes stress and how to best measure it (Cohen et al., 2016; Cohen et al., 2019; Epel et al., 2018; Kagan, 2016; Monroe & Slavich, 2019; Slavich, 2019). Within the stress paradigm certain influential theories are worth introducing: first is the theory of allostasis and allostatic load, a very influential biomedical theory in stress research (McEwen, 1998a, 1998b). This theory argues that the bodies' natural adaption in the face of adversity involves the activation of a broad range of mechanisms – allostasis – that when effectively turned on and off help the body to cope with stressors to sustain homeostasis (McEwen, 1998b). The situation in which allostatic system endures to many challenges is called 'allostatic load', which leads to 'wear and tear' on the body and ultimately to disease (Juster et al., 2010; Lupien et al., 2009; McEwen, 1998a). Allostatic load includes a too frequent activation, a failure to shut off systems, and an overarching response to stressors in the first place (McEwen, 1998b). In this sense allostatic load is biologically embedded in the nervous, endocrine, and immune system, and these alterations seem to persist into adulthood (Danese & McEwen, 2012). Next to biomedical approaches in stress research are sociological informed theories such as 'stress process' and 'stress proliferation' theories. These argue that stress itself should be understood as processes that increases the risk for later adversity and shapes life-trajectories (Pearlin, 1989; Pearlin et al., 1981; Pearlin et al., 2005; Turner et al., 1995). Combining these perspectives, other scholars have tried to integrate findings on 'toxic stress' into an eco-bio-developmental framework (Shonkoff et al., 2021; Shonkoff et al., 2012). Despite its conceptual imprecision, stress research offers a range of concepts and approaches which are fruitful to implement into research on health and well-being; however, as Pearlin et al. (1981, pg. 352) comments, "research into social stress needs to be raised to a level that matches the richness and intricacy of what it strives to explain", which still might hold true in light of recent debates.

1.3.4 The family risks and help systems perspectives - learning from those at highest risk and from those who care

Another line of research helpful in approaching the biopsychosocial sequel of adversity is research informed by the observation of child and familial risks for victimization, revictimization, and offending, which are common patterns often seen in research on the cumulation of adversity in high-risk populations. Research that shows abuse and neglect increase the risk for delinquency and criminal behavior became the theoretical foundation of the concept of a *cycle of violence* as a sequel of these exposures (Dodge et al., 1990; Widom, 1989a; Widom, 1989b). This earlier research is nowadays supported with methodologically stronger prospective findings that suggest that childhood victims of violence are at heightened risk for violent behavior when they grow up; however, this trajectory is not inevitable, and most victims of childhood violence do not become violent offenders themselves (Widom & Wilson, 2015). Next to the cycle of violence, there has been a huge interest in the phenomena of *revictimization*, specifically in the observation that victimized individuals are at increased risk for later revictimization during their life-course, with most literature focusing on sexual abuse (Widom et al., 2008). Further, the concept and observation of *poly-victimization*, defined as four or more different kind of victimizations in a single year, underlined the need to not only assess single types of victimizations, but also a broader range of exposures (Finkelhor et al., 2007a, 2007b). Including more types of victimization into analyses often decreases the impact of single exposures (Finkelhor et al., 2007a, 2007b). Therefore, research focusing on bullying should more thoroughly think about child maltreatment and vice versa, as poly-victimized individuals are often those with more trauma symptoms and a higher overall symptom burden (Finkelhor et al., 2007a, 2007b).

From a conceptual point of view, the '*risky families model'* argues that families characterized by conflict, aggression, and unsupportive and cold relationships create vulnerabilities that produce disruptions in psychosocial functioning (i.e. emotion processing and social competence), disruptions in stress-biology and poor health behaviors (Repetti et al., 2002). Family environments in this sense, are vital for our understanding of mental and physical health across the life span, as these disruptions leads to accumulations of further risk factors for adverse outcome (Repetti et al., 2002). Overall, this line of research argues that approaching victimization has to start by addressing family risks. These should be broad in its assessment and must consider the following: the possibility of multiple types of victimization; poly- and revictimization, as well as different developmental trajectories of these exposures; the risks for later offending; and the mechanisms that place children at risk for accumulation of further adversities including revictimization and offending.

1.2.5 The psychiatric perspectives – from categorical to dimensional transdiagnostic approaches

The psychiatric perspective is in constant debate on how its classification should conceptualize childhood adversity (early life stress, childhood maltreatment and trauma), and how integrate it into the classification of mental disorders. This perspective is broken into two major theories which are the classical descriptive categorical and the more recent transdiagnostic-dimensional approaches. Descriptive categorical perspectives include certain types of childhood adversities as traumatic exposure in their conceptualization of PTSD. In the last decades, there has been a huge controversy about the conceptualization of PTSD with differing approaches in DSM-5 and ICD-11 (Adam, 2013; Galatzer-Levy & Bryant, 2013; Young et al., 2014). Recent advances in DSM-5 included the broadening of the definition of Criterion A to open it up for the inclusion of series of prolonged exposures during childhood, the inclusion of a further symptom category of negative changes in cognition and mood following trauma exposure, and a new overall category of disorders called the 'trauma and stress-related disorders' as home for the diagnoses (American Psychiatric Association, 2013). Differently, ICD-11 proposed a new disorder 'complex PTSD' with three new symptom cluster (affect dysregulation, negative self-concepts and difficulties in relationships) on top of the classical PTSD symptoms (World Health Organization, 2018). Beyond the change in diagnosis of PTSD, others proposed childhood maltreatment to be an *ecophenotypic variant* within other categories of mental disorders (e.g., depression, anxiety disorders and substance disorders) (Teicher & Samson, 2013). In this sense, the maltreated subtype may be thought of as a clinically and neurobiologically distinct phenotypic specialization of a certain disorder as a result of environmental experience – an ecophenotype (Teicher & Samson, 2013).

Next to the categorical conceptualization of mental disorders, recent developments move towards a dimensional and transdiagnostic understanding of mental disorders. Following three important proposals: 1) that the focus should be on transdiagnostic and basic domains of functioning across multiple levels of analyses within the research domain criteria (RDoc) framework (Cuthbert & Insel, 2013); 2) one might conceptualize mental disorders as a general p-factor of psychopathology (Caspi et al., 2014); or 3) organize psychopathology within the hierarchical taxonomy of psychopathology (HiTOP) (Kotov et al., 2017). Following such an approach, childhood adversity (i.e. childhood trauma) can be theorized to be *transdiagnostic risk factor* related to internalizing and externalizing psychopathology mediated through different pathways – emotion regulation, social information processing, and accelerated aging (McLaughlin, Colich, et al., 2020). Despite the approach with which one might think about mental disorder – categorically or trans-diagnostically dimensionally – the understanding of childhood adversity and maltreatment as an etiological risk factor for distinct mental disorders or transdiagnostic psychopathology is crucial for prevention and intervention efforts. The

recent focus on transdiagnostic mechanisms, such as emotion regulation and social information processes, hold promise as interventions targets that reduce or buffer the long-term sequel of adversity across and above disorder boundaries and domains.

1.4 The resilience perspectives – looking from the other side on the same process?

Resilience is a dynamic and multilevel phenomenon and concept, which comprises the ability to 'bounce back' in the face of adversity and chronic stressors, incorporates personal growth after adverse experiences (American Psychological Association, 2020; Joyce et al., 2018), and therefore is crucial to foster understanding of the biopsychosocial sequel of adversity. With the steadily increasing attention to research on resilience in the last decades, a lively and interdisciplinary discussion about what constitutes resilience has emerged (Rutter, 2012; Southwick et al., 2014). Recent debates surround the definition, the subsequent operationalization and measurement of resilience, and discrepancies between the trait versus dynamic conceptualizations of resilience (Denckla et al., 2020; Kalisch et al., 2017). Current proposed definitions of resilience mostly share a common approach to conceptualize "resilience at multiple levels, from the biological to the social and policy level, a focus on the dynamic nature of resilience itself as a fluid, interacting process of adaptation, and a move away from conceptualizing resilience as an individual trait" (Denckla et al., 2020, p. 14). Certain theorists underline the need in resilience research to explicitly reference aspects of temporal trajectories (Bonanno et al., 2015). In light of these ideas, trajectory-based models of resilience and dysfunction following potential trauma show four different "likely phenotypic human stress responses": 1) with the resilience trajectory being the modus response, followed by 2) recovery, 3) chronic trajectories or 4) delayed onset trajectories (Bonanno et al., 2011; Galatzer-Levy et al., 2018). Other theorists underscore the complex ecological and multisystemic aspects of resilience with interactions across systems over development (Masten, 2019; Ungar & Theron, 2020). In this sense, "resilience depends just as much on the culturally relevant resources available to stressed individuals in their social, built, and natural environments as it does on individual thoughts, feelings, and behaviours" (Ungar & Theron, 2020, p.441).

Recent developments within the resilience field include the incorporation of biological processes over multiple phenotypic levels from stress and immune responses or neural circuitries, to their interaction with genetics (Choi et al., 2019; Feder et al., 2019; Rakesh et al., 2019). Recently, a affiliative neuroscience approach was proposed which states "that systems and processes that participate in tuning the brain to the social ecology and adapting to its hardships mark the construct of resilience" (Feldman, 2020, p.132). Considering this approach, biological systems of interest are the oxytocin system, the affiliative brain, and biobehavioral synchrony in the context of core features of resilience: plasticity, sociality and meaning (Feldman, 2020). Taken together, there is a rich literature on what constitutes resilience, yet

there still is no consensus of a shared definition of resilience or measurement. Current conceptualizations of resilience move towards understanding resilience as a dynamic, multilevel concept spanning biological-psychological-interpersonal-contextual processes. Recently, the incorporation of biological processes has gained additional attention. Advances in resilience research will help to further our understanding of trajectories of stress and resilience processes between adversity and disease.

1.5 Own research approaches

In light of this diverse body of empirical findings as well as theoretical perspectives introduced, my own research presented within this thesis aims to better understand adversities and their sequel to shape life-trajectories in order to target prevention and intervention efforts and to inform social policy making. Conceptually this work tries to incorporate these multiple perspectives and lines of thinking that go beyond specific disciplinary boundaries into an interdisciplinary understanding of adversities and their sequel. First and foremost, the developmental (psycho-)pathological framework strongly influences my work as every life-course approach and aging process has to start with a developmental process that is embedded into a family context and an environment. The approach taken towards psychopathology is through a dimensional transdiagnostic perspective. My work assumes that most prevention and intervention efforts have to start with supporting families, should be multisystemic, and focus on transdiagnostic risk and protective factors and mechanisms. Conceptually, my research tries to integrate factors of risk (adversity, maltreatment, and trauma) and protective factors (self-efficacy, self-care, and meaningfulness) to understand stress and resilience processes as they unfold over development and the life-course.

This thesis contains one line of my own research that aims to provide understanding of adversities in literature-based and large-scale studies. In a next line of applied research, which is not included in this thesis, we investigate high-risk samples within the residential care system in Switzerland and Germany. In this applied research, we try to transfer our understanding of adversities into high-risk populations and welfare systems to break the cascades of adversity in out-of-home-placed children and adolescents. We do this by implementing findings from our applied research into educational programs for professionals working in the child welfare systems with the idea that knowledge should be transferred and implemented (e.g., with trauma-pedagogical trainings and e-learning tools). The output resulting from this line of work and research is listed in the CV being enclosed to this dissertation. This line of work was left out of the main body of this thesis to be able to write a comprehensive and congruent overview of my main expertise and the theoretical framing in which this research is embedded, following the idea that less sometimes might be worth more.

1.6 Research objectives

As previously introduced, the research presented within this thesis aims to understand adversities, their incidence, distribution and sequel to shape an individual's subsequent trajectory. This research draws from the current body of literature and from large-scale, population-based samples.

Study 1: "A look into the heterogeneity of findings"

The main aim of this study was to review the fast-growing body of literature on the associations between adverse childhood experiences and telomere length in order to find explanations for the heterogeneity in findings. The included sample of studies was reviewed based on important study design characteristics and the "stressor exposure characteristics" proposed by Epel et al. (2018).

Study 2: "Compounding stress"

With this study, we investigated the associations between specific types of childhood adversities and specific adulthood traumatic exposures. In particular, our study aimed to (a) determine whether childhood adversity would be shown to increase the risk for adulthood traumatic exposures in a large-scale sample of older adults, with a focus on whether specific types of childhood adversities or cumulative childhood adversities were associated with specific or cumulative adulthood traumatic exposures, and (b) examine if these associations were moderated by gender.

Study 3: "Fact or artefact"

The aim of this study was to provide data on the prevalence of childhood adversity and adulthood trauma from a sample of older adults in the U.S. population-based Health and Retirement Study. We examined differences in exposure by exploring the distributions of the incidence of adulthood trauma across age and time-period and discussed observed findings in the context of major methodological and sampling artefacts inherent to older populations in an attempt to separate real cohort effects from methodological artefacts.

Chapter 2: Adverse Childhood Experiences and Telomere Length a Look into the Heterogeneity of Findings – A Narrative Review

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Adverse Childhood Experiences and Telomere Length a Look Into the Heterogeneity of Findings—A Narrative Review

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Background: Adverse childhood experiences (ACEs) have been associated with poor mental and somatic health. Accumulating evidence indicates that accelerated biological aging—indexed by altered telomere-related markers—may contribute to associations between ACEs and negative long-term health outcomes. Telomeres are repeated, non-coding deoxyribonucleic acid (DNA) sequences at the end of chromosomes. Telomeres shorten during repeated cell divisions over time and are being used as a marker of biological aging.

Objectives: The aim of the current paper is to review the literature on the relationship between ACEs and telomere length (TL), with a specific focus on how the heterogeneity of sample and ACEs characteristics lead to varying associations between ACEs and TL.

Methods: Multiple databases were searched for relevant English peer-reviewed articles. Thirty-eight papers were found to be eligible for inclusion in the current review.

Results: Overall, the studies indicated a negative association between ACEs and TL, although many papers presented mixed findings and about a quarter of eligible studies found no association. Studies with smaller sample sizes more often reported significant associations than studies with larger samples. Also, studies reporting on non-clinical and younger samples more often found associations between ACEs and TL compared to studies with clinical and older samples. Reviewing the included studies based on the "Stressor Exposure Characteristics" recently proposed by Epel et al. (2018) revealed a lack of detailed information regarding ACEs characteristics in many studies.

Conclusion: Overall, it is difficult to achieve firm conclusions about associations of ACEs with TL due to the heterogeneity of study and ACE characteristics and the heterogeneity in reported findings. The field would benefit from more detailed descriptions of study samples and measurement of ACEs.

Keywords: early adversity, adverse childhood experiences, stress, childhood trauma, accelerated aging, telomeres, telomere length

INTRODUCTION

Adverse childhood experiences (ACEs) (e.g., physical abuse, sexual abuse, emotional neglect, loss of a close family member) are a large societal problem, often with long-lasting health consequences. Previous research has shown that ACEs are highly prevalent. In the general population, more than half of people retrospectively report at least one, and more than a quarter two or more, types of ACEs (Felitti et al., 1998; Dube et al., 2001). In addition, ACEs are found to be related to poor health outcomes, including various mental health problems (e.g., depression, anxiety, post-traumatic stress disorder [PTSD], suicidal ideation), substance abuse problems, self-reported illness, obesity, and overall morbidity (Felitti et al., 1998; Widom, 1999; Dube et al., 2001, 2003; Anda et al., 2006, 2010; Widom et al., 2007; Brown et al., 2009; Green et al., 2010; Heim et al., 2010; Kessler et al., 2010; Heim and Binder, 2012; Moffitt and the Klaus-Grawe Think Tank, 2013). ACEs have also been found to be associated with increased risk for many somatic diseases, especially with diseases of aging including cancer, autoimmune, cardiovascular diseases and early mortality (Felitti et al., 1998; Brown et al., 2009; Rich-Edwards et al., 2012; Kelly-Irving et al., 2013; Tomasdottir et al., 2015). Although it is largely accepted that ACEs increase risk for poor health outcomes, mechanisms of the association are still not fully understood (Moffitt and the Klaus-Grawe Think Tank, 2013).

Following a pioneering study by Epel et al. (2004), research on the association of stress and telomere-related processes has rapidly emerged. Accelerated cell aging—indexed by altered telomere maintenance—might be one mechanism that partially explains the association between ACEs and long-term health complaints. Telomeres are repeated non-coding deoxyribonucleic acid (DNA) sequences—TTAGGG nucleotide tandem repeats – at the end of chromosomes, protecting the coded sequences (Blackburn, 1991). Telomeres shorten during cell division, caused by an incomplete replication of the chromosome ends (Blackburn, 2000, 2001). When telomeres are critically short, cells become genomically unstable and can malfunction in cell-specific ways (Blackburn, 2000). Telomeres tend to shorten with age, which makes telomere length (TL) an interesting marker of biological aging (Cawthon et al., 2003; Blackburn, 2005; Aubert and Lansdorp, 2008; Takubo et al., 2010). Interestingly, shorter telomeres are correlated with several psychiatric disorders (Lindqvist et al., 2015; Schutte and Malouff, 2015; Darrow et al., 2016; Ridout et al., 2016; Li et al., 2017a; Epel and Prather, 2018), somatic diseases (Honig et al., 2006; Willeit et al., 2010), and early mortality (Cawthon et al., 2003).

A fast-growing body of research describes the association between ACEs and TL over the life course. Various reviews in the broader context of the association between stress and TL have recently been published focusing in detail on early life stress and telomeres (Shalev, 2012; Price et al., 2013; Ridout et al., 2015), perceived stress and TL (Schutte and Malouff, 2014; Mathur et al., 2016), childhood exposure to violence and TL (Moffitt and the Klaus-Grawe Think Tank, 2013), violence and telomeres (Oliveira et al., 2016), caregiving experiences and telomeres (Blaze et al., 2015), and psychosocial factors and TL (Starkweather et al., 2014). Additionally, recent meta-analyses describe the association between early life adversity and TL (Ridout et al., 2017), childhood trauma and accelerated telomere erosion (Li et al., 2017b) and childhood psychosocial stressors and TL (Hanssen et al., 2017). Overall, these analyses reported negative associations between ACEs and TL with aggregated small effect sizes [Ridout et al. (2017) Cohen's d = −0.35; Hanssen et al. (2017) $r = -0.082$; and Li et al. (2017b) $r = -0.05$]. Epel and Prather (2018) summarized the current empirical evidence, concluding that "these meta-analyses demonstrate the robustness of the association [childhood stressors and telomere length] across published studies" (p. 5). However, all three meta-analyses reported a high between-study heterogeneity of effects, which they tried to explain in further moderator analyses. In their moderator analyses Ridout et al. (2017) showed "that differences in developmental timing of adversity exposure and comorbidities likely contributed to the heterogeneity" (p. 12), Li et al. (2017b) concluded that "the heterogeneous feature of childhood trauma may be one of the major potential sources of heterogeneity in outcomes" (p. 68), and Hanssen et al. (2017) found greater effect sizes for categorical compared to continuous measures of stressors, and for shorter durations between stressor and TL measures. Hence, a possible explanation for the observed heterogeneity in findings are attributes related to the characteristics and measurement of stressors. A deeper understanding about the different aspects of ACEs might help to explain the diversity in reported associations.

Epel and Lithgow (2014) stated that research must form a "common knowledge base and taxonomy for describing stressors and stress responses" (p. 11) to bridge the gap between basic and clinical research on aging and stress. Epel et al. (2018) further pointed out that "a large but disjointed literature shows that stress affects slow-acting biological processes in the brain and body, accelerating diseases of aging" (p. 146), but that despite this agreement one major barrier that prevents research progress is the "lack of consistency and thoroughness in stress measurement"(p. 146). This lack of a common knowledge base, consistency and thoroughness in stress measures can also be seen in the field of early life stressors and childhood adversities. Specifically, these conceptual issues lead to a large heterogeneity of reported prevalence and incidence rates of early traumatic stressors and ACEs (Heim and Binder, 2012; Moffitt and the Klaus-Grawe Think Tank, 2013). It can also be seen in the reviews and meta-analyses discussed here that use varying stress -frameworks but overall overlap to a great degree in their included studies.

In search of a common knowledge base and taxonomy, Epel et al. (2018) proposed a working model focusing on stress as "an emergent process that involves interactions between individual and environmental factors, historical and current events, allostatic states, and psychological and physiological reactivity" (p. 146). This model comprises different research perspectives on stress and introduces a more precise language for describing stress measures. Within this framework, stress consists of an exposure within in a specific context that elicits a stress-related response. Stressor exposure characteristics (SECs) are defined along different dimensions: timescale for stress measurements

(acute, event-based, daily, chronic), developmental life stages of stress exposures, stress assessment windows (measurement timeframe; proximity of assessment to the stressor in years), and stressor attributes (duration, severity, controllability, life domain, target of stressor, potential of the stressor to elicit harmful response). However, it is unknown to what extend the proposed SECs can be applied to a diverse body of literature focused on ACEs and TL.

Therefore, the main aim of the current paper is to review the fast-growing body of literature on the associations between ACEs and TL order to find explanations for the heterogeneity in findings. The included sample of studies will be reviewed based on important study design characteristics and the SECs proposed by Epel et al. (2018). This will help us to better understand the complex relationship between ACEs and TL.

METHODS

To be included in the current review, studies had to report on ACEs, assessed by means of a questionnaire or interview, on TL, and on a statistical measure of association between these two. Hereinafter, ACEs are defined as the broad array of harmful, perceived traumatic stressors during a child's development before the age of 18. This includes childhood traumatic experiences, all forms of childhood maltreatment including abuse and neglect, and childhood exposure to violence, and the combination of these factors with further potentially harmful circumstances. Multiple search methods were used to avoid biased retrieval of studies (Rosenthal, 1995). First, a computerized search of relevant databases was conducted: PubMed, PsycInfo, Web of Science, and Google Scholar up to the 26th of April 2018. The following key words were used in varying combinations: "childhood adversit*," "early life stress" or "childhood trauma" and "telomere length." Second, the combination of several instruments reported in the papers to assess ACEs with "telomere length" was examined: Childhood Trauma Questionnaire [CTQ] (Bernstein et al., 1994, 2003); Childhood Trauma Interview [CTI] (Foote and Lovejoy, 1995); Adverse Childhood Experiences [ACE] Questionnaire (Felitti et al., 1998); and the Early Trauma Inventory [ETI] (Bremner et al., 2000). Third, reference lists from relevant reviews on the association between ACEs and TL (Shalev, 2012; Price et al., 2013; Ridout et al., 2015, 2017; Oliveira et al., 2016; Epel and Prather, 2018) were examined for possible additional studies. Finally, reference lists of all included papers were checked for potentially relevant additional articles. One eligible paper by Schaakxs et al. (2015) was excluded, because another paper from the same research group (Schaakxs et al., 2016) used the same sample.

A total of 38 studies were eligible for inclusion in this review. First, we collected information on the following sample characteristics: sample size, sex, age (of the sample), sample origin, study design (cross-sectional [case-control], longitudinal), sample composition, telomere assay approach, and covariates. Additionally, we collected the following ACEs characteristics: questionnaire (specific instrument [e.g., CTQ], modified specific instrument, item, score, total score), and age at adversity exposure. Further, ACEs characteristics were assessed using the proposed SECs defined by Epel et al. (2018). This included: timescale of the used stress measurement (i.e., acute, event-based, daily, chronic); developmental life stages (i.e., childhood only, adolescence only, childhood and adolescence); stress assessment window (i.e., measurement timeframe [e.g., retrospective or prospective]; proximity of assessment to the stressor in years [i.e., duration in years between exposure and assessment]); and stressor attributes (duration, severity, controllability, life domain, target of stressor, potential of the stressor to elicit harmful response). For a detailed definition of the SECs, please refer to Appendix A. "Stress typology for stress measurement" within the model proposed by Epel et al. (2018) (p.163). Moreover, main findings of the ACEs-TL association were summarized and coded (shorter, none, longer, mixed). In a second step, studies were grouped into categories: sample size (<400, >400), age (<25, 25–45, >45), sex (male, female) and population (clinical vs. non-clinical) and reviewed regarding their overall findings.

Information regarding sample characteristics, ACEs characteristics and main findings are presented in **Table 1**. Further information regarding main and sub-findings are presented in **Table 2**. Additional supplementary characteristics including the type of adversity and nature of the ACEs-TL association are provided in the supplementary materials (**Supplementary Table 1**). Information was extracted and coded by the first author (DB) and double checked by one of the co-authors (Dd'H). Differences in extracted information and coding were solved by further discussing these issues.

RESULTS

Study Characteristics

A total of 38 studies were included in this review based on the criteria of eligibility defined in the method section (for an overview see **Table 1**). Sample sizes of included studies ranged from 31 (Tyrka et al., 2010) to 11,670 (Cai et al., 2015). Most studies ($N = 27$) reported on TL in both males and females, seven studies examined only females (Surtees et al., 2011; Malan-Müller et al., 2013; Cai et al., 2015; Mason et al., 2015; Levandowski et al., 2016; Oliveira et al., 2017; Mitchell et al., 2018), and three studies examined only males (Mitchell et al., 2014; Boks et al., 2015; Bersani et al., 2016; Osler et al., 2016). The included studies covered a wide age range of study participants at TL assessment from 5 years (Shalev et al., 2013; Drury et al., 2014) to 93 years of age (Schaakxs et al., 2016). Almost all of the included studies ($N = 32$) are of North-American or European origin, except for six studies that were conducted in Brazil (Levandowski et al., 2016; Oliveira et al., 2017), China (Cai et al., 2015), South-Africa (Malan-Müller et al., 2013), and New Zealand (Jodczyk et al., 2014; Shalev et al., 2014).

Reviewing the design of the studies, all studies, as defined within the inclusion criteria, had to report on TL at a minimum of one time point, and thus were able to associate ACEs and TL cross-sectionally. Of the 38 studies, 14 used a cross-sectional (case-control) approach to investigate differences in TL between groups (e.g., abused vs. non abused)

TABLE 1 | Study and stressor characteristics.

	Study characteristics							ACE characteristics												Findings
												Assessment window		Stressor attributes						
References	Sample size; sex	Age, mean (SD)	Sample origin	Design	Sample composition	Telomere assay	Covariates	Questionnaire	Age	Time scales	Life stage	Time frame	Proximity	Duration	Severity	Controllability	Life domain	Target	Potential	ACEs-TL
Bersani et al., 2016	$N = 76$ 0 f, 76 m	34.64 (9.17)	USA	Cross-sectional (case-control)	Combat-exposed subjects; 41 (healthy), 18 (PTSD), 17 (PTSD + MDD)	qPCR; granulocytes	Age, BMI, antidepressants and ethnicity	ETI-SR	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	17	X	X	X	X	X	X	shorter
Blom et al., 2015	$N = 117$ 64 f, 53 m	15.8 (1.32)	USA	Cross-sectional (case-control)	$n = 22$ (MDD) $n = 25$ (controls) (CTQ only 47 participants)	qPCR; saliva	Total brain volume, MDD and matched healthy controls	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	0	X	✓	X	X	X	X	none
Boks et al., 2015	$N = 96$ 0 f, 96 m	27.0 (9.1)	Netherland	Longitudinal	Clinical sample (PTSD); military combat exposure	qPCR; leukocyte	Baseline methyl. level, time interval, age, gender, alcohol consumption, cigarette smoking, military rank, length, weight, or medication	ETI-SR	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	9	X	X	X	X	X	X	none
Cai et al., 2015	$N = 11,670$ 11,670 f	NA	China	Cross- sectional	CONVERGE study of MDD	qPCR; saliva	NA	Score	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	NA	X	X	X	X	X	X	shorter
Chen et al., 2014	$N = 40$ 25 f, 15 m	36 (10.7)[a]	USA	Cross-sectional (case-control)	20 (MDD) 20 (controls)	qPCR; leukocyte	Age, sex- and ethnicity-matched controls	ACEs	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	18	X	X	X	X	X	X	mixed
Dagan et al., 2017	$N = 78$ 62 f, 16 m	20.5 (1.6)	USA	Cross-sectional	Undergraduate students	qPCR; buccal cells	Age, gender, ethnicity, current income, Health-related factors, smoking history, current physical activity level, and BMI	ACEs	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	2	X	X	X	X	X	X	mixed
Drury et al., 2014	$N = 80$ 39 f, 41 m	10.2 (2.9)	USA	Cross- sectional	High risk families	qPCR; buccal cells	Age, gender, maternal education, parental age at child conception, race	PAPA (mod.)	<15[b]	Event-based, chronic	Children and adolescents (5 to 15)	Retrospective period	0	X	X	X	X	X	X	shorter
Glass et al., 2010	$N = 1,874$ NA	NA	UK	Cross-sectional (case-control)	CM (123/1874) Physical abuse (20/540) Sexual abuse (34/550)	southern blot; leukocyte	Age, sex, BMI, smoking	Items	NA	Event-based, chronic	Whole childhood (NA)	Retrospective period	NA	X	X	X	X	X	X	none
Guarneri-White et al., 2018	$N = 108$ 60 f, 48 m	15.91 (1.65)	USA	Cross-sectional	Adolescence from larger suburban area recruited via school mailing lists and summer camps	qPCR; saliva	BMI, age, and sex	DIAS-VS CSEQ-SR	<19[a]	Event-based, chronic	Children and adolescents (age 11–19)	Retrospective period	0	X	X	X	X	X	X	shorter
Jodczyk et al., 2014	$N = 677$ females and males	Range: 28–30	New-Zealand	Cross-sectional	Population-based; longitudinal Birth cohort; Christchurch Health and Development Study (CHDS)	qPCR; leukocyte	Sex, ethnicity and family SES at birth	Reports; PBI; CTS (mod.); total score	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	0–5	X	X	X	X	X	X	none
Kananen et al., 2010	$N = 974$ 617 f, 357 m	49.8 (12.60)	Finland	Cross-sectional (case-control)	Epidemiological Health 2000 cohort; Anxiety disorder vs. control subjects	qPCR; leukocyte	Comorbidity, psychiatric medication, BMI, blood pressure, serum lipids, glucose, smoking, sleep, exercise	Items; total score	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	34	X	X	X	X	X	X	shorter

(Continued)

TABLE 1 | Continued

	Study characteristics							ACE characteristics												Findings
												Assessment window		Stressor attributes						
References	Sample size; sex	Age, mean (SD)	Sample origin	Design	Sample composition	Telomere assay	Covariates	Questionnaire	Age	Time scales	Life stage	Time frame	Proximity	Duration	Severity	Controllability	Life domain	Target	Potential	ACEs-TL
Kiecolt-Glaser et al., 2011	*N* = 132 95 f, 37 m	69.7 (10.14)	USA	cross-sectional	Caregivers vs. control subjects; 42/132 (abuse); 74/132 (adverse event)	southern blot; PBMCs	Age, sex, BMI, exercise, sleep, alcohol use, caregiving status	CTQ; total score	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	52	X	X	X	X	X	X	shorter
Kuffer et al., 2016	*N* = 120 57 f, 63 m	74.1 (6.1)[a]	Switzerland	Cross-sectional (case-control)	62 (child laborers, with or without PTSD), 58 (healthy controls)	qPCR; buccal cell	Age, sex, years of education, self-evaluated financial situation, depression, and mental and physical functioning	CTQ-SF	<18	Event-based, chronic	Whole childhood (<18)	Retrospective pe riod	56	X	✓	X	X	X	X	longer
Levandowski et al., 2016	*N* = 176 176 f, 0 m	Subst.: 28.6 (7.3)[a] Contr.: 68.3 (7.4)	Brazil	Cross-sectional (case-control)	Crack cocaine addiction: CRACK-ELS (*n* = 93) CRACK (*n* = 34) ELD (*n* = 49)	qPCR; blood	Age, educational level, BMI	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	11	X	X	X	X	X	X	shorter
Liu et al., 2017	*N* = 894 590 f, 304 m	Range: 28–60 Median = 46	Sweden	Cross-sectional (case-control)	Longitudinal population-based cohort study (PART); 337 (recent depress-ion diagnosis), 574 (non-depressed controls)	qPCR; saliva	Age, alcohol, number of somatic diseases, sex, education, BMI, smokers, physical exercise regularly	Items; total score	<18	Event-based, chronic	Whole childhood	Retrospective period	28	X	X	X	X	X	X	mixed
Malan-Müller et al., 2013	*N* = 128 128 f, 0 m	Range: 18–50 Mean = 29.8	South-Africa	Cross-sectional (case-control)	HIV-positive (83/128) Childhood Trauma (66/128)	qPCR; PBMCs	Age, education, BMI, trauma-subtype, traumatic life experiences, PTBS symptomatology, alcohol abuse	CTQ-SF	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	12	X	X	X	X	X	X	none
Mason et al., 2015	*N* = 1,135 1,135 f, 0 m	45.5 (4.1)	USA	Cross-sectional	Population-based Nurses' Health Study II (NHSII)	qPCR; leukocyte	Age, own and parental education, parental occupation, parental morbidity before age 60	CTS; SES	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	28	X	✓	X	X	X	X	mixed
McFarland et al., 2017	*N* = 1,108 594 f, 514 m	45.6 (11.6)	USA	Cross-sectional	Nashville Stress and Health Study (NSHS)	qPCR; leukocyte	Age, gender, depressive symptoms	LHC	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	28	X	X	X	X	X	X	shorter
Mitchell et al., 2018	*N* = 81 81 f, 0 m	25.48 (4.27)	USA	Cross-sectional	Pregnant women from the Ohio State University Wexner Medical Center (OSUWMC)	qPCR; PBMCs	Age, race, current household, income, education level, marital status, BMI, exercise, smoking and depressive symptoms	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	7	X	X	X	X	X	X	none
Mitchell et al., 2014	*N* = 40 0 f, 40 m	9	USA; African American Boys	Cross-sectional (case-control)	Fragile Families and Child Wellbeing Study (FFCWS)	qPCR; saliva	Mother's age at birth, BMI	CTS (mod.)	<10	Event-based, chronic	Childhood (<10)	Retrospective period	0	X	X	X	X	X	X	shorter
O'Donovan et al., 2011	*N* = 88 45 f, 43 m	30.55 (7.44)	USA	Cross-sectional (case-control)	43 adults with chronic PTSD (*n* = 18 with multiple childhood trauma) and 47 controls	qPCR; leukocyte	Age, sex, BMI, smoking, education	LSC (mod.)	<15	Event-based, chronic	Whole childhood (<15)	Retrospective period	16	X	X	X	X	X	X	shorter

(Continued)

TABLE 1 | Continued

	Study characteristics							ACE characteristics												Findings
												Assessment window		Stressor attributes						
References	Sample size; sex	Age, mean (SD)	Sample origin	Design	Sample composition	Telomere assay	Covariates	Questionnaire	Age	Time scales	Life stage	Time frame	Proximity	Duration	Severity	Controllability	Life domain	Target	Potential	ACEs-TL
Oliveira et al., 2017	$N = 83$ 83 f, 0 m	Range: 65–74	Brazil	Cross-sectional	42 women with less than secondary education and 41 with secondary or more education	qPCR; leukocyte	Age, parental abuse of alcohol	Items	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	54	X	X	X	X	X	X	longer
Osler et al., 2016	$N = 324$ 0 f, 324 m	56	Denmark	Cross-sectional	Copenhagen metropolitan birth-cohort	qPCR; leukocyte	Chronic diseases, and lifestyle, BMI, body weight and height	Items; total score	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	38	X	X	X	X	X	X	shorter
Puterman et al., 2016	$N = 4598$ 2,724 f, 1874 m	Median: 70 Range: 50–90	USA	Cross-sectional	US Health and Retirement Study: longitudinal, nationally representative sample of >26,000 US residents	qPCR; saliva (cell type not specified)	Age, ethnicity, sex, education, current partnership status, BMI, smoking, medical conditions, high blood pressure, diabetes, cancer, lung disease, heart disease, stroke, psychiatric problems, and arthritis	Items; total score	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	52	X	X	X	X	X	X	shorter
Revesz et al., 2016	$N = 2,936$ 1,950 f, 986 m	Baseline: 41.8 (13.1) Follow-up: 48.5 (13.0)	Netherlands	Longitudinal (6-year follow-up)	Population-based	qPCR; leukocyte	Sex, age, smoking, triglycerides, BP	CTI	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	26	X	X	X	X	X	X	mixed
Riley et al., 2018	$N = 66$ 27 f, 39 m	40.9 (9.8)		Cross-sectional (case-control)	48 adults with DSM-5 schizophrenia and 18 healthy controls	qPCR; lymphocytes	Age	ETI	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	23	X	✓	X	X	X	X	mixed
Robles et al., 2016	$N = 39$ 28 = f, 19 m	11.3 (1.5) Range = 8–13	USA	Cross-sectional	Population-based	qPCR; leukocyte	Age, gender, BMI, parent educational status and leukocyte composition	Score; total score	[8; 13]	Daily, chronic	Childhood (age 8–13)	Daily ratings for 56 days	0	X	X	X	X	X	X	shorter
Savolainen et al., 2014	$N = 1,486$ 817 f, 674 m	61.5 (2.9)	Finland	Cross-sectional	Population-based; Helsinki Birth Cohort Study	qPCR; leukocyte	Age, sex, stock of DNA, mental disorder, depression, education, alcohol, father's education and mother's age at delivery, coronary heart disease and stroke, BMI, diabetes II	National Archive Finland; TEC	Life time (median 10)	Event-based, chronic	Whole childhood + early childh., childhood and adolescence	Retrospective period, archive information	0 + 42	X	X	X	X	X	X	mixed
Schaakxs et al., 2016	$N = 496$ 323 f, 173 m	70.6 (7.4)	Netherlands	Cross-sectional	Netherlands Study of Depression in Older Persons (NESDO); 44.2% childhood abuse at least once, 23.4% one or more events	qPCR; leukocyte	Sex, age, chronic disease	Score	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	55	X	X	X	X	X	X	mixed
Shalev et al., 2013	$N = 236$ 116 f, 120 m	Baseline: 5 Follow-up: 10	UK	Longitudinal	Population-based; Environmental-Risk (E-Risk) Study, subset of epidemiological sample; 108/236 (Exp./N)	qPCR; buccal cells	Age, sex, BMI, SES	CTS; clinical interview; items; total score	[5; 10]	Event-based, chronic	Childhood (age 5–10)	Prospective, longitudinal + retrospective period	0	X	X	X	X	X	X	shorter

(Continued)

TABLE 1 | Continued

	Study characteristics							ACE characteristics												Findings
												Assessment window		Stressor attributes						
References	Sample size; sex	Age, mean (SD)	Sample origin	Design	Sample composition	Telomere assay	Covariates	Questionnaire	Age	Time scales	Life stage	Time frame	Proximity	Duration	Severity	Controllability	Life domain	Target	Potential	ACEs-TL
Shalev et al., 2014	$N = 1037$ 498 f, 539 m	Baseline: 26 Follow-up: 38	New-Zealand	Longitudinal	Population-based; Dunedin Multidisciplinary Health and Development Study, birth cohort; $n = 234$: int. dis. $n = 524$: no int. dis.	qPCR; leukocyte	CM, tobacco smoking, substance dependence, psychiatric medication use	Total Score	[3; 11]	Event-based, chronic	Childhood (age 3–11)	Prospective, longitudinal + retrospective periods	0–15	X	X	X	X	X	X	none
Surtees et al., 2011	$N = 4,441$ 4,441 f, 0 m	Median: 62 Range: 41–80	UK	Cross-sectional	European Prospective Investigation into Cancer (EPIC)-Norfolk Population Study	qPCR; lymphocyte	Age, physical health score, self- reported health, social class, obesity, smoking, preexisting disease	HLEQ	<17	Event-based, chronic	Whole childhood (<17)	Retrospective period	45	X	X	X	X	X	X	shorter
Tyrka et al., 2010	$N = 31$ 22 f, 9 m	26.9 (10.1)	USA	Cross-sectional (case-control)	No history of CM ($n = 21$) or a history of moderate or severe CM ($n = 10$)	qPCR; leukocyte	Age, sex, oral contraceptives, smoking, BMI, race, education, SES, perceived stress	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	9	X	X	X	X	X	X	shorter
Tyrka et al., 2016	$N = 289$ 177 f, 113 m,	31.0 (10.7)	USA	Cross-sectional (case-control)	No disorder/no adversity ($n = 113$) No disorder/ adversity ($n = 66$) Disorder/no adversity ($n = 39$) Disorder/adversity ($n = 72$)	qPCR; leukocyte	Race, smoking, oral contraceptive, psychiatric disorder	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	13	X	X	X	X	X	X	shorter
van Ockenburg et al., 2015	$N = 1,094$ 588 f, 506 m	53.1 (11.4)	Netherlands	Longitudinal (prospective)	Population-based	qPCR; leukocyte	Sex, age, comorbidity, BMI, smoking, exercise, education	LTE (mod.)	<12	Event-based, chronic	Childhood (<12)	Retrospective period	41	X	X	X	X	X	X	none
Verhoeven et al., 2015	$N = 2,936$ 1,950 f, 986 m	41.8 (13.1)	Netherlands	Cross-sectional	Longitudinal cohort study examining the course and consequences of depressive and anxiety disorders; 57% current depression	qPCR; leukocyte	Sex, age, comorbidity, depression, BMI, smoking, alcohol use, exercise, education	CTI; CTQ; score	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	26	X	X	X	X	X	X	none
Vincent et al., 2017	$N = 180$ 103 f, 77 m	50 (15.65)	UK	CROSS- sectional	80 depressed subjects and 100 control subjects	qPCR; blood (cell type not specified)	Age, sex	CTQ	<18	Event-based, chronic	Whole childhood (<18)	Retrospective period	32	X	X	X	X	X	X	mixed
Zalli et al., 2014	$N = 333$ 167 f, 166 m	63.2 (5.5)[a]	UK	Cross-sectional	Heart Scan Study, a subsample of the Whitehall II epidemiological cohort	qPCR; PBMC	Age, SES and BMI	Item	<16	Event-based, chronic	Whole childhood (<16)	Retrospective period	47	X	X	X	X	X	X	shorter

ACEs, adverse childhood experiences; BMI, body mass index; BP, blood pressure; BTL, buccal cell telomere length; CA, childhood adversity; CM, childhood maltreatment; CPA, child physical abuse; CSEQ, children's social experiences questionnaire; CTI, childhood trauma interview; CTQ, childhood trauma questionnaire; CTS, conflict tactics scale; DIAS-VS, direct and indirect aggression scale-victim version; DNA, deoxyribonucleic acid; DNAm age, DNA methylation age; ELD, elderly people; ELS, early life stress; ETI, early trauma inventory; Exp., exposed; f, female; HIV, human immunodeficiency virus; HC, healthy controls; HLEQ, health and life experiences questionnaire; int.dis., internalizing disorders; LHC, life history calendar; LSC, life stressor checklist; LTE, list of threatening events; LTL, leukocyte telomere length; m, male; MDD, major depressive disorder; mod., modified; N, number of participants; NA, not available; NLE, adulthood negative life events; PBI, parental bonding instrument; PAPA, preschool age psychiatric assessment; PBMC, peripheral blood mononuclear cells; PTSD, posttraumatic stress disorder; qPCR, quantitative polymerase chain reaction; SES, socioeconomic status; SF, short form; SR, self-report; SLE, stressful life events in early life; TA, Telomerase Activity; TEC, traumatic experiences checklist; TL, Telomere length; UK, United Kingdom; USA, United States of America.

[a] *weighted mean ages.*

[b] *Range up till the age of participants (oldest participant 15 years).*

(Glass et al., 2010; Kananen et al., 2010; Tyrka et al., 2010, 2016; O'Donovan et al., 2011; Malan-Müller et al., 2013; Chen et al., 2014; Mitchell et al., 2014; Blom et al., 2015; Bersani et al., 2016; Kuffer et al., 2016; Levandowski et al., 2016; Liu et al., 2017; Riley et al., 2018). Five studies measured TL at more than one time point and were therefore able to examine TL longitudinally (Shalev et al., 2013, 2014; Boks et al., 2015; van Ockenburg et al., 2015; Revesz et al., 2016). The type of samples and the sample composition of the included papers varied widely. Some studies examined general population samples, such as birth cohorts (Jodczyk et al., 2014; van Ockenburg et al., 2015; Osler et al., 2016), whereas others had a focus on specific clinical populations, such as on depressed patients (Chen et al., 2014; Blom et al., 2015; Cai et al., 2015; Liu et al., 2017; Vincent et al., 2017), patients with anxiety disorders (Kananen et al., 2010), patients with post-traumatic stress disorder (PTSD) (O'Donovan et al., 2011; Boks et al., 2015; Kuffer et al., 2016), or patients with substance use disorders (Levandowski et al., 2016).

Because there are different ways to measure telomere length (Montpetit et al., 2014), information on the telomere assay method was collected. In our sample of eligible papers, almost all studies ($N = 36$) investigated TL using a quantitative polymerase chain reaction (qPCR). Only two papers used a southern blot analysis as TL assay method (Glass et al., 2010; Kiecolt-Glaser et al., 2011). TL was examined in different cell types: six papers reported that DNA was extracted from saliva samples (Kiecolt-Glaser et al., 2011; Mitchell et al., 2014; Blom et al., 2015; Cai et al., 2015; Puterman et al., 2016; Liu et al., 2017; Guarneri-White et al., 2018), and four studies used epithelial buccal cells (Shalev et al., 2013; Drury et al., 2014; Kuffer et al., 2016; Dagan et al., 2017). The other studies ($N = 28$) extracted DNA from peripheral blood samples. Most of these studies assayed leukocyte DNA for TL ($N = 22$), four studies extracted DNA from peripheral blood monocular cells (PBMCs) (Kiecolt-Glaser et al., 2011; Malan-Müller et al., 2013; Zalli et al., 2014; Mitchell et al., 2018), and two studies extracted DNA from lymphocytes (Surtees et al., 2011; Riley et al., 2018). Although a wide variety of covariates were included across the studies, almost all studies controlled for age, sex, body mass index (BMI) and smoking.

ACEs Characteristics

Assessments of ACEs varied substantially across studies (see **Table 1**). Studies examined various age ranges: 18 studies included ACEs before the age of 18 (Tyrka et al., 2010, 2016; Kiecolt-Glaser et al., 2011; Malan-Müller et al., 2013; Chen et al., 2014; Boks et al., 2015; Mason et al., 2015; Bersani et al., 2016; Kuffer et al., 2016; Levandowski et al., 2016; Osler et al., 2016; Puterman et al., 2016; Dagan et al., 2017; Liu et al., 2017; McFarland et al., 2017; Vincent et al., 2017; Mitchell et al., 2018; Riley et al., 2018), one study reported on ACEs before the age of 17 (Surtees et al., 2011), eight studies investigated ACEs before the age of 16 (Kananen et al., 2010; Jodczyk et al., 2014; Zalli et al., 2014; Cai et al., 2015; Verhoeven et al., 2015; Revesz et al., 2016; Schaakxs et al., 2016; Oliveira et al., 2017), one study before the age of 15 (O'Donovan et al., 2011) and two studies before the age of 12 (Shalev et al., 2014; van Ockenburg et al., 2015). Additionally, six studies assessed ACEs up till the time of assessment (Shalev et al., 2013; Drury et al., 2014; Mitchell et al., 2014; Blom et al., 2015; Robles et al., 2016; Guarneri-White et al., 2018). Furthermore, the eligible papers used different ACEs assessments. About half of the studies ($N = 20$) used standardized validated questionnaires or interviews to assess adversities. The most commonly used questionnaire was the retrospective, self-report CTQ (Bernstein et al., 1994) that was used in 10 studies (Tyrka et al., 2010, 2016; Kiecolt-Glaser et al., 2011; Malan-Müller et al., 2013; Blom et al., 2015; Verhoeven et al., 2015; Kuffer et al., 2016; Levandowski et al., 2016; Vincent et al., 2017; Mitchell et al., 2018). The other studies ($N = 18$) used modified versions of other questionnaires or interviews or used novel items to create adversity scores (see **Table 1**, column assessment; **Supplementary Material**, column type of adversity).

TABLE 2 | Overview results.

	Shorter	None	Longer	Mixed
Total association				
ACEs and TL ($N = 38$)	18	9	2	9
ACEs and ΔTL ($N = 5$)	2	3	–	–
Sub-findings				
Sample size ($N = 38$)				
<400 ($N = 23$)	13	4	2	4
>400 ($N = 15$)	5	5	–	5
Sex ($N = 37$)				
Only male ($N = 3$)	2	1	–	–
Only female ($N = 7$)	3	2	1	1
Both ($N = 27$)	13	5	1	8
Age ($N = 36$)				
<25 ($N = 7$)	5	1	–	1
25–45 ($N = 13$)	5	6	–	2
>45 ($N = 16$)	7	1	2	6
Sample Composition ($N = 38$)				
Clinical ($N = 16$)	6	5	1	4
Non-clinical ($N = 22$)	12	4	1	5

ΔTL, telomere attrition or within subject TL change.

With the SECs in mind, it was shown that almost all studies ($N = 37$) either had an event-based, or event-based/chronic stress measurement timescale. The only exception was Robles et al. (2016), who based their adversity score on current ratings of daily emotions to family conflict. Regarding the developmental life stage, all papers reported on ACEs before the age of 18. Most studies did not differentiate between childhood and adolescence. However, certain studies only included ACEs in childhood or did differentiate between childhood and adolescence (Shalev et al., 2013; Drury et al., 2014; Mitchell et al., 2014; Blom et al., 2015; Robles et al., 2016; Guarneri-White et al., 2018). Some studies used smaller age ranges (Shalev et al., 2014) or built subcategories of their larger ranges (Savolainen et al., 2014; van Ockenburg et al., 2015). Looking at the stress assessment window—in particular the measurement timeframe of ACEs assessments—most studies ($N = 34$) assessed ACEs retrospectively. Some studies used combined retrospective and prospective assessments (Shalev et al., 2013, 2014), a combination of retrospective

self-reports and archive information (Savolainen et al., 2014), or an adversity score based on daily ratings (Robles et al., 2016). In terms of the time between the ACEs exposure and the age at ACEs assessment, the duration varied between 0 and 56 years. Aggregating all duration measures across studies, the mean time between the end of the ACEs measure and age at ACEs assessment was approximately 23 years.

Regarding the six reviewed stressor attributes, almost no information is included and specified in the included sample of studies. First, only one study reported on the duration of ACEs (the duration of being separated from their parents) (Savolainen et al., 2014). Second, four studies reported on the severity of ACEs on a continuous scale (Blom et al., 2015; Mason et al., 2015; Kuffer et al., 2016; Riley et al., 2018). Most studies ($N = 34$), however, did not report on the severity of the stressor on a continuous measure. Instead, they reported exposure categories, defined by using self-developed items or certain cut-off scores on continuous measures. Third, none of the studies explicitly measured controllability on a continuous scale. Fourth, looking at specific life-domains, no study reported on ACEs from a specific life-domain. However, many ACEs in childhood are of interpersonal and interpersonal-intimate nature, resulting from multiple life domains, mainly family, peers and school. Fifth, no study explicitly reported on the attribute "target of the stressor," though, most studies assessed ACEs that targeted participants themselves, or close others. Last, focusing on the attribute "potential of the stressor to elicit potential harmful responses," none of the study described in detail the qualities inherent to the adversities that were measured.

Overall, the eligible studies reported on stressors from a broad range of potentially harmful experiences. However, a lot of information is unknown, missing or not specified. Therefore, more research using a common language and taxonomy to describe certain characteristics of stressors—in particular with regard to ACEs—is needed.

Main Findings: ACEs and TL

In total, 18 paper reported a negative association between ACEs and TL or higher odds for shortened TL among individuals reporting exposure to ACEs compared to those who were less or non-exposed (Kananen et al., 2010; Tyrka et al., 2010, 2016; Kiecolt-Glaser et al., 2011; O'Donovan et al., 2011; Surtees et al., 2011; Shalev et al., 2013; Drury et al., 2014; Mitchell et al., 2014; Zalli et al., 2014; Cai et al., 2015; Bersani et al., 2016; Levandowski et al., 2016; Osler et al., 2016; Puterman et al., 2016; Robles et al., 2016; McFarland et al., 2017; Guarneri-White et al., 2018). Additionally, nine papers showed no association between ACEs and TL (Glass et al., 2010; Malan-Müller et al., 2013; Jodczyk et al., 2014; Shalev et al., 2014; Blom et al., 2015; Boks et al., 2015; van Ockenburg et al., 2015; Verhoeven et al., 2015; Mitchell et al., 2018). Furthermore, two studies even reported a trend toward longer telomeres among individuals reporting more ACEs (Kuffer et al., 2016; Oliveira et al., 2017). Finally, nine papers reported mixed findings, with studies reporting some associations within their data, but no conclusive association within their total sample (Chen et al., 2014; Savolainen et al., 2014; Mason et al., 2015; Revesz et al., 2016; Schaakxs et al., 2016; Dagan et al., 2017; Liu et al., 2017; Vincent et al., 2017; Riley et al., 2018).

Beyond that, five studies have examined TL at more than one time point (Shalev et al., 2013, 2014; Boks et al., 2015; van Ockenburg et al., 2015; Revesz et al., 2016). Hence, these studies were able to assess telomere attrition, which is the change in telomere length within a subject. Two of these studies showed ACEs to be associated with TL change (Shalev et al., 2013; Revesz et al., 2016), whereas three papers reported no association between ACEs and TL change (Shalev et al., 2014; Boks et al., 2015; van Ockenburg et al., 2015).

Possible Moderators

To attempt to explain the variety in findings, comparisons were made based on sample size, age, sample composition, and sex of study samples. First, focusing on the study characteristics, the results of studies with more than 400 participants ($N = 15$) seemed to be less conclusive than studies with <400 participants ($N = 23$). Of these studies with larger samples, five papers reported a cross-sectional association between early adversity and TL (Kananen et al., 2010; Surtees et al., 2011; Cai et al., 2015; Puterman et al., 2016; McFarland et al., 2017), five studies reported mixed results (Savolainen et al., 2014; Mason et al., 2015; Revesz et al., 2016; Schaakxs et al., 2016; Liu et al., 2017), and five reported no associations (Glass et al., 2010; Jodczyk et al., 2014; Shalev et al., 2014; van Ockenburg et al., 2015; Verhoeven et al., 2015). Second, subdividing the age of study samples indicated that studies investigating TL during childhood, adolescence or emerging adulthood ($N = 7$) more often find associations of ACEs and shorter TL (Shalev et al., 2013; Drury et al., 2014; Mitchell et al., 2014; Blom et al., 2015; Robles et al., 2016; Dagan et al., 2017; Guarneri-White et al., 2018). Findings in older samples are more inconclusive. Third, considering the sample composition, comparing clinical (with mental disorders) ($N = 16$) and non-clinical samples (without mental disorders) ($N = 22$) indicated that studies in non-clinical samples more often find negative associations between ACEs and TL than do studies in clinical populations. Fourth, with regard to the sex of participants, there were no observable differences in reported results.

DISCUSSION

The aim of the current review was to review the literature on the associations between ACEs and TL in an attempt to highlight how heterogeneity in sample and stressor characteristics contributes to findings. Overall, the sample of studies we reviewed indicates a negative association between ACEs and TL, although many papers presented mixed findings and a quarter of eligible studies found no relationship between ACEs and TL. These findings are consistent with recently published meta-analyses investigating the association between early adversity, childhood trauma and childhood psychosocial stressors and TL. All three studies showed significant small negative associations with TL (Hanssen et al., 2017; Li et al., 2017b; Ridout et al., 2017). These meta-analyses further reported high between-study heterogeneity of effects. Considering possible moderators within our sample of

studies indicates that results of larger samples seem to be less conclusive than results of smaller samples. In addition, studies investigating participants younger than 25 more often find ACEs to be negatively associated with TL compared to older samples. Furthermore, results from studies of non-clinical samples more often report negative associations between ACEs and TL than do studies of clinical samples. Using the SECs proposed by Epel et al. (2018) to examine characteristics of the included ACEs shows a lack of detailed information on SECs in many studies. At least four findings (sample size, age, psychopathology, and ACEs characteristics) need to be discussed in more detail to find explanations for the heterogeneity and inconclusiveness of reported findings.

First, with regard to sample size, we observed that findings of larger samples are less conclusive compared to findings of smaller samples. This might be explained by the fact that larger samples can control for more additional variables and potential confounds. These additional factors might moderate, mediate, conceal or suppress the direct, independent impact of ACEs, as many of these variables in larger models are inter-correlated (e.g., adversities, mental health problems, negative life-styles, and smoking status).

Second, we observed that studies with younger participants more often find negative associations than studies with older participants. This is in line with Ridout et al. (2017) who reported in their moderator analyses that the smaller the duration between ACEs exposure and age at TL assessment, the larger the magnitude of effect sizes. They explained this finding by pointing to the fact that studies of children assume no smoking amongst participants, and that adversities early in childhood tend to be associated with larger effects (Ridout et al., 2017). Similar results were found by Hanssen et al. (2017). Another potential explanation, according to the healthy survivor effect, might be that participants within older samples drop out due to morbidity or early mortality, which is in turn associated with shorter telomeres (Mather et al., 2011; Kuffer et al., 2016; Schaakxs et al., 2016; Oliveira et al., 2017). Moreover, Schaakxs et al. (2016) argued that "a possible explanation for these null findings in older adults may be that older adults have been exposed to numerous competing causes for shortened TL, such as somatic diseases or an unhealthy lifestyle over the life span. These other TL-damaging factors may suppress the independent impact of psychosocial stressors." (p. 441).

Third, the sample composition of included studies varied strongly. Some of the studies focused on specific clinical populations and the impact of psychiatric disorders on TL. These studies included ACEs in their models as control variables. In contrast, other studies focused on the impact of ACEs on TL controlling for psychiatric conditions. We observed that studies with non-clinical populations more often report negative associations between ACEs and TL. This is in line with Ridout et al. (2017), who found effect sizes of smaller magnitude regarding the association of ACEs and TL in their moderator analyses, when looking at studies that included subjects with mental disorders. Epel and Prather (2018) recently proposed a triad model of stress exposures, psychopathology and telomere biology combining the meta-analytic evidence between the associations of stress and telomeres, stress and psychopathology, and psychopathology and telomeres. Having this triad in mind, when approaching TL from a psychopathological perspective, studies have to acknowledge that "expression of psychopathology may be strongly influenced by exposure to maltreatment" (Teicher and Samson, 2013, p. 1,114). This distinctive phenotypical expression of a psychiatric disorder (with vs. without maltreatment) might reveal distinct subtypes of disorders that are important to account for when determining the biological bases of these mental disorders (Teicher and Samson, 2013; Teicher et al., 2016). Moreover, possible direct associations of ACEs on TL might be mediated by the later development of mental disorders. Assuming that early adversities often precede psychopathology, psychiatric disorders might mediate the association of ACEs and TL. Hence, research on TL should acknowledge both perspectives: distinct subtypes of psychiatric disorders (with vs. without maltreatment) within clinical samples and the potential mediating effect of psychopathology in non-clinical samples.

Fourth, the current study further examined ACEs using the SECs recently proposed by Epel et al. (2018). Results showed an overall lack of details and lots of missing information. This makes it indeed very difficult to understand the adverse nature of these experiences with important characteristics and attributes not being measured or articulated. Differentiating between event-based and chronic exposures, the target of the exposure, and the duration, for instance, is very important in the context of trauma research as many childhood adversities are interpersonal and traumatic in nature (e.g., abuse and neglect, interpersonal loss, interpersonal conflict, interpersonal violence) and are targeted at either participants themselves or at close others (e.g., siblings or family members) (Widom et al., 2008; Moffitt and the Klaus-Grawe Think Tank, 2013). Chronic-occurring interpersonal events are often followed by a broad range of trauma-associated psychopathologies that are not captured within the classical framework of PTSD (Cook et al., 2005). These harmful responses can lead to diverse behavioral and emotional alterations, often referred to as complex trauma symptoms, as for example affective dysregulation, attentional and behavioral problems, self and relational deregulation (Briere et al., 2008; Greeson et al., 2011; Schmid et al., 2013). For this reason many experts emphasized the need for a more developmentally sensitive diagnostic system that takes account of the heterogeneity of psychopathology following early trauma (Cloitre et al., 2009; van der Kolk et al., 2009; D'Andrea et al., 2012; Schmid et al., 2013). This led to the inclusion of complex trauma symptoms within the PTSD section in the Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition (DSM-5) and the inclusion of a complex PTSD disorder in the International Classification of Diseases 11th Revision (ICD-11). These complex trauma symptoms contain symptoms of affect dysregulation, negative self-concepts and interpersonal problems that are related to the traumatic exposure (Cloitre et al., 2013). Overall, the adversities included are all of a stressful, adverse, and traumatic nature. Most of these stressors have the potential to elicit harmful emotional responses (e.g., social threat, loss of control, shame) and behavioral alterations

(e.g., role-change, impulsivity), but detailed and differentiating information is missing.

Limitations

The current review needs to be seen in light of some limitations. First, this review is not a systematic review as defined by PRISMA or Cochrane guidelines. The narrative approach, however, allowed us to discuss the complexity of exposure characteristics in an overall heterogenous sample of studies and adds to recently published systematic meta-analyses. Second, most studies assessed ACEs retrospectively with self-reported questionnaires, sometimes with several decades between adversity and assessment of adversity, which leads to recall biases. Hardt and Rutter (2004) extensively discussed biases of retrospective self-reports and concluded that they easily lead to an underreporting of events and that the validity of details assessed retrospectively might be low, but false-positive reports are rare. In contrast, a recently published meta-analysis reported only weak associations between prospective and retrospective measures of adversity concluding that these measures identify different groups of individuals (Baldwin et al., 2019). This should be taken into account in future studies. Third, this review focused on the ACEs part of the ACEs-TL association. Besides that, methodological issues with regard to the TL measurement approach are also of high interest and might explain some of the heterogeneity in findings. These issues are extensively reviewed and discussed elsewhere and beyond the scope of this review (Montpetit et al., 2014; Lai et al., 2018). Fourth, publication bias is likely to occur because we only included papers that were published in peer-reviewed journals. Last and most important, as described in the method section, studies were included that measured ACEs before the age of 18 by means of a questionnaire or an interview. Studies reporting on early adversities solely based on high-risk status, on low socio-economic status (SES), on neglectful, non-supportive parenting styles, on maternal depression, and on maternal stressors during pregnancy, were not included due to their lack of direct measurement of adverse experiences. Being at risk for ACEs is highly correlated with incidence of ACEs but not all at-risk individuals are exposed. This approach was used because the focus of this review was on the harmful long-term consequences of experiencing ACEs. Still, as a substantial overlap between different operationalization's of stressors exist, it is therefore very difficult to draw clear boundaries.

Implications

Future research might benefit from a differentiated look into ACEs, articulating multiple domains of stressors such as in the SECs (Epel et al., 2018). This will help to improve our understanding of the adverse nature of these exposures and uncover different exposure-related emotional and behavioral responses that mediate the association between ACEs and long-term health outcomes. This might help to further our understanding of the complex associations of stress and TL, beyond what can be explained by simply summing potentially harmful incidents in childhood. In addition, resilience factors that protect children and adolescents from sustained physiological consequences need further investigation.

CONCLUSION

Overall, the included sample of studies indicates a negative association between ACEs and TL, but the diversity in sample and stressor characteristics makes it difficult to achieve a final and confident conclusion. From a developmental perspective, a more comprehensive evaluation of adversities using a common language and dimensional approaches to SECs might help to improve understanding of the complex associations between (early) stressors and health outcomes. Individuals are exposed to numerous competing and interacting exposures that might shorten TL over the life course. A focus on developmental trajectories combining early adversities, psychopathology and protective factors might help to develop enhanced approaches to reduce the stress-related health burden of our societies.

AUTHOR CONTRIBUTIONS

DB, CB, MS, and KS contributed to the conception of the paper. DB extracted all study and stressor characteristics and wrote the first draft of the manuscript. AOD, CB and DdH wrote sections of the manuscript and edited the paper. AOD, AE, JF, AdG, MS, KS, and CB critically revised the paper. All authors contributed to manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnins.2019.00490/full#supplementary-material

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Chapter 3: Compounding Stress: Childhood Adversity as a Risk Factor for Adulthood Trauma Exposure in the Health and Retirement Study

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Compounding Stress: Childhood Adversity as a Risk Factor for Adulthood Trauma Exposure in the Health and Retirement Study

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Childhood adversity (CA) and adulthood traumatic experiences (ATEs) are common and unequally distributed in the general population. Early stressors may beget later stressors and alter life-course trajectories of stressor exposure. Gender differences exist regarding the risk of specific stressors. However, few studies have examined the associations between specific types of CA and ATEs. Using a large-scale sample of older adults, we aimed to (a) determine if specific or cumulative CA increased the risk for specific or cumulative ATEs and (b) examine whether these associations were moderated by gender. In a sample from the U.S. Health and Retirement Study ($N = 15{,}717$; $M_{age} = 67.57$ years, $SD = 10.54$), cross-sectional Poisson and logistic regression models were fitted to assess the specific and cumulative associations between CA and ATEs. Overall, cumulative CA was associated with a larger risk ratio of ATEs, adjusted for covariates: a*RRR*s = 1.28, 1.63, and 1.97 for 1, 2, and 3–4 adverse events in childhood, respectively. Cumulative CA was particularly strongly associated with adulthood physical attacks, a$OR = 5.66$, and having a substance-abusing spouse or child, a$OR = 4.00$. Childhood physical abuse was the strongest independent risk factor for cumulative ATEs, a$RRR = 1.49$, and most strongly associated with adulthood physical attacks, a$OR = 3.41$. Gender moderated the association between cumulative CA and cumulative ATEs, with slightly stronger associations between cumulative CA and ATEs for women than men. Given that CA and ATEs perpetuate health disparities worldwide, reducing their incidence and effects should be major priorities for public health.

Childhood adversity (CA) and adulthood trauma exposure (ATE) are highly prevalent in the general population (Benjet et al., 2016; Copeland et al., 2007; Green et al., 2010; Hussey et al., 2006; Kilpatrick et al., 2013). These stressful experiences, particularly those that occur during childhood, such as physical abuse and parental substance abuse, have been linked to negative long-term outcomes ranging from mental health problems and suicide attempts to major medical illnesses and even premature mortality (Anda et al., 2006; Brown et al., 2009; Clemens et al., 2018; Dube et al., 2001, 2003; Felitti et al., 1998; Johnson et al., 2020; Logan-Greene et al., 2014; O'Donovan et al., 2015; Puterman et al., 2020; Riedl et al., 2019). Despite the strong effects of CA on mental and physical health outcomes, our understanding of the various pathways that link adverse events during childhood to ill health remains incomplete. One possibility is that early adversity alters the trajectories of stress exposure in later life, increasing the risk for trauma exposure in adulthood. Therefore, to further our understanding of stress exposures and their associations across the life-course, we investigated the association between CA and ATEs in a large, community-based sample of older adults from the Health and Retirement Study (HRS).

Population-based studies have shown high prevalence rates of CA and ATEs worldwide (Kessler et al., 2010, 2017). Approximately 50%–70% of children in the United States are exposed to some kind of adverse event during childhood, with multiple adversities common among those affected (Copeland et al., 2007; Felitti et al., 1998; Green et al., 2010; Hussey et al., 2006). In these studies, the CA construct includes a broad array of experiences, including items directly related to emotional and physical abuse, neglect, family instability, and parental substance abuse, which are typically summed to create

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a cumulative index of different exposure types (Dube et al., 2001; Felitti et al., 1998). Worldwide studies of life-course trauma exposure have demonstrated that over two-thirds of individuals experience at least one traumatic event in their life course, and approximately one-third of the population experiences four or more such events (Benjet et al., 2016; Kessler et al., 2017). The lifetime prevalence of traumatic experiences in the United States is high—60%–90%—with multiple exposures being very common (Benjet et al., 2016; Breslau et al., 1998; Kilpatrick et al., 2013; Norris, 1992). In light of these exposure rates, it is important to understand how stressful childhood events are related to ATEs.

Two related theoretical models attempt to explain the potent impact of CA on health: early embedding in critical periods and life-course stress models. First, childhood is a critical period for the development and integrity of major biological systems and psychological processes. Childhood is a particularly vulnerable phase of high plasticity, as there are major shifts in the development of brain structure and functioning, the hormonal system and stress responses, and many other important systems (Heim et al., 2010; Kolb & Gibb, 2014; McCrory et al., 2017; McCrory & Viding, 2015). Furthermore, childhood is a critical period for the development of cognitive and emotional processes, and emotional and social information processing enables personal and social functioning in adulthood. However, interruptions in such development could lead to maladaptation and latent vulnerability in adulthood (McCrory et al., 2017; McCrory & Viding, 2015; McLaughlin et al., 2019, 2020). In line with such models, recent studies have shown that adverse experiences that occur during specific age ranges in childhood are associated with altered neurodevelopment, accelerated maturation, and epigenetic changes (Callaghan & Tottenham, 2016; Dunn et al., 2018; Hambrick et al., 2019; McCrory et al., 2017; Szyf & Bick, 2013).

Second, CA may alter later trajectories of stress exposure, increasing the overall lifespan burden of stressor exposure. Life-course stress theories, such as cumulative inequality theory, state that "social systems generate inequality, which is manifested over the lifespan via demographic and developmental processes, and that personal trajectories are shaped by the accumulation of risk, available resources, perceived trajectories, and human agency" (Ferraro & Shippee, 2009, p. 334). Similarly, stress proliferation theories argue that people who experience adversity are at an increased risk of experiencing additional later adversities, including traumatic stress exposures (Pearlin et al., 2005). In line with these life-course perspectives, studies have shown that CA is associated with increased adult life stress exposures and perceived distress (Manyema et al., 2018; Nurius et al., 2015). The evidence for a life-course stress accumulation perspective is further supported by dose–dependent effects that link cumulative CA to later adverse outcomes (Anda et al., 2006; Berens et al., 2017; Dube et al., 2001, 2003; Felitti et al., 1998; Logan-Greene et al., 2014). Understanding the distributions of exposures from a life-course perspective might open up possibilities for strategic interventions to counteract maladaptation and latent vulnerability following early adverse experiences.

Although the overall cumulative number of trauma exposures tends to be higher in men than in women, additional gender differences in exposure can be found when focusing on specific categories of events, such as sexual abuse (Benjet et al., 2016; Hatch & Dohrenwend, 2007; Tolin & Foa, 2008). Several reviews and large-scale studies on gender differences in overall trauma exposure have shown that women are less likely to experience traumatic events compared to men (Breslau, 2002; Breslau et al., 1998; Hatch & Dohrenwend, 2007; Tolin & Foa, 2008). However, when examining specific types of exposure, women have been found to have a higher risk than men of experiencing adverse sexual incidents and equal risk of experiencing nonsexual abuse (Olff, 2017; Tolin & Foa, 2008). Furthermore, women have been shown to be less likely to be exposed to accidents and disasters, nonsexual assaults, witnessing death or injury, and military trauma than men (Tolin & Foa, 2008). During childhood specifically, no significant gender differences in overall cumulative exposure have been found; however, girls were found to experience more sexual abuse than boys (Tolin & Foa, 2008). Despite the higher rates of overall trauma exposure in men, women have a higher risk of developing posttraumatic stress disorder (PTSD), which may partly be due to differences in the types of traumatic events men and women experience (Breslau, 2002; Breslau et al., 1998; Olff, 2017; Tolin & Foa, 2008). Overall, the literature has demonstrated differences in trauma exposure with regard to gender as well as the importance of focusing not only on cumulative exposure scores but also on specific exposure types.

Despite the high prevalence rates of CA and ATEs, their associations with increased risks for diseases of aging, and the rapid aging of the global population, only a small number of studies have investigated the prevalence of CA and ATEs in older populations. Little is known about how CA alters the risk for ATEs across the life-course, which is particularly important because CA and ATEs are some of the strongest known risk factors for a broad range of adverse health outcomes in later life (Clemens et al., 2018; Johnson et al., 2020; Logan-Greene et al., 2014; Riedl et al., 2019). Many previous studies have lacked a life-course perspective and have had insufficient sample sizes to investigate specific combinations and patterns of trauma exposure. In addition, beyond well-known gender differences in exposure to adverse events in childhood and ATEs, little is known about gender and its impact on the associations between specific types of CA and ATEs. We add to this growing literature by investigating associations between specific types of CA and specific ATEs. In particular, our study aims were to (a) determine whether CA would be shown to increase the risk for ATEs in a large-scale sample of older adults, with a focus on whether specific types of CA or cumulative CA were associated with specific or cumulative ATEs, and (b) examine if these associations were moderated by gender.

Method

Participants

In the HRS, a longitudinal study of a population-based U.S. sample, more than 40,000 individuals over 50 years of age and their spouses were interviewed (Fisher & Ryan, 2018) from 1992 through the present. The original HRS study population included community-dwelling adults in the contiguous United States born during the years 1931 to 1941, with a 2:1 oversampling of African American and Hispanic populations. This sample has been refreshed with new birth cohorts over the years with participants born during 1890–1931 and 1941–1959, leading to the current HRS population (Fisher & Ryan, 2018; Sonnega et al., 2014). The actual panel of HRS participants at each wave of data collection is much smaller than the total amount of participants, as some participants have already died, and others entered the panel at a later date. Therefore, the sample size of each wave is approximately 20,000 (HRS, 2017c). The HRS is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan.

Procedure

Starting in 2006, the HRS implemented a psychosocial questionnaire that included assessments of CA and ATEs (Clarke et al., 2008; Smith et al., 2017). After the interview section of the HRS, which is conducted at each wave of data collection, participants answered a questionnaire on different psychosocial domains, called the "leave behind" (LB) questionnaire (Clarke et al., 2008; Smith et al., 2017). Response rates for these questionnaires were high: Between 73% and 88% of eligible participants responded to the LB questionnaire over the course of assessments (Smith et al., 2017). At the start of each interview, respondents received a written informed consent document, were read a confidentiality statement, and gave oral consent to take part in the interview. Ethical approval for the HRS was granted from the University of Michigan Institutional Review Board and the study has been conducted according to the principles of the Declaration of Helsinki.

For the current study, data from respondents of the assessments administered in 2008, 2010, and 2012 were analyzed (HRS, 2014b, 2017a, 2017b). Missing CA and ATE values in the 2010 wave were replaced with data from the 2006 wave (HRS, 2014a). All participants from the original sample who had completed all ATE-related measures and were at least 50 years old at the time of their assessment were included in the analyses. A total of 15,717 participants met these inclusion criteria: In the final analytic sample, 40.1% of all participants were from the 2008 assessment, 46.1% were from the 2010 wave, and 13.4% were from 2012.

Measures

Childhood Adversity

Childhood adversity was evaluated using four items from a list of lifetime potentially traumatic events (Krause et al., 2004). Participants indicated whether they had ever experienced any of four adverse events before the age of 18 years. These incidences included: repeating a year of school, having had trouble with the police (added in 2008), parental alcohol or drug use that caused family problems, and physical abuse by a parent (Clarke et al., 2008; Smith et al., 2017). We examined the reliability of this measure by assessing the 4-year test–retest reliability of these items in more than 10,000 participants. We found high agreement in scoring on these items, which ranged from 92.4% and 96.0%. The cumulative index was created by summing different childhood exposures. We combined three to four types of CA into one category to have a group that was sufficiently large (i.e., 1.9% of the total sample).

Adulthood Trauma Exposure

Adulthood traumatic experiences were assessed using seven items from a list of lifetime potentially traumatic events (Krause et al., 2004). Respondents reported whether they had experienced each of seven events at any point during their life. If participants experienced an incident, they were asked to indicate the year the most recent exposure occurred. We excluded events that were reported to have occurred before 18 years of age from the ATE scores. The potentially traumatic events included: having lost a child; having experienced a major fire, flood, earthquake, or natural disaster; having fired a weapon in combat or been fired upon in combat; having had a spouse, partner, or child addicted to drugs or alcohol; having been the victim of a serious physical attack or assault; having had a life-threatening illness or accident; and having had a spouse or child who experienced a life-threatening illness or accident (Clarke et al., 2008; Smith et al., 2017). A cumulative ATE index was created by summing the different adulthood exposure types.

Covariates

All covariates were derived from the RAND HRS Detailed Imputations File 2014 (Version 2; RAND, 2018). These files were developed at RAND with funding from the National Institute on Aging and the Social Security Administration. We extracted the following variables from the RAND HRS data: age (i.e., year of trauma exposure assessment minus year of birth) and gender (i.e., participants self-identified as men or women). As in previous studies of HRS participants with regard to CA and ATEs (Puterman et al., 2016), race/ethnicity (Caucasian [non-Hispanic], African American [non-Hispanic], Hispanic, other [non-Hispanic]) and childhood socioeconomic status (SES) were included as covariates. Childhood SES was

Table 1
Study Characteristics, by Gender

	Total	
	n[a]	%[b]
Gender		
Women	9,164	58.3
Men	6,553	41.7
Race/ethnicity		
Caucasian	11,159	71.1
African American	2,478	15.8
Hispanic	1,628	10.4
Other	433	2.8
Missing	19	–
Parental educational attainment (years)		
< 8	1,950	13.3
≥ 8	12,742	86.7
Missing	1,025	–

Note. [a]Number of observations.
[b]Percentages are based on observed cases without missing data.

measured using information on parental educational attainment, defined as fulfilling at least 8 years of school. Parental educational attainment for both parents was queried; the higher score was used for parental education if data from both parents, and the single available value was used if only one parent responded to the item.

Data Analysis

Demographic characteristics, study descriptive information, and prevalence rates of CA and ATEs, by gender, are provided in Tables 1 and 2. Several different sets of cross-sectional analyses were conducted: Poisson regressions for the cumulative ATE index and logistic regressions for specific ATEs as outcomes. Adjusted relative risk ratios (a*RRR*s) are reported for Poisson regressions, and adjusted odds ratios (a*OR*s) are reported for logistic regressions, with respective 95% confidence intervals (CIs). Adulthood trauma exposure scores (i.e., count of trauma types) markedly decreased from reporting zero ATEs to seven ATEs, and the mean and standard deviation of cumulative ATEs was very similar ($M = 1.199$, $SD = 1.202$), suggesting the data were not overdispersed and met the assumption for Poisson models. First, we examined whether cumulative CA was associated with cumulative and specific ATEs, controlling for age, gender, race/ethnicity, and parental educational attainment (see Table 3). Each row in Table 3 indicates a distinct multivariate regression model. Second, we examined whether specific types of CA were associated with cumulative and specific ATEs, controlling for age, gender, race/ethnicity, and parental educational attainment (see Table 4); in these models, the effects of specific types of CA were independent (i.e., mutually adjusted) of each other. Third, all models were recalculated including an interaction term for CA and gender. If the findings indicated significant interactions, the models were rerun stratified by gender, and these findings were subsequently reported. Tables and plots for all other findings resulting from gender-stratified analyses are available in the Supplementary Materials. All statistical analyses were conducted in R through RStudio (Version 3.5.2; 2018). The plots were created using the R-packages "sjPlot" (Lüdecke, 2018) and "ggplot2" (Wickham, 2016). The proportions of missing items regarding descriptive information and CAs are reported in Table 1. As the proportion of missingness was small (i.e., 7%) and the missingness was largely unrelated to study demographics, we decided to do complete case analyses. The p values for all models are indicated at the levels of $< .05$, $< .01$, and $< .001$. However, as large sample sizes may cause very small effects to be highly significant, we have focused our interpretation of the data on the largest effect sizes of our findings (i.e., a*RRR*s and a*OR*s). We did not adjust p values for multiple testing; therefore, all analyses were descriptive and exploratory in nature.

Results

Descriptive Statistics

In total,15,717 participants were included in the present analyses. The mean participant age was 67.57 years ($SD = 10.55$, range: 50–101 years). Table 1 presents the distributions of gender, race/ethnicity, and parental educational attainment. Regarding CA, 29.3% of participants were exposed to one of the four potentially traumatic childhood events listed; for ATEs, 61.1% were exposed to one of the seven events. Men were more likely to experience cumulative CA than women; however, there were no gender differences in cumulative ATEs on the descriptive level (see Table 2). When focusing on specific types of CA, women were less likely to repeat a year of school or have had trouble with the police than men, and they were slightly more likely to have been physically abused. With regard to gender differences for specific ATEs, women were more likely than men to have lost a child and less likely to have experienced a major disaster. Compared to men, women were much less likely to report experiencing combat-related trauma; much more likely to report a substance-addicted spouse, partner, or child; slightly more likely to have been physically attacked; less likely to report an illness or accident; and more likely to report a family member's illness or accident (see Table 2).

Associations Between Childhood Adversity and Adulthood Trauma Exposure

Cumulative CA and ATEs

Overall, cumulative CA was associated with cumulative ATEs (see Table 3). Compared to experiencing no CA, experiencing one type of CA was related to a higher relative risk of cumulative ATEs, a$RRR = 1.28$, 95% CI [1.23, 1.32]. The addition of more types of CAs further heightened the risk for

Table 2
Childhood Adversity (CA) and Adulthood Traumatic Experiences (ATEs), by Gender

	Total		Gender							
			Women		Men					
Cumulative CA	n[a]	%[b]	n[a]	%[b]	n[a]	%[b]	Statistical test	Cramer's V	ϕ	p
0	10,350	66.5	6,422	70.7	3,928	60.5				
1	3,849	24.7	2,054	22.6	1,795	27.7				
2	1,080	6.9	506	5.6	574	8.8				
3–4	297	1.9	102	1.1	195	3.0	$\chi^2(3, N = 15{,}576) = 226.75$	.12		$< .001$
Missing	141	0.9								
Cumulative ATEs										
0	5,926	37.7	3,489	38.1	2,437	37.2				
1	4,806	30.6	2,815	30.7	1991	30.4				
2	2,954	18.8	1,726	18.8	1,228	18.7				
3	1,383	8.8	779	8.5	604	9.2				
≥ 4	648	4.1	355	3.9	293	4.5	$\chi^2(4, N = 15{,}717) = 6.49$	.02		.166
Specific types of CA										
Repeat school year	2,460	15.7	1,055	11.6	1,405	21.5	$\chi^2(1, N = 15{,}664) = 285.41$		$-.14$	$< .001$
Missing	53	0.3								
Trouble with police	874	5.6	142	1.6	732	11.2	$\chi^2(1, N = 15{,}642) = 671.26$		$-.21$	$< .001$
Missing	75	0.5								
Parental substance abuse	2,551	16.3	1,508	16.5	1,043	15.0	$\chi^2(1, N = 15{,}650) = 0.77$		.01	.382
Missing	67	0.4								
Parental physical abuse	1,101	7.0	702	7.7	399	6.1	$\chi^2(1, N = 15{,}649) = 14.1$		.03	$< .001$
Missing	68	0.4								
Specific ATEs										
Child died	2,461	15.7	1,577	17.2	884	13.5	$\chi^2(1, N = 15{,}717) = 39.73$		.05	$< .001$
Major disaster	2,544	16.2	1,412	15.4	1,132	17.3	$\chi^2(1, N = 15{,}717) = 9.67$		.02	.002
Military combat	838	5.3	28	0.3	810	12.4	$\chi^2(1, N = 15{,}717) = 1{,}097.70$		.26	$< .001$
Family member with substance addiction	2,828	17.0	1,963	21.4	865	13.2	$\chi^2(1, N = 15{,}717) = 174.43$		.11	$< .001$
Physical attack	948	6.0	586	6.4	362	5.5	$\chi^2(1, N = 15{,}717) = 4.96$		.02	.026
Illness/accident	3,874	24.7	1,958	21.4	1,916	29.2	$\chi^2(1, N = 15{,}717) = 127.07$		.09	$< .001$
Family member illness/accident	4,163	26.5	2,609	28.5	1,554	23.7	$\chi^2(1, N = 15{,}717) = 44.14$		.05	$< .001$

Note. [a]Number of observations.
[b]Percentages for "missing" information is based on all cases; percentages for exposure items are based on observed cases only.

Table 3
Associations Between Cumulative CA and Adulthood Traumatic Experiences (ATEs)

	1 type of CA			2 types of CA			3–4 types of CA		
Type of ATE	a*RRR*	a*OR*	95% CI	a*RRR*	a*OR*	95% CI	a*RRR*	a*OR*	95% CI
Cumulative ATEs	1.28***		[1.23, 1.32]	1.63***		[1.54, 1.72]	1.97***		[1.80, 2.15]
Death of child		1.21***	[1.09, 1.35]		1.63***	[1.36, 1.94]		1.89***	[1.36, 2.59]
Disaster		1.30***	[1.17, 1.44]		1.55***	[1.31, 1.82]		1.53**	[1.13, 2.03]
Military combat		1.05	[0.87, 1.26]		1.55**	[1.18, 2.02]		2.13***	[1.39, 3.17]
Family member substance addiction		1.74***	[1.58, 1.92]		2.71***	[2.33, 3.15]		4.00***	[3.08, 5.17]
Illness/accident		2.07***	[1.76, 2.43]		3.94***	[3.19, 4.84]		5.66***	[4.09, 7.72]
Family member illness/accident		1.27***	[1.17, 1.39]		1.53***	[1.32, 1.77]		1.86***	[1.43, 2.41]

Note. $N = 14{,}552$. Analyses controlled for age, gender, race/ethnicity, and parental educational attainment. a*RRR* = adjusted relative risk ratio (from Poisson regressions); a*OR* = adjusted odds ratio (from logistic regressions).
** $p < .01$. *** $p < .001$.

reporting more cumulative ATEs: a*RRR* = 1.63, 95% CI [1.54, 1.72] for two types of CA and a*RRR* = 1.97, 95% CI [1.80, 2.15] for three or four types of CA. Similar patterns were observed when examining specific ATEs, with participants who experienced more adverse events during childhood having higher odds of reporting subsequent specific ATEs (see Table 3). The largest effects were seen in the associations between cumulative CA (i.e., three or four types of CA) and a substance-addicted family member, a*OR* = 4.00, 95% CI [3.08, 5.17], and experiencing a physical attack, a*OR* = 5.66, 95% CI [4.09, 7.72].

Specific Types of CA and ATEs

Assessing different types of CAs showed each event to be associated with cumulative ATEs independently (i.e., mutually adjusted; see Table 4). Physical abuse had the strongest association with cumulative ATEs, a*RRR* = 1.49, 95% CI [1.42, 1.57], followed by parental drug or alcohol problems, a*RRR* = 1.28, 95% CI [1.23, 1.33]; trouble with the police, a *RRR* = 1.25, 95% CI [1.18, 1.34]; and repeating a year of school, a*RRR* = 1.08, 95% CI [1.04, 1.13], after adjusting for age, gender, race/ethnicity, and parental educational attainment. Specific types of CA had distinct associations with specific ATEs; the association patterns can be seen in Table 4 and Figure 1, 2. The largest effects were found in the association between physical abuse in childhood and adulthood physical attacks, a*OR* = 3.41, 95% CI [2.82, 4.12], and the association between parental substance abuse during childhood and a substance-addicted spouse, partner, or child later in life, a*OR* = 1.80, 95% CI [1.55, 2.08].

Gender-Moderated Association Between CA and ATEs

To investigate gender-moderations, we added an interaction term of Gender x Cumulative CA into the previously described models; if this interaction term was significant (i.e., $p < .05$), we report herein on these specific findings from subsequent gender-stratification. Overall, we found higher adjusted relative risk ratios in women for the association between cumulative CA and cumulative ATEs: one type of CA, a*RRR* = 1.30, 95% CI [1.24, 1.36]; two types of CA, a*RRR* = 1.69 95% CI [1.56, 1.82]; three or four types of CA, a*RRR* = 2.10 95% CI [1.81, 2.42], compared to men: one types of CA, a*RRR* = 1.24 95% CI [1.17, 1.31]; two types of CA, a*RRR* = 1.57 95% CI [1.45, 1.70]; three or four types of CA, a*RRR* = 1.92 95% CI [1.71, 2.15]. Physical abuse was strongly associated with adulthood physical attacks overall, but the association was stronger in women compared to men, a*OR* = 3.91, 95% CI [3.10; 4.91] for women and a*OR* = 2.60, 95% CI [1.64; 3.08] for men. All models with Gender x CA interactions as well as the models from the gender-stratified analyses are reported in the Supplementary Materials (Supplementary Tables S5–S8, Supplementary Figures S1–S4). Most models that were used to investigate the association between CA and ATEs, however, were not moderated by gender (see Supplementary Materials).

Table 4
Associations Between Specific Types of Childhood Adversity (CA) and Adulthood Traumatic Experiences (ATEs)

	CA type											
	Repeat of school year			Trouble with police			Parental substance abuse			Parental physical abuse		
Type of ATE	a*RRR*	a*OR*	95% CI	a*RRR*	a*OR*	95% CI	a*RRR*	a*OR*	95% CI	a*RRR*	a*OR*	95% CI
Cumulative ATEs	1.08***		[1.04, 1.13]	1.25***		[1.18, 1.34]	1.28***		[1.23, 1.33]	1.49***		[1.42, 1.57]
Death of child		1.32***	[1.16, 1.49]		1.18	[0.94, 1.46]		1.15*	[1.01, 1.31]		1.36***	[1.13, 1.62]
Disaster		1.11	[0.99, 1.26]		1.21*	[1.00, 1.45]		1.18**	[1.05, 1.33]		1.47***	[1.25, 1.72]
Military combat		1.18	[0.98, 1.42]		1.28	[0.98, 1.64]		1.17	[0.94, 1.45]		1.36	[0.99, 1.84]
Family member substance addiction		1.10	[0.98, 1.25]		1.72***			1.97***	[1.77, 2.19]		1.80***	[1.55, 2.08]
Physical attack		1.25*	[1.04, 1.49]		1.92***	[1.51, 2.43]		1.54***	[1.30, 1.82]		3.41***	[2.82, 4.12]
Illness/accident		1.12*	[1.00, 1.24]		1.27**	[1.08, 1.49]		1.37***	[1.24, 1.52]		1.70***	[1.48, 1.96]
Family member illness/accident		0.94	[0.84, 1.05]		1.27**	[1.07, 1.50]		1.28***	[1.15, 1.41]		1.65***	[1.43, 1.90]

Note. $N = 14{,}552$ observations. Analyses controlled for age, gender, race/ethnicity, and parental educational attainment. a*RRR* = adjusted relative risk ratio (from Poisson regressions); a*OR* = adjusted odds ratio (from logistic regressions).
*$p < .05$. **$p < .01$. ***$p < .001$.

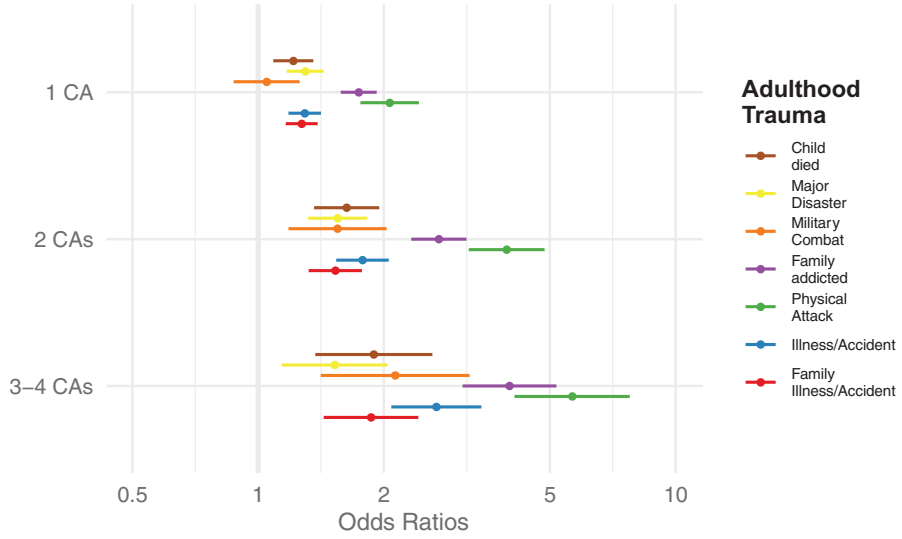
Discussion

In this cross-sectional large-scale study of over 15,000 older adults, we found that more cumulative childhood adversity was associated with more cumulative adulthood trauma exposure across the life course. Exposure to three or more of the four categories of CA almost doubled an individual's risk for experiencing an additional ATE compared to no CA exposure. We also observed that the association between cumulative CA and ATEs varied depending on the specific ATE assessed. The largest associations between CA and specific ATEs were observed for having a substance-addicted spouse or child and experiencing adulthood physical attack. Moreover, physical abuse in childhood was the strongest independent contributor to cumulative ATEs (mutually adjusted for other CA items) as well as for the specific ATE of a physical attack. Finally, these associations of cumulative CA and cumulative ATEs were moderated by gender, with CA more strongly associated with ATEs in women compared to men. With regard to specific stressors, cumulative childhood adversity was more strongly associated with physical attacks in women compared to men. However, most of the specific associations between CA and ATEs were not moderated by gender. These results emphasize the important role that CA may play in determining the pattern of life-course trauma exposure and highlight that associations between CA and ATEs are generally similar in men and women, with some important exceptions.

Our findings add to the current literature of large-scale and population-based studies that have found associations between early adversity and adulthood stressors and perceived distress, suggesting that CA might lead to circumstances that heighten the risk for later stressor exposure (Manyema et al., 2018; Nurius et al., 2015). Moreover, adult stressor exposure might then moderate or mediate the direct association between CA and psychological distress in young adulthood (Manyema et al., 2018) and in this way may lead to long-term adverse outcomes. Given that stressors in adulthood increase the risk for mental health problems, such as depression and suicide (Fowler et al., 2013; Jeon et al., 2014; Panagioti et al., 2009), as well as physical ill-health (e.g., poor health behaviors, inflammation, and telomere length; Lee & Park, 2018; Lin et al., 2016; Puterman et al., 2016), these findings are particularly important to disentangle.

We found parental physical abuse and parental substance abuse to be strongly associated with ATEs, particularly with regard to being physically attacked in adulthood and having a substance-abusing child or partner in later life. Previous findings have shown that adversities often co-occur and cluster in families and that these clusters of maladaptive family functioning are strongly related to the onset of mental disorders (Green et al., 2010; Kessler et al., 2010). A cohort study of over 80,000 Danish children born in 1966 showed that parental alcohol abuse was associated with multiple adverse outcomes, such as increased mortality, self-destructive behaviors, hospitalization due to violence, higher rates of teenage pregnancy,

Figure 1
Associations Between Cumulative Childhood Adversity and Specific Types of Adulthood Traumatic Experiences



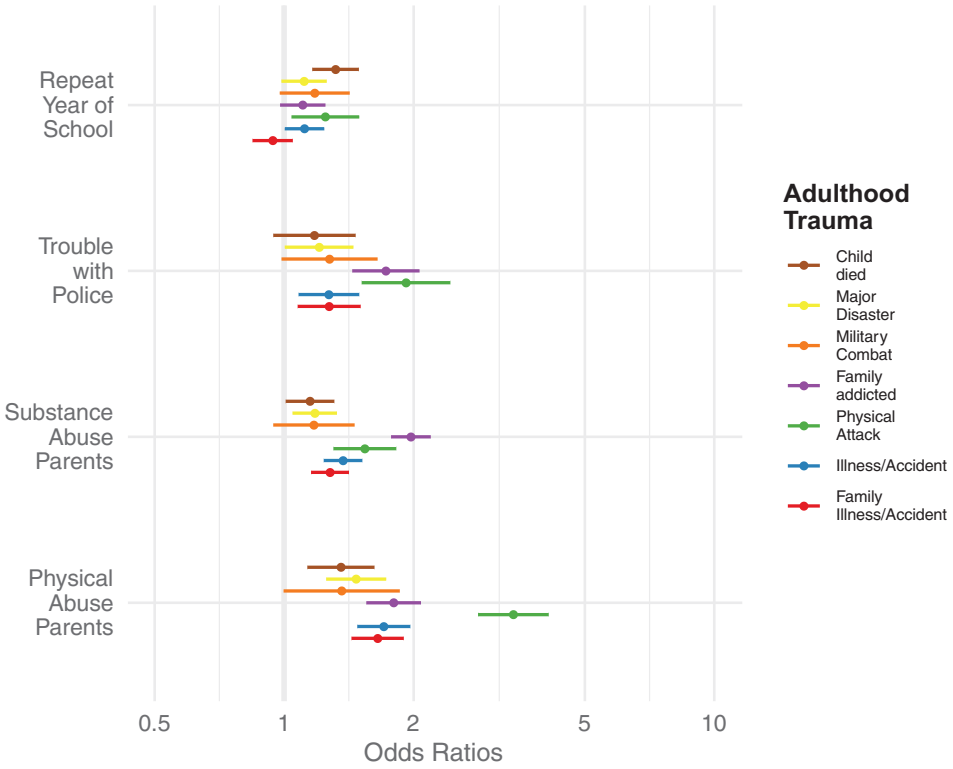
Note. All analyses controlled for age, gender, race/ethnicity, and parental education. Error bars indicate 95% confidence intervals of the corresponding odds ratios.

and unemployment (Christoffersen & Soothill, 2003). In fact, just under 50% of the participants in our analysis who reported physical abuse also reported parental substance abuse. The high rates of co-occurrence make it unsurprising that these types of CA were the two most strongly associated contributors to adulthood trauma exposure.

Our findings regarding gender differences in exposure to our subset of types of CA and ATEs support previous population-based studies that have reported that women have a lower cumulative incidence of potentially traumatic exposures than men (Breslau, 2002; Breslau et al., 1998; Hatch & Dohrenwend, 2007; Tolin & Foa, 2008). However, it is important to note that these overall differences are small compared to the differences in exposure between women and men for specific categories of traumatic experiences (Hatch & Dohrenwend, 2007; Tolin & Foa, 2008). Women in our study were much less likely than men to repeat a year of school or to have had trouble with the police, and they were slightly more likely to be physically abused. Beyond differences between genders with regard to CA and ATE exposure, we found that gender significantly moderated the association between cumulative CA and ATEs. Overall, our findings show that CA is related to ATEs for both men and women. However, the risk for women was slightly higher overall compared to men, particularly the risk of adulthood physical attacks for women who were physically abused in childhood.

From a theoretical point of view, our data are in line with both the early embedding and life-course stress theories. First, our data support life-course stress theories that state that inequality cumulates across a life course (Ferraro & Shippee, 2009; Ferraro et al., 2009; Pearlin et al., 2005; Schafer et al., 2011). In particular, our data indicate that individuals who experience CA are more likely to experience later trauma exposure. These associations in our sample extended even into old age. Unsurprisingly, the largest effects were found for the two types of CA that originated in the family, were interpersonal in nature, and often co-occurred (i.e., physical abuse and parental substance abuse). The effects observed for these exposures are consistent with the concept of revictimization, which states and supports the idea that early abuse and neglect are closely related to later revictimization (Widom et al., 2008). In particular, types of CA that are relatively more traumatic in nature, such as physical abuse, might influence social information processing (e.g., enhanced threat detection and hostile attribution biases), emotion processing (e.g., heightened reactivity with poor regulation), and accelerated aging (e.g., early pubertal timing and later cellular aging), which might, in turn, predict psychopathology (McLaughlin et al., 2020) and increase the risk for later exposure. In this sense, the adaption to unsafe and hostile environments, such as growing up with parental substance abuse, might cause social, emotional, and neurocognitive alterations that confer vulnerability (McCrory et al., 2017; McCrory & Viding, 2015). It is also possible that the effects of deprivation, neglect, and interpersonal adversities might occur by impairing attachment security (Fox et al., 2017; McLaughlin, 2016). Other sociological explanations might include lower SES, neighborhood stress, discrimination, and education, which might moderate and mediate the association between early and later exposure. Thus, there are diverse mechanisms by which CA may increase the risk of ATEs. Our findings add to the growing

Figure 2
Associations Between Specific Types of Childhood Adversity and Specific Types of Adulthood Trauma Exposure



Note. All analyses controlled for age, gender, race/ethnicity, and parental education. Error bars indicate 95% confidence intervals of the corresponding odds ratios.

research that is uncovering important domains that can be leveraged in preventive strategies and interventions to target these specific mechanisms of interest (McLaughlin et al., 2019).

Our findings should be interpreted in light of several important limitations. First, differences in the prevalence rates of stressors, particularly those that occur in childhood, are common in the literature due to the use of different measures (Miller et al., 2011; Moffitt & Klaus-Grawe Think, 2013). The current study used a narrow measure of CA and ATEs, with only four items to assess CA and seven to assess ATEs. This measure lacked many important other exposure types, such as sexual abuse and neglect/deprivation. Future research might benefit from advanced methods of measuring childhood adversity that include more specific characteristics of these experiences, such as the timing, duration, and severity of the exposure (Crosswell & Lockwood, 2020; Slavich & Shields, 2018; Teicher & Parigger, 2015). Second, the present analyses were only cross-sectional, and the measures of trauma exposure were retrospective, with multiple decades between exposure and recall, which can lead to recall biases (Hardt & Rutter, 2004). A recent meta-analysis reported only a small overlap between prospective and retrospective assessments of adversity, which raises questions regarding the validity of retrospective assessments (Baldwin et al., 2019); however, the authors found a higher agreement for clear-cut forms of adversity. The potentially traumatic events analyzed in the present study had a high agreement over time as they mostly referred to distinct events; this was demonstrated by the high test–retest agreement we found for the four types of CA included in our measure. Third, sampling weights were not implemented; therefore, the findings are not true population-based estimates. Finally, studies that investigate older populations might find biased estimates due to methodological artifacts as selection effects (e.g., selective mortality and survivor effects) inherent to older populations, which might lead to underestimated trauma incidence among the oldest participants (Arrighi & Hertz-Picciotto, 1994; Bürgin et al., 2020; Heiss, 2011; Picciotto & Hertz-Picciotto, 2015; Zajacova & Burgard, 2013). Furthermore, varying prevalence rates for different traumatic exposures across certain age ranges in old age might be observed due to age, period, or cohort effects (Bürgin et al., 2020; Creamer & Parslow, 2008; Krause et al., 2004).

Our data indicate that CA and ATEs may be inextricably linked. Studies that consider the life-course effects of CA may

need to consider ATEs as a potential contributor to any findings, and studies that consider the effects of ATEs need to consider that individuals who report more ATEs are likely to have experienced a larger burden of CA. In addition, a shared and clearer nosology and taxonomy of stressors in general, and of associations between CA and ATEs in particular, would lay the conceptual groundwork for future investigations (Epel et al., 2018; McLaughlin, 2016). Further, recent studies have analyzed life-course stressors using person-oriented approaches (e.g., latent class/profile/trajectory models; (Hajat, et al., 2020); these approaches or a combination of person- and item-oriented models might help disentangle exposure trajectories. Of further interest for future research are factors that moderate and mediate associations between CA and ATEs, such as adult SES, substance abuse, and attachment style. Another interesting topic that needs further investigation is the clustering of stressors and traumatic experiences within households and in couple dyads; such analyses are possible using HRS data (Crosswell et al., 2018) but were beyond the scope of the present study. Further, given the older age of the HRS population and the history of the military draft in the United States, future research might investigate differences in the relation between CA and military combat exposure in pre- versus postdraft cohorts. As CA was related to ATEs, our data provide additional evidence that early prevention and intervention should be a major priority for public health. In particular, cumulative CA, physical abuse, substance abuse by parents were strongly related to later ATEs. As stressful childhood experiences often cluster within families (Green et al., 2010; Kessler et al., 2010), programs aimed at improving family functioning and preventing parental substance abuse and physical abuse may be particularly beneficial.

The current study adds to existing evidence of the associations between CA and ATEs, extends these findings into older age, and suggests differences in the associations between specific types of exposure. Both men and women who have experienced multiple types of CA were shown to have increased odds for later ATEs; however, the effects were stronger for women. As CA is unequally distributed in the population and highly intertwined with later adversities, targeting the impact of CA at its roots is warranted. Safe childhoods confer lifelong benefits.

Open Practices Statement

For this study, we analyzed archival data from the larger HRS requests to access the data should be directed to the relevant archive. All datasets analyzed in this study are openly available and referenced within the manuscript. Data is accessible online after registration at https://hrspubs.sites.uofmhosting.net. Requests for the complete analysis scripts and code can be sent via email to the lead author at david.buergin@upk.ch .

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Chapter 4: Fact or artefact? Childhood adversity and adulthood trauma in the U.S. population-based Health and Retirement Study

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Fact or artefact? Childhood adversity and adulthood trauma in the U.S. population-based Health and Retirement Study

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ABSTRACT

Background: Despite the well-known deleterious health effects of childhood adversity (CA) and adulthood trauma (AT) and ageing of the global population, little is known about self-reported CA and AT in older populations. Existing findings are mixed due to methodological and sampling artefacts, in particular, recall and selection biases, and due to age-period-cohort effects.

Objectives: We aim to first, provide data on the prevalence of retrospective self-reported CA and AT in a large population-based sample of older adults and, second, to discuss the data in the context of major methodological and sampling artefacts, and age-period-cohort effects.

Method: Data are derived from the U.S. population-based Health and Retirement Study (N = 19,547, mean age = 67.24 ± 11.33, 59% female). Seven birth-cohorts were included (<1924, 1924–1930, 1931–1941, 1942–1947, 1948–1953, 1954–1959, >1959).

Results: Overall, 35% of participants reported CA and 62% AT, with strong variability among birth-cohorts. Opposing trends were observed regarding prevalence of CA and AT. As age of cohorts increased, prevalence of CAs decreased while that of ATs increased. Investigating the distributions of incidence of specific ATs across age and period per cohort revealed incidence of exposure was associated with (1) age (e.g. having lost a child), (2) time-period (e.g. major disaster), and (3) cohort (e.g. military combat).

Conclusions: Retrospective self-reported CA and AT in older samples should be interpreted with caution and with regard to major methodological challenges, including recall and selection biases. Untangling fact from artefact and examining age, period, and cohort effects will help elucidate profiles of lifetime exposures in older populations.

¿Realidad o artefacto? Adversidad en la infancia y trauma en la adultez en Estudio de Población de Salud y Jubilación en EE.UU

Antecedentes: A pesar de los ampliamente conocidos efectos nocivos de la adversidad en la infancia (AI) y el trauma en la adultez (TA) y el envejecimiento de la población global, se sabe poco respecto a AI y TA auto-reportados en poblaciones mayores. Los hallazgos existentes son heterogéneos debido a artefactos metodológicos y de muestreo, en particular sesgos de memoria y de selección, y debido a efectos de la edad, período y cohorte.

Objetivos: Apuntamos primero a entregar información sobre la prevalencia de AI y TA retrospectivos auto-reportados en una amplia muestra poblacional de adultos mayores y, segundo, discutir los datos en el contexto de los mayores artefactos metodológicos y de muestreo, y de los efectos de la edad, período y cohorte.

Método: Los datos provienen del Estudio de Población de Salud y Jubilación en EE.UU. (N=19,547, edad promedio = 67.24±11.33, 59% mujeres). Fueron incluidas siete cohortes de nacimiento (<1924, 1924-1930, 1931-1941, 1942-1947, 1948-1953, 1954-1959, >1959).

Resultados: En términos generales, 35% de los participantes reportó AI y un 62% TA, con una marcada variabilidad entre las cohortes. Se observaron tendencias opuestas en relación a la prevalencia de AI y TA. A medida que la edad de las cohortes aumentó, la prevalencia de AI disminuyó, mientras que la de TA aumentó. Al investigar las distribuciones de incidencia de AI específicos según edad y período por cohorte se reveló que la incidencia de exposición se asoció con (1) la edad (por ej. Perder un hijo), (2) período de tiempo (por ej. desastre grave), y (3) la cohorte (por ej. combate militar).

Conclusiones: AI y TA retrospectivos auto-reportados en muestras de adultos mayores deberían ser interpretados con precaución y en consideración de importantes dificultades metodológicas, incluyendo sesgo de memoria y de selección. Distinguir entre hecho y artefacto y examinar los efectos de edad, período y cohorte ayudará a elucidar los perfiles de exposición a lo largo de la vida en poblaciones mayores.

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Childhood adversity; trauma; prevalence; incidence; cohort effects; age-period-cohort; old age; elderly; population-based

PALABRAS CLAVES
Adversidad en la Infancia; Trauma; prevalencia; poblacional; edad-periodo-cohorte; edad mayor; ancianos

关键词
童年期逆境; 创伤; 流行率; 基于人群; 年龄-时期-队列; 老龄; 老年人

HIGHLIGHTS

- Childhood adversity were reported by 35% and adulthood trauma by 62% of participants in a large U.S. population-based study of older adults
- Distinct effects of age and generation on reports of stress exposure appear to cause both over- and underestimation of exposure.

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事实还是伪象？美国人群健康与退休研究中的童年期逆境和成年期创伤

背景：尽管童年期逆境 (CA) 和成年期创伤 (AT) 对健康的有害影响以及全球人口老龄化众所周知，但对于老年人群自评CA和AT知之甚少。由于方法学和抽样误差，特别是回忆和选择偏差，以及年龄-时期-队列的影响，现有结果混杂。
目标：我们首先旨在提供大量老年人群样本回溯性自评CA和AT流行率的数据，其次，在主要方法学和抽样误差以及年龄-时期-队列效应的背景下讨论数据。
方法：数据来自美国人群的健康与退休研究 (样本量N = 19,547, 平均年龄= 67.24±11.33, 女性占59%)。入组七个出生队列 (<1924, 1924-1930, 1931-1941, 1942-1947, 1948-1953, 1954-1959, > 1959)。
结果：总体而言，参与者中35%报告了CA, 62%报告了AT, 在出生队列之间有巨大差异。观察到关于CA和AT流行率的相反趋势。随着队列年龄增加，CA流行率下降而AT流行率上升。每个群体进行跨年龄，跨时期针对特定AT发生率分布的考查，发现暴露的发生率与 (1) 年龄 (例如丧子), (2) 时间段 (例如重大灾难) 和 (3) 队列 (例如军事战争) 相关。
结论：在老年样本中，回溯性自评CA和AT应谨慎解释，并应考虑主要的方法学挑战，包括回忆和选择偏差。从表象中厘清事实并考查年龄，时期和队列的影响，将有助于阐明老年人群终身暴露情况。

1. Introduction

Childhood adversity (CA) and adulthood trauma (AT) are common in the general population and are known to have deleterious effects on health across the lifespan and into late life (Anda et al., 2006; Dube et al., 2001; Dube, Felitti, Dong, Giles, & Anda, 2003; Felitti et al., 1998; Glaesmer, Brähler, Gündel, & Riedel-Heller, 2011; Green et al., 2010; Kessler et al., 2009; Kessler, Alonso, Benjet, Bromet, & Cardoso et al., 2017). Due to major demographic shifts in the last century, the ratio of people over, compared to under, age 65 increased dramatically, especially in western societies (Bongaarts, 2009). Despite the widely reported serious negative health impact of CA and AT and the ageing of the world's population, little is known about prevalence and incidence of self-reported CA and AT in older populations. Moreover, methodological challenges in the measurement of CA and AT may have led to inconsistent findings across the studies that have examined this issue. Therefore, the aim of the current study is to present data on the prevalence of CA and AT from a large, population-based study of older adults from the US, and to discuss them in the context of methodological artefacts that may influence the data.

Population-based studies of CA and AT show varying prevalence and incidence rates due to differences in conceptualization and assessment of these experiences. The prevalence of CA has been found to be high, with 40-70% of children and adolescents being exposed to some kind of adversity, and multiple adversities are more common than singular (Copeland, Keeler, Angold, & Costello, 2007; Green et al., 2010; Hussey, Chang, & Kotch, 2006; Kessler et al., 2010). The prevalence of lifetime trauma is also high with 60-90% of the general population being exposed to traumatic experiences, of which about a third experience four or more events (Benjet et al., 2016; Kilpatrick et al., 2013; Norris, 1992; Ogle, Rubin, Berntsen, & Siegler, 2013). CA and AT have been found to increase risk for a broad range of psychiatric disorders across the life-course (Carr, Martins, Stingel, Lemgruber, & Juruena, 2013; Green et al., 2010; Kessler et al., 2010; McLaughlin, Conron, Koenen, & Gilman, 2010). Moreover, CA and AT increase risk for major medical illnesses and premature mortality (Brown et al., 2009; Clemens et al., 2018; Dube et al., 2003; Felitti et al., 1998; Glaesmer et al., 2011; O'Donovan et al., 2015; Riedl et al., 2019). Thus, CA and AT are highly prevalent risk factors for ill health.

In contrast with the reasonable assumption that people accumulate more traumatic experiences as they age, a review of more than 30 studies found a trend across samples of decreasing self-reported traumatic life events and stressful life events with age (Hatch & Dohrenwend, 2007). Population-based data from 68,894 participants assessed in 24 countries in the World Mental Health Survey indicated that younger cohorts (age<65) had lower odds of self-reported exposure to collective violence, but higher odds for self-reported exposure to interpersonal violence, sexual violence, accident/injuries, unexpected death of a loved one, or being mugged (Benjet et al., 2016). However, other studies support this assumption and have found increasing lifetime prevalence rates with age. Data from 10,641 participants in the Australian National Survey of Mental Health showed a linear increase of self-reported trauma exposure with age only in the men and an inverted U-shaped distribution in women due to combat-related exposures in men only (Creamer & Parslow, 2008). A population-based study of 2,510 participants in Germany also found older cohorts (both males and females) to have greater exposure to self-reported trauma (Hauffa et al., 2011). Others observed varying prevalence rates across various age ranges for self-reported specific traumatic events rather than for overall trauma scores (Krause, Shaw, & Cairney, 2004). In regard to age distribution of specific events, it has been shown that some events (e.g. sexual assaults) occurred more often at younger ages, whereas other events (e.g. unexpected death of a loved one) were more frequent after the transition to adulthood (Ogle

et al., 2013; Ogle, Rubin, & Siegler, 2013). Taken together, these studies suggest high but varying prevalence of CA and AT across samples. Contrasting data exists to support either increasing or decreasing prevalence rates with age, depending on the specific events assessed, characteristics of the sample, and the location.

While major differences in prevalence of CA and AT may be due to differences in measurement and study samples, studies also contain some specific methodological and sampling artefacts. For example, recall biases due to prolonged periods of recall or cognitive decline, and selection biases due to selective mortality and institutionalization may both lead to an underreporting of exposures (Arrighi & Hertz-Picciotto, 1994; Brown et al., 2017; Buckley, Keil, McGrath, & Edwards, 2015; Hardt & Rutter, 2004). Furthermore, cohort differences might be apparent due to effects of age, time-period, or an interaction between these effects. Age effects are variations due to changes across the life course that are internal to individuals (Keyes & Li, 2012; Yang & Land, 2013). Age-specific stages in life exist at which individuals are at highest risk for a specific incident; therefore, pure age effects should be consistent across cohorts (e.g. miscarriage, having a spouse with dementia). Period effects emerge related to changes over time in certain events or social and epidemiologic circumstances (e.g. the AIDS epidemic) (Keyes & Li, 2012; Yang & Land, 2013). Age x period interactions are period effects that vary with age-related vulnerabilities (e.g. military combat during war times occurring in young adulthood). Cohort effects are differences among individuals defined by shared temporal experiences (e.g. the baby boom generation's increase in suicide and depression risk)(Keyes & Li, 2012). In the epidemiological literature, the age-period-cohort identification problem describes the problem that relates from the perfect collinearity between these variables in some cases and therefore the difficulty of separating these effects (Bell & Jones, 2013; Yang & Land, 2013).

Despite the large prevalence of CA and AT, the well-known risk to population health caused by CA and AT, and the rapid ageing of the worlds' population, we know relatively little about the prevalence of childhood adversity and trauma in older individuals. Existing findings are mixed due to differences in assessments, methodological artefacts, and due to the collinearity of age-period-cohort effects. Therefore, the aim of the current study is to provide data on the prevalence of CA and AT from a sample of older adults in the U.S. population-based Health and Retirement Study (HRS). Further, we will examine differences in exposure by exploring the distributions of the incidence of AT across age and time-period and discuss observed findings in the context of major methodological and sampling artefacts inherent to older populations in an attempt to separate real cohort effects from methodological artefacts.

2. Methods

2.1. Participants

Participants were drawn from HRS, a U.S. population-based longitudinal study of more than 43,000 Americans over the age of 50 and their spouses (spouses can be younger than 50) (Fisher & Ryan, 2018). The original study population, the HRS cohort, was sampled in 1992 and included all adults in the USA born during the years 1931–1941 who resided in households, with a 2:1 oversample of African American and Hispanic populations and a slight oversampling of Florida state residents. The HRS sample is based on a 'multi-stage area probability design involving geographical stratification and clustering and oversampling of certain demographic groups' (Sonnega et al., 2014, p. 577). Later, a second study, called 'Asset and Health Dynamics Among the Oldest Old' (AHEAD), was conducted to capture the cohort born between 1890 and 1923. These two studies were then merged with two new cohorts the 'Children of the Depression' (CODA, 1924–30), and the 'War Babies' (1942–47) building up the total HRS sample. HRS now undertakes a steady-state design, refreshing the overall sample every 6 years with younger birth cohorts not previously represented in the sample. Early Baby Boomers (1948–53) were added in 2004, and Mid Baby Boomers (1954–59) were included in 2010 (Sonnega et al., 2014). Spouses of these cohorts, can either be part of a specific birth cohort, or might have been born after 1954 (n = 777) (Fisher & Ryan, 2018; Sonnega et al., 2014). HRS is sponsored by the National Institute on Ageing (grant number NIA U01AG009740) and is conducted by the University of Michigan. Starting in 2006, the study implemented a psychosocial questionnaire that included assessments of CA and AT (Clarke, Fisher, House, Smith, & Weir, 2008; Smith, Ryan, Sonnega, & Weir, 2017).

2.2. Procedure

After the phone-interview section of HRS took place, participants were given a leave-behind questionnaire assessing psychosocial domains (Clarke et al., 2008; Smith et al., 2017). Response rates for these questionnaires were high over the waves and varied between 73-88% (Smith et al., 2017). Prior to each interview, participants were provided with written study information, all respondents were read a confidentiality statement, and they gave their oral consent by agreeing to do the interview. Ethical approval for the HRS Study was granted from the University of Michigan Institutional Review Board, and the study has been conducted according to the principles of the Declaration of Helsinki.

For the analyses in the current paper, data were combined from the assessments of 2008 and 2010 (Health and Retirement Study, 2008 HRS Core (Final) (v.3.0)

public use dataset); Health and Retirement Study (2010) HRS Core (Final) (v.5.1) public use dataset. If participants did not take part in these waves or did not fill out the questionnaires, data from the 2006 wave (Health and Retirement Study, 2006 HRS Core (Final) (v.3.0) public use dataset) were used for missing values of the 2010 wave, and from the 2012 assessments (Health and Retirement Study, 2012 HRS Core (Final) (v.2.0) public use dataset) for missing values of the 2008 wave. We selected participants from the original sample who had completed all items for either CA or AT. A total of 19,547 participants met these inclusion criteria; 9.52% of participants were included from 2006, 35.58% from the year 2008, 41.85% from the year 2010, and 13.05% from 2012 assessments. Number of participants included from each cohort varied (n per cohort: AHEAD = 1,369; CODA = 2,171; HRS = 6,181; War-Babies = 2,570; Early-Baby-Boomers = 3,440; Mid-Baby-Boomers = 3,039; Later-Birth-Years = 777).

2.3. Measures

2.3.1. Childhood adversities

CAs were evaluated between 2006 and 2012 using all items from the measure developed by Krause et al. (2004). Respondents were presented with four potentially adverse exposures and asked whether they experienced each one before the age of 18. These exposures included: repeating a school year, having trouble with the police (item added in 2008), having parents who drank alcohol or used drugs so often that it caused problems in the family, and physical abuse by a parent (Clarke et al., 2008; Smith et al., 2017).

2.3.2. Adulthood trauma

ATs were assessed using all items from the questionnaire developed by Krause et al. (2004). Participants were presented seven potentially traumatic experiences and were asked if they experienced each one at any point in their life. Participants that were exposed were supposed to indicate the year of *most recent* incidence. Experiences that were reported before the age of 18 were excluded from the adulthood trauma scores. AT included: having lost a child; experiencing a major fire, flood, earthquake or natural disaster; firing a weapon in combat or been fired upon in combat; having a spouse, partner, or child addicted to drugs or alcohol; being a victim of a serious physical attack or assault; having or having had a life-threatening illness or accident; having a spouse or child that experienced a life-threatening illness or accident (Clarke et al., 2008; Smith et al., 2017).

2.3.3. Sociodemographic variables

All other variables were derived from the RAND HRS Detailed Imputations File 2014 (V2). These files were developed at RAND with funding from the National Institute on Ageing and the Social Security Administration. The following variables were retrieved from this file for analyses in the current paper: Age (year of trauma assessment – year of birth), gender (male/female), race/ethnicity (Caucasian [non-Hispanic], African American [non-Hispanic], Hispanic, Other [non-Hispanic]) and parental education (<8 years vs. ≥8 years of education; if data regarding the education of the father was missing, data from maternal education was used instead).

2.4. Analytic plan

Sample demographics are reported, followed by total scores for CA and AT, and an overall combined score. Prevalence rates of specific CAs and ATs are reported as percentages of total and cohort-specific participants exposed. Distributions of incidences of most recent ATs by age of participants are displayed by plotting the ratio of number of participants exposed per age divided by the total number of participants exposed to the respective AT (Figure 4). Due to the decreasing sample size among older ages, we upweighted exposures in older ages in Figure 4. Upweighting was achieved by multiplying the ratio (exposure per age/number exposed) by the invert of the proportion of the remaining sample at a specific age (e.g. if 10% of the sample reached the age of 80, each exposure at this age was upweighted by the factor 10, or if 20% of the sample reached the age of 70, each exposure at this age was upweighted by the factor 5). We plotted the distribution of the ages of incidence to ATs to the point at which 10% of the sample was left, limiting the largest adjusting weight to factor 10. Furthermore, in Figure 5 the distributions of incidences to ATs over time-period per cohort are displayed until 2006. This plot was created using the 'densityplot'- function from the lattice-package (Sarkar, Sarkar, & KernSmooth, 2018), the selected bandwidth of the kernel function was 1. The statistical software used was R (Version 3.5.2, 2018), Boston, MA, USA. Missing data was deleted listwise (R Core Team, 2013).

3. Results

3.1. Sociodemographic

In total, 19,547 participants were included in the analyses. Participants mean age was 67.24 years (SD 11.33) with an age range from 25 to 105 (96% >50 years). More than half of the participants were female (59%). Over two thirds of participants were non-Hispanic Caucasian (71%), 16% were non-Hispanic African American, 11% were Hispanic, and 3% reported 'Other' as race/ethnicity. One-fifth of the

participants reported their parents had less than 8 years of school (20%).

3.2. Childhood adversity and adulthood trauma across cohorts

Overall, 35% of the sample reported having experienced at least one CA. Looking at cohort-specific rates, we observed a difference between cohorts with the youngest cohort having the highest rate (43%) and the oldest cohort having the lowest rate (18%). Similar trends were found when investigating cumulative scores: older cohorts reported fewer CAs compared to younger cohorts (see Figure 1). The opposite trend was observed for AT. In the full sample, 62% reported exposure to at least one AT. The highest rates were found for the oldest two cohorts with almost 70% reporting an exposure, compared to slightly over 50% in the youngest cohort. The same trend was found for the cumulative ATs with more exposure in older cohorts (see Figure 1 and Table 1). Combining both CAs and ATs into an overall cumulative stressor score levelled these contrary trends, resulting in almost similar levels of overall stressor exposure across the cohorts.

3.3. Prevalence of specific childhood adversities across cohorts

Prevalence rates of CAs across cohorts differed greatly, with linear trends towards higher rates among younger cohorts for all four CAs investigated (see Figure 2 and Table 1). The largest difference between oldest and youngest cohorts was observed for substance abuse of parents, the second largest for parental physical abuse, the third largest for trouble with the police, and the smallest for repeating a year of school.

3.4. Prevalence and incidence of specific adulthood trauma

Prevalence rates of ATs differed largely among cohorts (Figure 3 and Table 1). Some exposures were found to be more prevalent in older cohorts, namely losing a child, having had an illness/accident, and having a spouse, partner or child have an illness/accident. Being exposed to a major disaster was equally prevalent in all cohorts. Military combat had a distinct pattern with the youngest cohort showing smaller prevalence rates compared to older cohorts. Having a family member with substance abuse problems was less prevalent in the oldest two cohorts and equally prevalent in the other cohorts. The prevalence for physical attack was higher in younger cohorts than in older cohorts (specific prevalence for ATs across cohorts is displayed in Figure 3).

If participants reported an AT, they were asked to indicate the exact year of the *most recent* exposure. Response rates for the exact year varied between 73-92%. The highest response rate was observed for loss of a child and the lowest for substance abusing family members (Child died: 91%, Major Disaster: 85%, Military Combat: 79%, Family addicted: 74%, Physical Attack: 78%, Illness/Accident: 87%, Family Illness/Accident: 86%). Participants that did not indicate an exact year of most recent exposure were excluded from further analyses.

Overall, the oldest two cohorts had slightly decreased response rates for the indication of the exact year compared to younger cohorts (AHEAD: 77%; CODA: 81%; HRS: 83%; War-Babies: 87%; Early-Baby-Boomers: 86%; Mid-Baby-Boomers: 84%; Later-Birth-Years: 85%). Distributions of age at incidence of most recent exposures to AT are shown in Figure 4. The distributions of AT incidences showed distinct patterns. Incidence of losing a child peaked in young adulthood, followed by a decline in mid-life and an increase towards old age. The incidence of experiencing a major disaster was equally

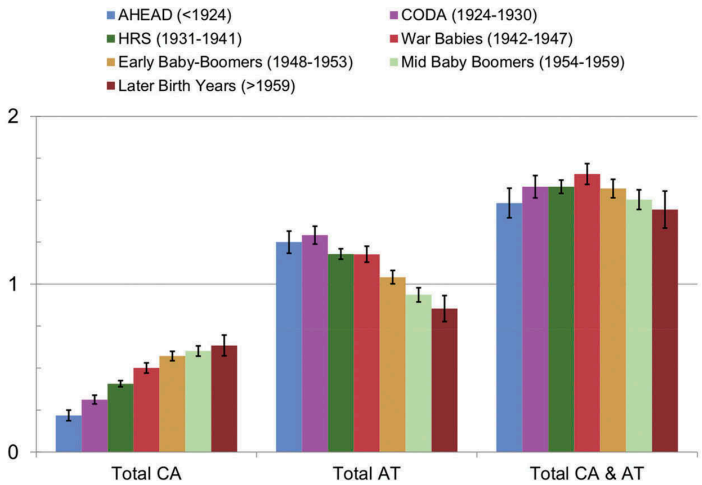

Figure 1. Means of total self-reported CA, AT and CA&AT scores by birth-cohort. Error bars indicate 95% confidence intervals.

Table 1. Prevalence of childhood adversities and adulthood trauma across birth-cohorts.

	Total sample	AHEAD Cohort <1924	CODA Cohort 1924–1930	HRS Cohort 1931–1941	War babies 1942–1947	Early baby boomers 1948–1953	Mid baby boomers 1954–1959	Later birth years >1959
Repeat year of School	15.85%	10.52%	12.99%	16.07%	15.60%	17.44%	17.41%	18.02%
Trouble with Police	6.16%	0.73%	2.07%	3.53%	5.68%	7.82%	10.76%	9.14%
Substance abuse Parents	16.43%	6.36%	10.27%	14.11%	19.46%	20.41%	21.09%	22.39%
Physical abuse Parents	7.52%	2.99%	4.24%	5.53%	8.68%	10.26%	10.20%	13.26%
Any CA	34.93%	18.37%	26.14%	31.55%	37.20%	40.84%	41.81%	43.39%
Total CA – Mean (CI)	0.47 (.46-.48)	0.22 (.19–.25)	0.31 (.29-.34)	0.41 (.39–.42)	0.50 (.47-.53)	0.57 (.54–.60)	0.60 (.57–.63)	0.63 (.57–.70)
Child died	15.91%	24.69%	24.14%	19.71%	13.31%	10.17%	8.03%	8.49%
Major disaster	16.44%	14.83%	13.68%	14.77%	18.33%	17.30%	17.24%	15.83%
Military combat	5.64%	13.15%	10.46%	4.29%	6.81%	5.47%	1.61%	1.42%
Family addicted	18.23%	11.32%	15.52%	18.83%	20.12%	18.23%	19.55%	17.89%
Physical attack	6.44%	2.70%	3.50%	4.22%	5.80%	9.16%	10.63%	10.30%
Illness/Accident	25.38%	27.61%	29.39%	26.71%	25.37%	22.94%	19.78%	15.96%
Family Illness/Accident	26.76%	31.78%	32.98%	29.59%	27.55%	22.56%	19.05%	17.63%
Any AT	62.38%	66.98%	68.61%	64.24%	65.41%	59.57%	54.59%	52.79%
Total AT – Mean (CI)	1.12 (1.11–1.14)	1.25 (1.18–1.31)	1.29 (1.24-1.34)	1.18 (1.15–1.21)	1.18 (1.13-1.22)	1.04 (1.00–1.08)	0.94 (.89–.98)	0.85 (.78–.93)
Total CA&AT – Mean (CI)	1.56 (1.54–1.59)	1.48 (1.39–1.57)	1.58 (1.51-1.65)	1.58 (1.54–1.62)	1.66 (1.59-1.72)	1.57 (1.51–1.62)	1.50 (1.44–1.56)	1.44 (1.33–1.55)

Abbreviations: CA, Childhood Aversity; AT, Adulthood Trauma; CI-95%-Confidence Interval.

distributed across ages. Military combat peaked in young adulthood. Incidence of substance abuse of a spouse, partner, or child increased until the age of 40, after which it stayed stable for the rest of the lifetime. Incidence of physical attacks peaked in young adulthood followed by a decline over the life-course. Incidence of having an illness/accident, and having a family member with illness/accident, increased steadily over the life-course (see Figure 4).

Density plots for the distribution of the year of incidence of ATs for each birth cohort are displayed in Figure 5. These plots combine the perspective of age at incidence of most recent AT for each cohort across time-periods and allow certain observed age-specific effects to be seen for different cohorts across time-periods. For example, the incidence of losing a child peaked in young adulthood and in old age for all cohorts; however, the older the cohorts, the smaller the peak in young adulthood. Major Disasters, however, peaked across all birth cohorts in the same specific years (e.g. in 2005, with Hurricane Katrina). For military combat, certain cohorts show specific incidence patterns that are likely specific to the US. The AHEAD and CODA cohort likely fought in WWII (1944–1945); the CODA and HRS cohorts likely fought in the Korean War (1950–1953); and the HRS, War Babies and Early Baby Boomer cohorts likely fought in the Vietnam War (1965–1973), explaining the three major peaks. Incidence of spouse, partner or child with substance abuse increases over the life-course for all cohorts. Most cohorts tend to have peaks at the start of each decade starting in 1970. For incidence of severe physical attacks, all the cohorts show the same age-dependent curve that peaks in young adulthood and declines over the rest of the life. For the AHEAD cohort, the physical attack incidence curve mirrors the cohorts' combat-exposure curve, suggesting the incidence of physical attack may be due to war-related aggression. The incidence of personal illness or accidents peaks for all cohorts in old age with an additional smaller peak in young adulthood, and incidence of family member illness or accident displays almost the same pattern.

4. Discussion

In this large population-based study of 19,547 older adults, we found that 35% of participants reported exposure to at least one CA and 62% reported exposure to at least one AT. Lifetime prevalence rates varied strongly among cohorts; in regard to CA, an overall trend of decreasing lifetime prevalence rates across age cohorts was found. In contrast, prevalence of AT increased with the age of cohorts. In the case of specific CAs, the largest differences in prevalence between earliest and latest birth-cohort were observed for substance abuse of parents followed by physical abuse of parents. For specific ATs, it would be reasonable to predict higher rates in older cohorts due to their longer duration of risk for

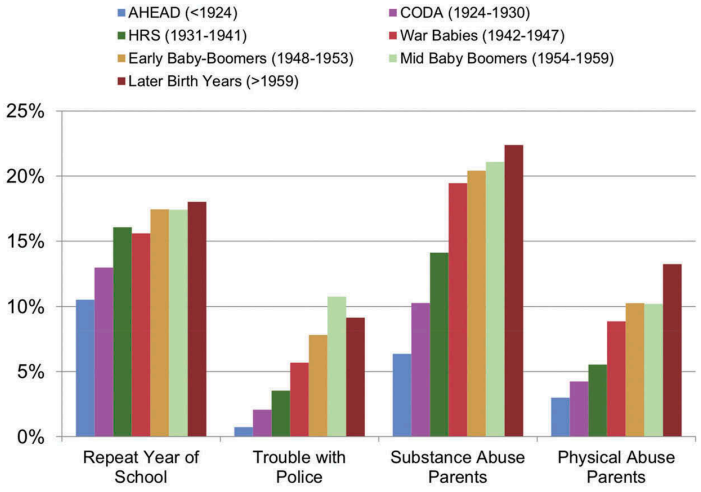

Figure 2. Self-reported prevalence rates in per cent of per CA across birth-cohorts.

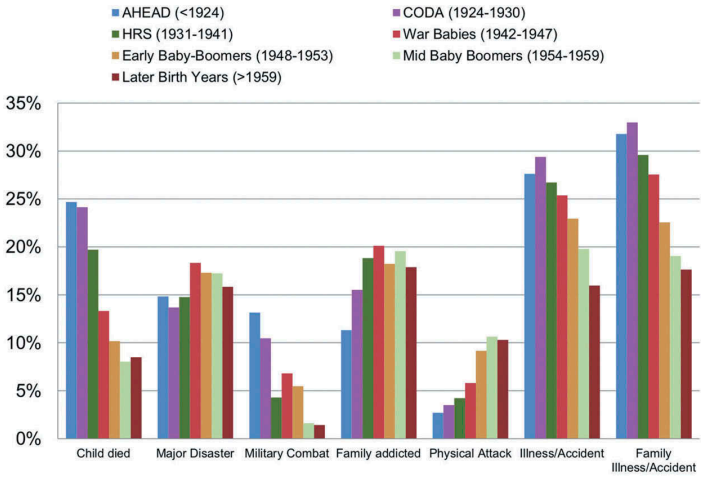

Figure 3. Self-reported prevalence rates in per cent per AT across birth-cohorts. Family relates to spouse, partner, or children.

exposure. However, findings did not support this assumption. Some ATs are more prevalent in older cohorts than expected, such as loss of a child, illness/accident, and family illness/accident. Others are almost equally distributed across cohorts, such as exposure to a major disaster. Furthermore, some ATs were even more prevalent in younger cohorts (e.g. having a family member with substance abuse, and serious physical attacks). Finally, military combat shows a distinct pattern related to major wars during certain periods. Overall, these data indicate that reports of CA tend to decrease, and reports of AT tend to increase with cohort age, with variation in the patterns for specific CAs and ATs.

The overall observed prevalence rates are in line with previous research; however, findings are at the lower boundary of what other studies have found regarding prevalence of both CA (Copeland et al., 2007; Green et al., 2010; Hussey et al., 2006; Kessler et al., 2010) and AT (Benjet et al., 2016; Kilpatrick et al., 2013; Norris, 1992; Ogle et al., 2013). Possible explanations include the rather narrow conceptualization and operationalization of CA and AT, as well as the methodological and sampling artefacts inherent in studies of older populations. With regard to overall trends in prevalence across age or cohorts, other studies found evidence of both decreasing (Benjet et al., 2016; Hatch & Dohrenwend, 2007) and increasing prevalence with age (Creamer & Parslow, 2008; Glaesmer et al., 2011; Hauffa et al., 2011). In our study, we observed both major trends of decreasing and increasing prevalence rates of earlier and later cohorts depending on the stressor. Decreasing prevalence with age of cohorts was observed for CA but increasing prevalence with age of the cohorts for AT. Combining CA and AT scores levelled these opposing trends.

Several different explanations could underlie our observed results. First, observed cohort differences in prevalence rates might be explained by real cohort differences in occurrences of CAs or ATs. In the case of ATs,

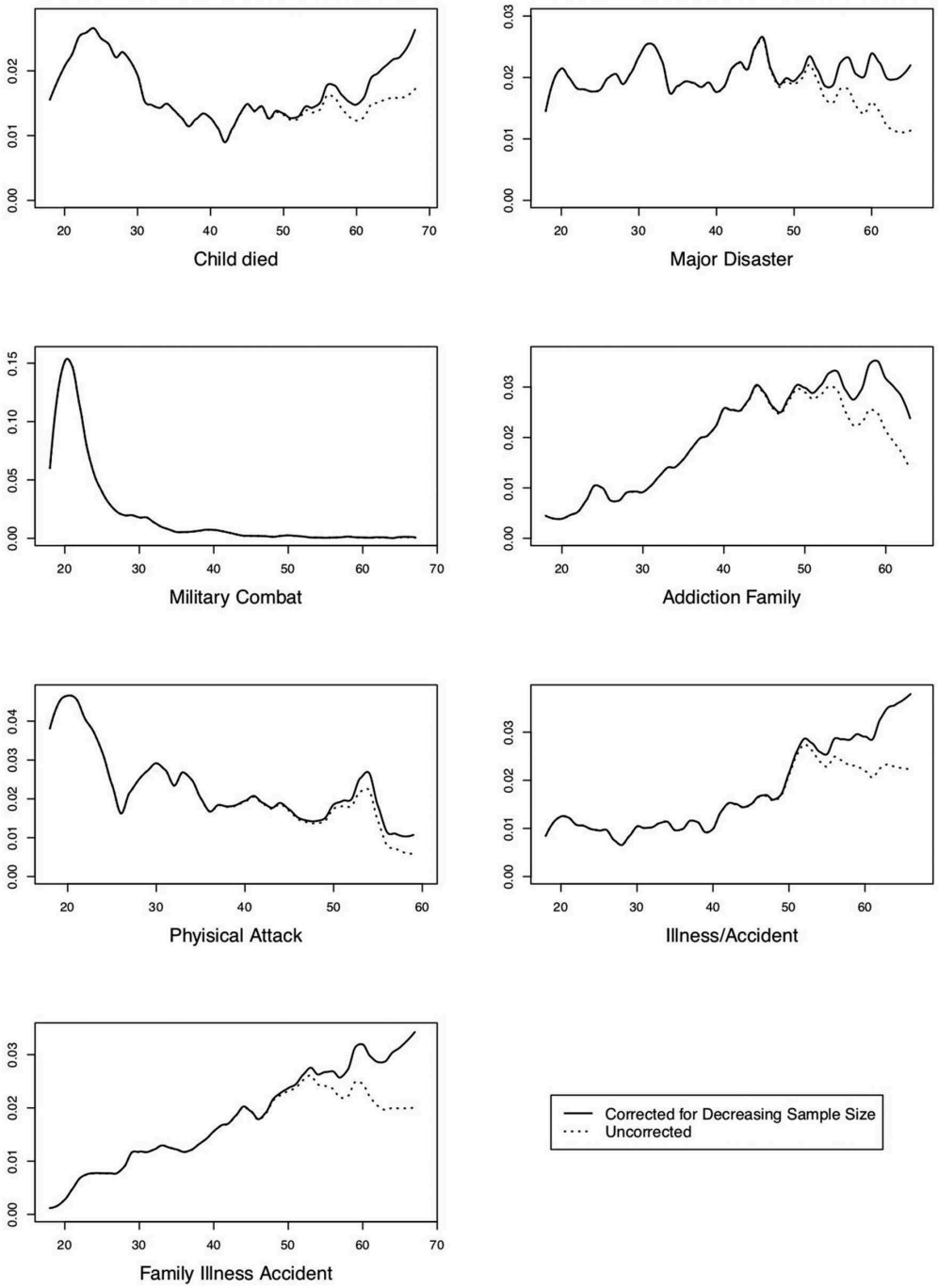

Figure 4. Distribution of age at incidence of most recent AT. Ratio of number of exposures per age and total number exposed. Plot is smoothened to account for variations between years to see overall trends.

differences might also be due to the separate or combined influence of age and time-period on incidence of an AT, which leads to observed cohort differences in prevalence. Influence of age, for example, can be seen for loss of a child and personal illness/accident, which both have very specific distributions of incidence. As the incidence of these events is much more likely to have occurred by older ages, early birth cohorts are less likely to have already experienced such an exposure. Effects of period might influence a cohorts' prevalence, as some events could have happened before the birth of some participants. Furthermore, an interaction between age and period effects might explain the incidence of military combat, which likely occurred only in those who were young enough to deploy to combat at the time of major conflicts. These data highlight the importance of

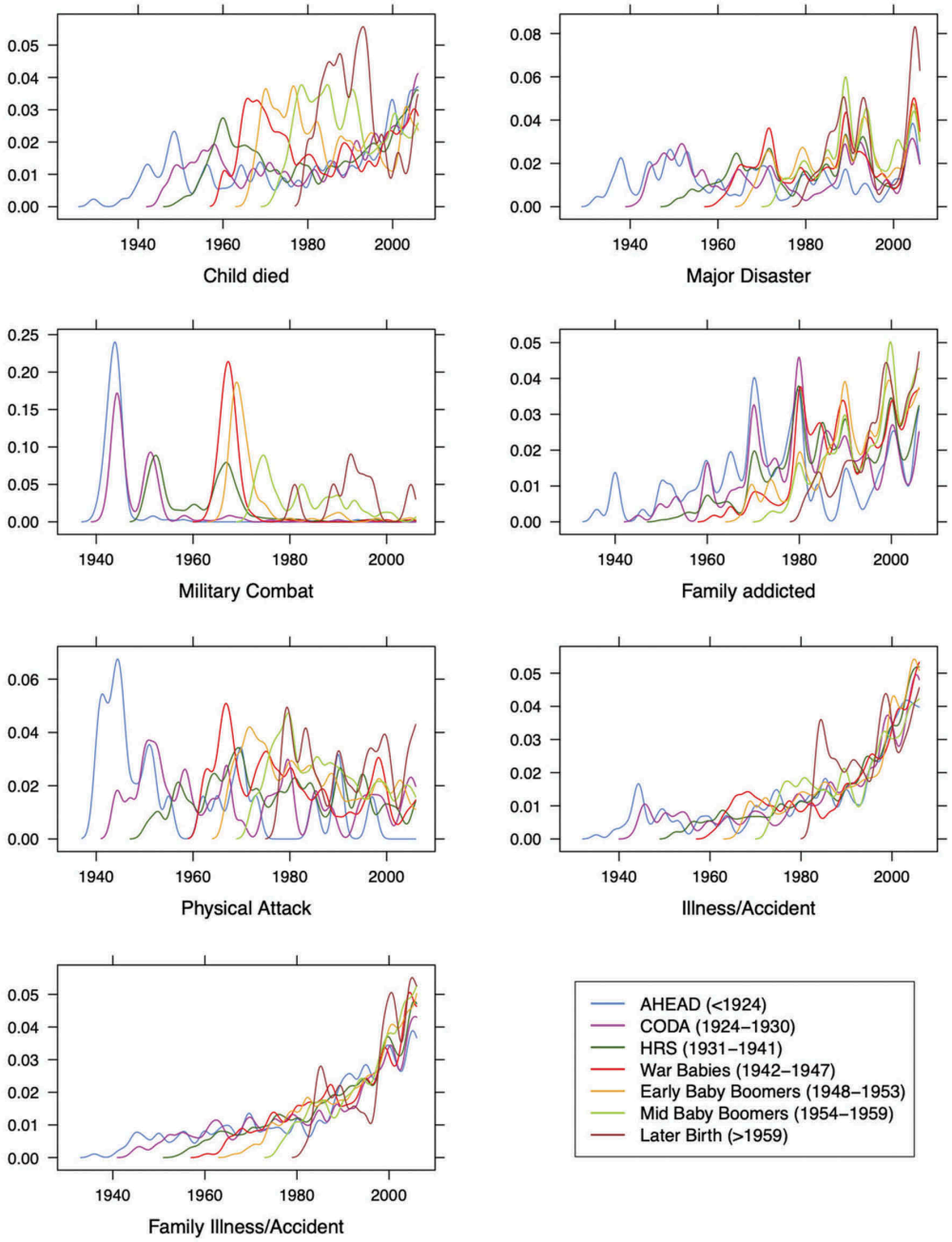

Figure 5. Distribution of year of incidence of AT per birth-cohort. Lines are kernel density distributions with bandwidth=1 for each AT per cohort, created with 'densityplot' from the lattice package.

accounting for age and period in stress research, even in samples with a restricted age range, such as our sample of mostly older individuals.

Second, differences in reported prevalence might be a result of cohort effects in the perception and willingness to report certain events. While debating possible cohort effects in the prevalence of depression in the 1980s, Klerman et al. (1985) argued that people in different cohorts, attribute different meaning and display different attitudes towards certain phenomena, and therefore might label and remember them differently. Older people for instance were shown to be less likely to report emotional problems such as depression compared to younger individuals (Hasin & Link, 1988). For example, some cohorts might be less likely to reveal certain events due to shame, fear of prejudice, or social desirability. Retrospective accounts of previous events might also be desirable reconstructions and narratives that are more consistent with current behaviour, as has been discussed in relation to family violence (Widom, 1989). Thus,

beyond cohort effects in occurrence, our findings may in part be a result of cohort effects in perception and reporting.

Third, methodological and selection artefacts might contribute to the observed differences in prevalence between cohorts. We expect recall bias to lead to an overall underreporting of exposures (Hardt & Rutter, 2004). This effect might be strongest for CAs and ATs with incidence in early adulthood (e.g. physical attack), due to prolonged recall periods. Additionally, age-related cognitive decline may lead to a recall bias of even larger magnitude in the older cohorts. This argument is supported by the observation that older cohorts overall were less likely to indicate the exact year of exposure to AT (response rate oldest cohort: 77%, and youngest cohort: 85%). Selection bias, in particular, selective mortality and institutionalization or healthy survivor effects, may in part explain the low prevalence of CA and AT, especially in older cohorts (Heiss, 2011; Zajacova & Burgard, 2013). In occupational cohorts, it has been shown that individuals who remain in a cohort tend to be healthier than those who drop out, which is known to decrease estimates of the adverse effect of an exposure (Arrighi & Hertz-Picciotto, 1994; Picciotto & Hertz-Picciotto, 2015). CA has previously been reported to be associated with morbidity and premature mortality (Brown et al., 2009; Clemens et al., 2018; Felitti et al., 1998; Riedl et al., 2019). In particular, the accumulation of adversities and inequalities 'may lead to premature mortality; therefore, nonrandom selection may give the appearance of decreasing inequality in later life' (Ferraro & Shippee, 2009, p. 336). Our data are consistent with the idea that self-report of stressors across the lifespan might underestimate the actual prevalence of stressors in older cohorts due to recall biases and loss of participants with high levels of past stressor exposure due to morbidity and mortality.

In the case of CAs investigated, we observed an overall trend of lower prevalence in older cohorts. As discussed, these effects might be related to methodological artefacts associated with long recall periods, cognitive decline, and selective attrition due to morbidity and mortality. Nonetheless, the magnitude of cohort differences varied greatly among specific CAs with the largest differences for substance abuse by parents. A review conducted by Keyes, Li, and Hasin (2011) showed that younger birth cohorts, especially those born after WWII, were more likely to engage in more risky drinking behaviours. A large US population-based survey also showed alcohol use and dependence to be more common in birth-cohorts born after Prohibition (1933) and after World War II (1945) (Grant, 1997). This is in line with our findings of largely increasing prevalence rates for 'parental substance abuse in childhood' and 'having a family member with substance abuse in adulthood' especially for the HRS (1931–1941) and the War Babies (1942–1947), compared to the earlier cohorts. In the case of parental physical abuse, our findings are consistent with previous research that also found lower rates of retrospectively reported physical abuse in older participants (Draper et al., 2008; Dube et al., 2003; Logan-Greene, Green, Nurius, & Longhi, 2014). Beyond recall and selection biases, three major trends in the US might explain these findings. First, corporal punishment was long viewed as the norm and therefore not as abuse. In 1968, 94% of parents physically punished their children, this rate declined to 68% in 1994 (Straus & Mathur, 1996), and further to 37% in 2014 (Finkelhor, Turner, Wormuth, Vanderminden, & Hamby, 2019). Second, efforts around child protection and awareness of abuse grew greatly around the 1960s (Myers, 2008). Third, U.S. Department of Health and Human Services (1999) found that between one-third and two-thirds of child maltreatment cases were affected in some way by substance use. This is in line with our finding of about half of the cases with parental physical abuse also reporting parental substance abuse. The decline in corporal punishment alongside the change in awareness of physical abuse might have led to cohort differences in the perception, the willingness to report, and labelling of early life physical punishment. Combined with an increase in parental substance abuse and methodological and sampling artefacts, this might explain the higher rates of self-reported parental physical abuse in younger cohorts.

In the case of the specific ATs investigated, differences in prevalence of having lost a child are largely due to the difference in age of incidence of such an experience, which peaks in young adulthood and towards old age. Furthermore, fertility rates strongly declined from the 1960s onwards (Guyer, Freedman, Strobino, & Sondik, 2000), child mortality rates dropped (Behrman & Field, 2003), and overall life expectancy grew (Guyer et al., 2000), all explaining the lower prevalence in younger birth cohorts. Regarding major disasters, we assume the findings of rather stable prevalence across cohorts to be related to two factors. First, recall bias may reduce reports of early experiences of natural disaster in older cohorts, and second, data exists showing an actual increase in natural disasters in the second half of the last century worldwide (Emergency Events Database, 2019). Cohort differences for combat-related exposures are mainly explained by age-period interactions in incidence, in that young adults in specific periods (major wars) volunteered or were drafted into war regions for limited time periods in young adulthood (see Figure 4, military combat). After conscription ended in 1973 and the military moved to an all-volunteer army, military personnel nowadays often do multiple tours in different war zones. Overall about 40% military service members were deployed multiple times into recent conflict zones,

suggesting the age of incidence for most recent military traumatic exposures may be increasing (Institute of Medicine of the National Academies, 2010).

5. Limitations

Beyond the strengths of having a large population-based sample of older individuals that fell into several distinct cohorts and reported on both CA and AT, our findings need to be considered in light of some important limitations. First and foremost, compared to the broad concepts of trauma and stress, the implemented questionnaire with eleven items (four in childhood and seven in adulthood) is a rather narrow assessment of mostly event-based measures of potentially adverse and traumatic exposures. Additionally, the indication of the exact year of exposure for AT focused only on the *most recent* incidence. Furthermore, the items asking for substance abuse of parents in childhood and family members in adulthood focus on prolonged stressors, which makes it hard to indicate the exact year of exposure, leading to artefacts in the data (peaks occurred around full decades: 1970, 1980, 1990, 2000). Second, and related to the first limitation, assessments of CA and AT are based on retrospective self-reports and therefore subject to numerous problems, such as prolonged recall periods, cognitive decline, false memory, and bias due to mood state and symptomatology, that have been extensively discussed in previous literature (Baldwin, Reuben, Newbury, & Danese, 2019; Hardt & Rutter, 2004; Maughan & Rutter, 1997; Reuben et al., 2016; Sheikh, 2018). A recent meta-analysis reported a poor overlap between prospective and retrospective measures of childhood maltreatment (Baldwin et al., 2019). However, they found greater agreement for more clear-cut forms of adversity, meaning that most of the exposures in our study – the major traumas – might still have a high level of agreement over time (Baldwin et al., 2019). Third, the sample is U.S. population-based; therefore, some findings and patterns might only be representative for the U.S. (e.g. military combat) and others only for certain areas (e.g. Hurricanes in southeastern states). Additionally, upon study enrolment, participants had to be fully registered household residents, which might lead to an underestimation of prevalence rates due to exclusion of people with temporary or no housing. Lastly, as the HRS study only recruited adults over 50 and their spouses, less than 4% of the total sample are younger than age 50. Having additional younger birth cohorts would increase generalizability of findings.

6. Implications

The present data highlight the high prevalence of lifespan trauma exposure in older samples. However, there are stark differences in lifetime prevalence based on age, period, and cohort effects. Thus, studies of self-reported CA and AT in older samples have to be interpreted in the light of methodological limitations highlighted in our study. Methods from sociology and epidemiology will be useful in making sense of self-reported stressor exposure data. For example, new models, methods and empirical applications from age-period-cohort (APC) analysis might be fruitful to apply in lifespan stress and trauma research (Keyes & Li, 2012; Yang & Land, 2013). Our work here adds to a growing literature that highlights problems with some stress measurement techniques (Epel et al., 2018; Kagan, 2016; Slavich, 2019). In future studies, a combination of prospective and retrospective, as well as self- and observer-rated measures might help to reduce recall biases. Using more sophisticated stress and trauma measurement questionnaires (Slavich & Shields, 2018; Teicher & Parigger, 2015), conducting interviews with trained raters and employing memory enhancement techniques might be of interest for future research. A better understanding of the timing and distribution of stressors, and differences among age, period, and cohort effects in the population will allow us to target interventions that aim to reduce the negative impact of stressors to those most likely to benefit. As little is known about CA and AT in older populations, further research is warranted to tackle these important issues.

7. Conclusion

Conflicting findings on the prevalence of CA and AT in older populations might be due to both facts, because the specific age and period of a sample will influence results, and artefacts, because there are several potential methodological issues that might cause biases in the data. Data on retrospective self-reported exposure to CA and AT in older samples should be interpreted with caution and with regard to their major methodological challenges. Recall biases might lead to underreporting of events and in this way conceal real cohort effects. Selection biases due to selective mortality of the most highly exposed individuals likely lead to underestimates of overall prevalence in the oldest-old. Untangling fact from artefact and differentiating among age-period-cohort effects will help distinguish more accurate profiles of lifetime stressor exposures in older populations.

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Data availability

The Health and Retirement Study was conducted by the University of Michigan. All data analyzed in this study is openly available. Data is accessible at https://hrspubs.sites.uofmhosting.net.

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Chapter 5: General Discussion

This chapter will conclude the thesis with a general discussion of what we found; how it adds to the current body of research on theory, measurement and modelling; where it shows a need for future research; and what's left to be done.

5.1 The need for conceptual and theoretical work – about the necessity of integrating risk and protective factors into the process of stress and resilience

In light of the ever-increasing and, in recent years, exponentially growing number of publications and replications of the long-term sequel of childhood adversity, strong heuristics, interdisciplinary frameworks and concepts are needed to integrate this broad, diverse and at times fragmented body of literature on risk and protective factors. These heuristics should draw upon existing theories from different research fields and lines of conceptualizing and theorizing; should address the questions of what constitutes risks, in particular stressors, adversity and trauma; and should elucidate best ways to approach these overlapping concepts. Next to the broad body of evidence focusing on risk and disease, probably equally or even more important, theoretical work and conceptualization have to address the questions of what constitutes protective factors and what constitutes healthy functioning. Answering both these questions regarding what constitutes risk and protective factors may open up new ways of thinking about stress and resilience processes, trajectories, and how to shape these trajectories from disease towards health and from stress towards resilience.

In our own literature research looking into the heterogeneity of findings on childhood adversity and telomere length, we had quite a hard time finding suitable search terms to include the relevant body of studies – as the field suffers greatly from a clash of concepts and differing terminology. This diversity in terminology and concepts is in part a result of the diverse theoretical perspectives and fields of research involved the study of biological consequences of adversity. Resulting from this issue, the current literature on the association of adversity and telomere length consists of many studies, summarized in numerous reviews and meta-analyses investigating some form of adversity – childhood adversity, early life-stress, childhood psychosocial stressors, childhood trauma, childhood exposure to violence, adverse caregiving environments, chronic social stress, perceived stress – with great overlap of included studies making it difficult to draw firm conclusions.

To move the field forward, a shared, clear conceptualization of stressors and adversity might result in a common nosology and taxonomy, as well as working models that may lay the conceptual groundwork for future investigations (Epel et al., 2018; McLaughlin, 2016; Slavich, 2020). For example, recent conceptualizations of childhood adversity underline two major aspects of adversity: an absence of expected positive input (i.e. neglect and/or deprivation) and the presence of unexpected negative inputs (i.e. violence, abuse, and trauma)

(Humphreys & Zeanah, 2015; McLaughlin, 2016; McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). In particular the presence of unexpected negative inputs is understood to be mediated by threat-related processes with adverse negative outcomes, including both psychopathological and general health outcomes (Colich et al., 2020; McLaughlin, Colich, et al., 2020; McLaughlin & Lambert, 2017; Slavich, 2020). Compared to examinations of negative inputs, there is a lack of research looking into the absence of expected positive inputs, in particular following neglect and deprivation (Gilbert et al., 2009). The limited studies that have been completed found neglect and deprivation to increase the risk for indiscriminate social behavior, are related to reactive attachment disorder and disinhibited social engagement disorder and are associated with neural correlates (as inhibitory control, cortical hypoactivation and reduced amygdala discrimination) (Fox et al., 2017; Humphreys & Zeanah, 2015). In this sense, disrupted emotional interactions from close caregivers with their infants (e.g. affective communication errors, role confusion, negative intrusive behavior, disorientation or withdrawal in interactions) conveys risk for later functioning (Humphreys & Zeanah, 2015), probably beyond that of threat-related processes. Investigating these two pathways – threat and deprivation – their specific mechanisms and interaction of these might help in moving the field forward.

Having those two pathways in mind, two approaches seem promising to integrate the affiliative neuroscience approach of resilience (Feldman, 2020) and the social safety theory of stress (Slavich, 2020). The affiliative neuroscience approach to resilience “aims to direct attention to systems that sustain our capacity to form affiliative bonds, enter into social groups, and use relationships to manage stress, as core features of the human capacity to withstand, even thrive, in the face of trauma” (Feldman, 2020, p.145). Social safety theory argues that “developing and maintaining friendly social bonds is a fundamental organizing principle of human behavior and that threats to social safety are a critical feature of psychological stressors that increase risk for disease” (p. 265), and suggests, that “social safety and social threat lie at the heart of life’s most impactful experiences” (Slavich, 2020, p. 287). Both of these approaches, one coming from the stress side of the story (Slavich, 2020) the other one from the resilience side of the story (Feldman, 2020), underline the importance of belonging, affiliation, cohesion and sociality, and by doing this move beyond the concrete behavior-based approaches to cognition and action and shift the focus of attention towards the social (Feldman, 2020).

Next to that, meta-analysis on trajectory-based approaches of resilience and dysfunction following potential trauma across studies have shown four types of trajectories with the resilience trajectory being the modal response, followed by recovery, chronicity and delayed onset (Galatzer-Levy et al., 2018). Therefore, from a public health perspective, building up resilience might help to combat the high prevalence of stress-related disorders over

and beyond intervention for specific disorders (Kalisch et al., 2017). From a theoretical stand, advancements in the conceptualization of stress and resilience, in particular good heuristics that help to integrate stress responses, resilience processes, and risk processes with protective mechanisms and vice versa, might help to combine the bodies of evidence on risk factors and adverse outcomes with those regarding resilience trajectories and protective mechanisms. The need to integrate these perspectives is far from being new as risk research is, and was, paradigmatic of developmental psychopathology; however, "attention, increasingly, came to be drawn to the need to consider both risk and protective mechanisms […], to understand the developmental operation of the complex mix of influences that give rise to resilience in the face of adversity" (Rutter & Sroufe, 2000, p.266).

5.2 The need for methodological work – about better measurements of clearer concepts

Related to and building upon the need for clearer concepts is the need for higher resoluting measures of stressors, adversities and traumatic exposures, as well as for protective factors and resilience. In regard to stress, some scholars argue to restrict the use of the concept of stress for limited, select events that pose a serious threat, or to abandon it all together (Kagan, 2016). Others argue to revise the stress term and plead for the use of better higher-resoluting measures of stress and the articulation of important characteristics (Epel et al., 2018; Slavich, 2019), or anchor the term stress within biological systems (McEwen & McEwen, 2016). Epel et al. (2018) proposed a stress typology as a transdisciplinary working model underlining the need to clearly separate stress exposures and their characteristics, from the responses to these stressors. These stressor exposure characteristics include important domains such as the timescale (acute, life-events, daily events, chronic stressors), life period (in utero, childhood, adulthood, lifespan), assessment windows (measurement timeframes and proximity of assessment to exposure) and important stressor attributes (duration, severity, controllability life domain, target of the stressor, and potential to elicit harmful stress responses) (Epel et al., 2018).

Our research looking into the heterogeneity of findings on adversity and telomer length has shown that there is an abundance of ways to assess childhood adversity, that major important domains of these stressors are not assessed well, and that this imprecision is related to the heterogeneity in findings looking at biological correlates (Bürgin et al., 2019). Our investigations into childhood adversities and adulthood trauma in the HRS study have shown that childhood adversity and adulthood trauma are inextricably linked, and that incidence to certain exposures follows age, others are more closely linked to the time period or might be related to both and therefore to the birth-cohorts themselves (Bürgin et al., 2021; Bürgin, Boonmann, et al., 2020).

In regard to specific measures, two rather recent questionnaires might be helpful to move the field forward by providing broad and higher resoluting measures of life-course

stressors and adversity ('STRAIN') (Slavich & Shields, 2018) and on maltreatment chronologies of exposures in childhood ('MACE') (Teicher & Parigger, 2015). These measure a broad array of stressors, adversities, and types of maltreatment along with their severity and multiplicity, the age of incidence, and durations. Next to the measurement of stressors, there is a great need for strong and commonly accepted measures of resilience, as current measures are relatively low in congruence (Nishimi et al., 2020). Looking at methodological biases, large-scale longitudinal studies with prospective and well-constructed measures of stressors and adversity might help to overcome the bias of retrospective measures of adversity (Baldwin et al., 2019). In particular, reliable and valid retrospective measures of neglect and deprivation might help to foster our understanding of mechanisms mediating neglect and its sequel. Better measures of sound concepts and heuristics will help to improve our understanding of the adverse nature of certain exposures, and to uncover different exposure-related mechanisms that mediate the association between childhood adversities and long-term (health) outcomes.

5.3 The need for different analytical approaches – about the cumulation of specifics and the trajectories of individuals

Inspired by old theories and informed by the increasing-openly accessible large-scale and longitudinal data bases; new working models, concepts, and measures must be rethought building on advances in statistical modelling in order to adequality analyze stressor exposure, adversity data, and their sequel. When working on our compounding stress paper, we were stunned to see that summed childhood adversity and summed adulthood trauma scores were only weakly correlated. We started to look into the patterns and combinations of specific types of childhood and adulthood exposures, and found specific childhood adversities to be more strongly associated with specific adulthood trauma exposures (Bürgin et al., 2021). In the in-between of specific impacts of certain types of exposures and the cumulation of all types of exposures, might be an important story of the cumulation of specifics being associated with divergent trajectories of outcomes. Recently, more and more studies use person-oriented statistical modelling (e.g., latent class/profile analyses) and investigate the association of latent classes our profiles of exposures with certain outcomes (Bürgin et al., 2021). Further, the use of trajectory-based approaches (e.g., latent class mixture models and latent class growth analysis) is gaining popularity to investigate the impact of certain exposures over time, and focuses on latent divergent trajectories in functioning (Galatzer-Levy et al., 2018). Each of these approaches, singularly and combined-the latent cumulation of specifics on the exposure side, and the divergent latent trajectories on the outcome side – might be fruitful in moving the field forward.

When working on our fact or artefact paper, we were intrigued by the descriptive patterns of incidence of specific types of adverse exposure across the life-course. We were surprised to find out that there is a huge statistical and methodological literature on applications

and modelling approaches around age-period-cohort (APC) analysis that we haven't seen applied in lifespan stress and trauma research (Bürgin, Boonmann, et al., 2020). Approaching and tackling APC effects within stress, ageing and lifespan research beyond static linear effects of age as co-variable might be worth further methodological and statistical consideration, and will move the field from a lifespan to a true life-course perspective. Person-oriented modelling approaches – on both risk and outcome side of the equation – might be promising to help address the developmental psychopathological concept of multifinality in that "individuals may begin on the same major pathway and, as a function of their subsequent 'choices', exhibit very different patterns of adaptation or maladaptation" (Cicchetti & Rogosch, 1996). As Cicchetti and Rogosch (1996, p.598) already noted over 25 years ago, "this more person-oriented level of analysis of a differential pathways approach is vital for achieving a primary mission of developmental psychopathology, implied in its definition as the study of the origins and course of *individual* patterns of behavioral maladaptation". Novel modelling approaches might help to move the field forward by doing that.

5.4 Going truly interdisciplinary - in theory, measurement and modelling

Understanding the sequel of childhood adversities needs true interdisciplinary science on all three levels discussed: in theory, in measurement and in modelling. New and integrative theories, frameworks, models and concept will help to integrate the exponentially growing amount of evidence and research papers published. Over and above one's own research fields' boundaries might lie an abundance of good – maybe even old – ideas, that wait to be combined, integrated, and included into truly interdisciplinary bio-psycho-social models. Great existing theories and excellent scholars from sociology have tried to integrate the 'psycho' and 'bio' into the 'social' (Ferraro et al., 2009; McEwen & McEwen, 2017; Pearlin, 1989; Pearlin et al., 1990), with recent theories increasingly integrating the 'social' into the 'bio' and 'psycho' (Feldman, 2020; Slavich, 2020). Beyond this, recent theories on stress and resilience show the need to integrate different levels of the social world with its dimensions (from macro, over meso, to micro) into once individual psychological systems (mental health, functioning, personality and life-experiences) that interact with once individual biological functioning (Slavich, 2020; Ungar & Theron, 2020). Such multisystemic perspectives might open possibilities for intervention across social systems in which individuals are embedded (Slavich, 2020). In particular, mechanisms that mediate and moderate at the intersection between the bio-psycho-social are of interest and warrant further investigation.

Beyond theory, measurement of stress and resilience, adversity and trauma, needs interdisciplinary efforts towards measurement and assessment with agreed upon gold standards and reporting guidelines. A shared nosology and taxonomy of stressors and stress responses, and agreed upon working models including important characteristics are a first step in this direction (Epel et al., 2018). Next to stress, conceptual models of childhood adversity

that conceptually try to separate the influence of abuse and neglect, threat (trauma) and deprivation along dimensions, might help to understand different trajectories and sequels following different types of adversity (Humphreys & Zeanah, 2015; McLaughlin, Sheridan, et al., 2020; McLaughlin et al., 2014; Sheridan & McLaughlin, 2014). In particular, reliable and valid measures of neglect and deprivation are needed that overcome the strong biases of retrospective measurement, which are most apparent when investigating neglect (Baldwin et al., 2019).

Next to theory and measurement, interdisciplinary efforts are needed to make best use of available data in the context of their major flaws and artefacts. Theory-driven person-oriented modelling approaches hold promise to understand divergent trajectories over time as well as to understand the cumulation of specifics within a developmental perspective. Next to these approaches, data-driven approaches with new machine learning algorithms and artificial intelligence might help to generate new hypotheses and ideas that might need subsequent theoretical framing. New approaches towards measurement of stress and resilience using novel technologies might help to get real time information of these processes while they unfold. The bio-psycho-social sequel of childhood adversity is an interdisciplinary sequel by definition, and therefore the research tackling this sequel needs to keep up with the problem it tries to address.

5.5 Filling the gap between risk factors and outcomes – about mediators, moderators, and the necessity to go high-risk

Two research strings are getting more and more attention: the focus on mechanisms, moderators and mediators that explain the link between adversity and distal outcomes, and research on high-risk populations. Following the CDC-Kaiser ACE study in the last two decades, a huge publication effort around the long-term sequel of childhood adversities emerged. Many studies replicated the obvious finding that cumulated childhood adversities have long-lasting and deleterious effects throughout an individual's life-course across bio-psycho-social domains. Recent research more and more focuses on important mediators and moderators such as following the exposure to threat (childhood trauma). Important bio-psycho-social mechanisms that mediate long-term psychopathological outcomes include social information processing, emotion processing, and accelerated biological aging, while social support serves as a transdiagnostic protective mechanism (McLaughlin, Colich, et al., 2020). This line of research tries to fill the gap between adversity and outcome by addressing important mechanisms examining how distal risk factor might increase the risk for proximal risk factors (Dennison et al., 2019; Lee & Park, 2018; Moffitt et al., 2016; Rakesh et al., 2019). Compared to research on mechanisms following abuse and trauma, less attention is given to mechanisms following neglect and deprivation, which will be important to address in future research.

Next to the focus on mechanisms, recent research increasingly highlights the stark differences in exposure rates of childhood adversities, in particular the higher cumulation of stressors and adversities in those living in poverty, being part of a racial or ethnical minorities, those living in low-resource neighborhoods, and those in contact with the child-welfare system, which are all underrepresented in research (Hughes & Tucker, 2018; Kim & Drake, 2018; Lanier et al., 2014; McEwen & McEwen, 2017). Out-of-home placed children and adolescents and those leaving care are at particular high risk to be exposed to adversity with three-quarters reporting some type of adversity and trauma, and most of these reporting multiple forms (Fischer et al., 2016; Garcia et al., 2017; Jaritz et al., 2008; Woods et al., 2013). With our research in high-risk samples (listed in the CV enclosed) we try to address this need and to add to this rather small body of research investigating children, adolescents and young adults within residential youth care and those leaving care (Bürgin, Kind, et al., 2020; Clemens et al., 2020; Jäggi et al., 2021; Kind, Bürgin, Clemens, et al., 2020; Kind, Bürgin, Fegert, et al., 2020). Both these lines of research – the focus on mechanisms, mediators and moderators and research on high-risk population – will help to further our understanding of adversities and will inform the best ways to prevent and intervene in those most at risk.

5.6 Societal and clinical implications

Better understanding the bio-psycho-social sequel of childhood adversity from multiple perspectives leaves us with the clear obligation and mandate to address this sequel as a major priority for public health and social policy making. As multisystemic as the sequel of adversity presents itself, so to must be the multisystemic solution strategies – from the biology of the individual to the micro-, meso- and macro-system in which the individual is embedded. Beyond the ethical obligation to prevent harm from those who can't protect themselves, and respecting the developing autonomy in children (Beauchamp & Childress, 2001), there is a financial consideration for early intervention. The prevention of adversity and maltreatment might lead to a huge reduction in long-term cost (Bellis et al., 2019), well in line with Benjamin Franklin (1736) famous quote, "an ounce of prevention is worth a pound of cure". If harm can't be prevented and autonomy strongly gets disrespected, there are certain ethical obligations and a clear mandate to intervene, to do good; these mandates pertain to relieving, lessening, and preventing further harm, as well as to strive for justice whilst distributing benefits, risks, and costs (Beauchamp & Childress, 2001). Following Franklin's idea that prevention is better than intervention, in regard of the sequel of adversity a kilo of early prevention might be worth a ton of early intervention, both of which might still pay off compared to the prize of starting to intervene decades later or doing neither of both.

Justice stands out being particularly relevant in discussing childhood adversity, in light of these four biomedical ethical principles – respect for autonomy, nonmaleficence, beneficence and justice (Beauchamp & Childress, 2001). As introduced, research has shown

the high co-occurrence of adversities in individuals, the clustering within families and neighborhoods, and the co-occurrence of poverty and adversity (Green et al., 2010; Hughes & Tucker, 2018; Kessler et al., 2010; Kim & Drake, 2018). Next to that, the exposure to risks such as poverty is one of the factors driving the overrepresentation of minority groups in the child welfare and juvenile justice system (Kim & Drake, 2018; Lanier et al., 2014). Childhood adversities, poverty and the cumulation of inequality impacts physical systems and brain development through recurrent stress leading to the embodiment of inequalities, earlier mortality and even intergenerational transmission of such (Brown et al., 2009; Dowd et al., 2011; Fritzell et al., 2015; Jackisch et al., 2019; Johnson et al., 2020; Kondo et al., 2009; McEwen & McEwen, 2017). Given these findings and societal trends one might ask oneself how well do we do – as modern and enlightened societies – with the principle of justice? Better understanding the biopsychosocial sequel of adversity leaves a clear mandate to care and take action, as *combating childhood adversity is ethically imperative and an issue of social justice.*

5.7 Conclusions

Childhood adversities cast long shadows through the life-course of those being exposed. These early deviations in expectable environments – be it through an absence of expected input, the presence of unexpected inputs, or both – are followed by a broad range of bio-psycho-social sequel of dysfunctional outcomes. From a theoretical stand, advancements in the conceptualization of stress and resilience will help to integrate stress responses and resilience processes, and risk processes with protective mechanisms, and vice versa. This might help to combine the – at times – separate bodies of evidence on risk factors and adverse outcomes meeting resilience trajectories and protective mechanisms. Next to theory, better measures of clearer concepts and heuristics will help to improve our understanding of the adverse nature of certain types of exposures and to uncover different exposure-related mechanisms that mediate the association between childhood adversities and long-term bio-psycho-social outcomes. Over and above theory and measurement, new approaches for statistical modelling, in particular theory-driven, person-oriented modelling approaches, hold promise to improve our understanding of divergent trajectories over time as well the cumulation of specifics within a developmental perspective. Addressing the bio-psycho-social sequel of childhood adversity – as an interdisciplinary sequel by definition – is imperative. Research tackling this sequel however has to keep up with the complexity and interdisciplinary nature of the problem it tries to address. Targeting childhood adversity at its roots is nothing less than an ethical imperative, should be a major public health concern, and is an issue of social justice. When targeting adversity, a kilo of early prevention might be worth a ton of early intervention, however both of which might still pay off compared to the costs of starting to intervene decades later or doing neither of both.

Looking back onto the roots of developmental psychopathology Rutter and Sroufe (2000) stated over twenty years ago that:

> Developmental psychopathology arose out of a *recognition of the value* of combining developmental and clinical perspectives but also out of an *appreciation of the limitations* of the grand theories of the day. There is a continuing need to remain skeptical about the new evangelisms that have come to take their place, but equally the imperative must be to replace doubt with programmatic research that truly tests competing hypotheses and which has the potential of providing a real understanding of the range of causal processes as they apply across the span of behavioral and developmental variation. (Rutter & Sroufe, 2000, p.287).

Concluding this thesis, great interdisciplinary science needs the appreciation of different perspectives and the recognition of the value of combining such. It needs a good portion of skepticisms with the new evangelisms of this time – which might be 'stress' and 'trauma' and their overly extensive use in explaining the world. But on the other hand, it needs programmatic, well designed, enthusiastic research that is theory-driven, implements cutting edge methodology, and tests competing ideas and hypotheses to provide a real and better understanding of processes and how they unfold over development and the life-course. Continuing this odyssey of discovery of developmental (psycho-)pathology and resilience, it still holds true that there are many miles to go and promises to keep before one might go to sleep (Cicchetti, 2004). There is more to be done, as safe childhoods confer lifelong benefits.

Those who have a ‘why’ to live, can bear with almost any ‘how’.
Viktor E. Frankl

Chapter 6: Curriculum Vitae

Personal Information

Name:	David Bürgin
Date and Place of Birth:	29th June 1994; Lörrach (Germany)
E-Mail:	david.buergin@upk.ch; d.buergin@unibas.ch
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Education

09/2017 –	Clinical Research PhD Program, PhD Program Health Sciences (PPHS), Faculty of Medicine, University of Basel, Switzerland, Supervisor: *Prof. Dr. Klaus Schmeck, Prof. Alain Di Gallo*
08/2015 – 07/2017	Master's Program Faculty of Psychology; Major in Clinical Psychology and Neuroscience; University of Basel, Switzerland; Final grade: 5.8 (equivalent: A); Department of Clinical Psychology and Psychotherapy, Faculty of Psychology, University of Basel, Supervisor: *Prof. Dr. Jens Gaab*
08/2012 – 07/2015	Bachelor's Program Faculty of Psychology; University of Basel, Switzerland; Final grade: 5.5 (equivalent: A) Department of Clinical Psychology and Psychotherapy, Faculty of Psychology, University of Basel, Supervisor *Prof. Dr. Jens Gaab*

Employment

09/2017 – 09/2021	PhD Candidate and Project Coordinator, Psychiatric Hospital of the University of Basel, Research Department of the Child and Adolescent Psychiatric Clinic; Supervisor: *Prof. Klaus Schmeck, Dr. Marc Schmid,*
01/2020 – 02/2020 09/2018 – 10/2018	Visiting PhD Student, THRIVE Lab, University of California San Francisco (UCSF), Supervisor: *Prof. Aoife O'Donovan*
01/2016 – 08/2017	Research Assistant, Psychiatric Hospital of the University of Basel, Supervisor: *Dr. Marc Schmid*
01/2010 – 12/2015	Private Tutor – High school and secondary school (mathematics, physics and chemistry), Bachelor and Master level (statistics)

Teaching

01/2020 –	Supervisor of a Master Project at the Department of Clinical Psychology at the Psychological Faculty of the University of Basel in collaboration with *Prof. Jens Gaab*
09/2020 – 12/2020	Lecturer in Theory Seminary for Master students at the Psychological Faculty of the University of Basel

References

Prof. Dr. Aoife O'Donovan (UCSF San Francisco, aoife.odonovan@ucsf.edu)
Prof. Dr. Klaus Schmeck (UPK Basel, klaus.schmeck@upk.ch)
Dr. Marc Schmid (UPK Basel, marc.schmid@upk.ch)
Prof. Dr. Jens Gaab (Faculty of Psychology, University of Basel, jens.gaab@unibas.ch)

Academic Training

Scientific Courses

2020	**Journal Editing in Health Sciences** – Prof. Dr. Nino Künzli, Dr. Anke Berger at the Swiss TPH
	Writing a journal article and getting it published – PD Dr. Jürgen Barth, at the Child and Adolescent Psychiatric Research Department of the Psychiatric Hospital (UPK) Basel
2019	**Structural equation modeling with lavaan** – Prof. Dr. Yves Rosseel, at the University of Zurich
	Statistical Power Analyses: Basic and Advanced Use of G*Power and MultiTree – Prof. Dr. Edgar Erdfelder, at the University of Basel
	Good scientific conduct in health sciences – Prof. Dr. Christian Lengeler, at the Swiss TPH
	Applied Statistics Using R – Dr. Gilles Dutilh, at the University of Basel
2018	**Mediation, Moderation, and Conditional Process Analysis** – Prof. Dr. Andrew Hayes, at the University of St. Gallen
	Essentials in Health Research Methodology – Prof. Dr. Mathias Briel, at the University of Basel
2017	**Good Clinical Practice (GCP) Basic Course - Investigator Level Certificate** – Dr. Sandra Kohlmaier, at the Clinical Trials Unit of the University Hospital Basel
	Academic Writing in the Health Sciences – PD Dr. Annegret Mündemann, at the University of Basel
	Writing a PhD thesis proposal in Health Sciences – PD Dr. Amena Briet, at the Swiss TPH Basel

Personal Skill Courses

2020	**Project Management for Researchers** – Dr. Dimitrije Krstic, at the University of Basel Transferable Skills Program
2019	**Self-Branding and Self-Promotion** – Dr. Andrea Wüst, at the University of Basel Transferable Skills Program

Skills

Research Skills	Statistics, oral presentations, scientific writing (ethic and project grants, papers and scientific reports), project coordination, participant recruitment, clinical interviews (e.g., SCID-5, SCID-II)
Computer Skills	R, SPSS, EndNote, MacOS, Windows, Microsoft Office
Language Skills	German (native), English (fluent), French & Spanish (basics)

Research Output

International publications

2021

*** Bürgin, D.**, Boonmann, C., Schmid, M., Schmeck, K., Tripp, P., & O'Donovan, A. (2021). Compounding Stress: Childhood adversity as a risk factor for adulthood trauma in the population-based Health and Retirement Study. *Journal of Traumatic Stress*.

Jäggi L., Schmid M., **Bürgin D,** Saladin N., Grob A. & Boonmann. (2021). Shared Residential Placement for Child Welfare and Juvenile Justice Youth: Current Treatment Needs and Risk for Adult Criminal Conviction. *Child and Adolescent Mental Health.*

2020

Bürgin D., Kind N., Clemens V., Fegert J.M., Eckert A., Buchheim A., O'Donovan A., Boonmann C.* & Schmid M.* (2020). The Stress of Caring – Resilience and HPA-axis activity in hair samples of youth residential caregivers. *Frontiers in Psychiatry.*

*** Bürgin, D.**, Boonmann, C., Schmid, M., Tripp, P., & O'Donovan, A. (2020). Fact or artefact? Childhood adversity and adulthood trauma in the U.S. population-based Health and Retirement Study. *European Journal of Psychotraumatology*.

Kind N., **Bürgin D.**, Clemens V., Jenkel N., & Schmid M. (2020). Disrupting the disruption cycle - a longitudinal analysis of aggression trajectories, quality of life, psychopathology and self-efficacy in closed youth residential care. *Children and Youth Services Review.*

Kind N., **Bürgin D.**, Fegert J. M. & Schmid M. (2020). What protects youth residential caregivers from burning out? A longitudinal analysis of individual resilience. *International Journal of Environmental Research and Public Health.*

Clemens V., **Bürgin D.**, Eckert A., Kind N., Dölitzsch C., Fegert J.M. & Schmid M. (2020). Hair cortisol in a high-risk population of adolescents and young adults: Associations with adverse childhood experiences linked to missing continuity of care and mental health problems. *Psychiatry Research*.

2019

*** Bürgin, D.**, O'Donovan, A., d'Huart, D., di Gallo, A., Eckert, A., Fegert, J., Schmeck, K., Schmid, M., & Boonmann, C. (2019). Adverse Childhood Experiences and Telomere Length: A Look into the Heterogeneity of Findings. *Frontiers in Neuroscience*.

Gaab J., **Bürgin D.**, Locher C., Werner C., Urech S., Bratschi C., Bartolomé Garcia L., Hauke M., Bitter S., Bohny M. & Bentz. D. (2019). Endogenous Cortisol and Conditioned Placebo Effects on Pain – A Randomized Trial. *Journal of Psychosomatic Research.*

*** Included as a part of this cumulated dissertation**

Book Chapters

Schmid M. & **Bürgin D.** (2021) Spezifische Förderung von Resilienzfaktoren in der stationären Kinder und Jugendhilfe und Transition. Modul zur Resilienz-orientierten Pädagogik, E-Learning: Jugendhilfeverläufe: Aus Erfahrung Lernen (JAEL): Ein Online-Kurs zur Sensibilisierung für Risiko- und Schutzfaktoren im sozialpädagogischen Alltag

Presentations (scientific) congresses

Bürgin D., Boonmann C., Fegert J. M., Jenkel N., Schmeck K., & Schmid M. (2019). The relationship between traumatic experiences and adverse adult functional outcomes of children and adolescents in residential care-preliminary results from a Swiss-wide longitudinal prospective study. 16th European Society of Traumatic Stress Studies (ESTSS) Conference, Rotterdam, Netherlands.

O'Donovan A., Lin J., **Buergin D.**, Niles A., Epel E., & Neylan T., (2019). Early life adversity as a risk factor for ill health and elevated inflammation: Risk and protective factors. 77th Annual Scientific Meeting, American Psychosomatic Society, Vancouver, Canada.

Boonmann C., Jenkel N., Bachmann T., **Bürgin D.**, Erb J., Fux E., d'Huart D., Habersaat S., Palix J., Schröder M., Seker S., Zala E., Fegert J.M., Schmeck K. & Schmid M (2019). JAEL – Jugendhilfeverläufe: Aus Erfahrung Lernen, PSY Kongress, Swiss Society for Psychiatry and Psychotherapy, Bern, Switzerland.

Posters (scientific) congresses

Bürgin D., Kind N., Fegert J., & Schmid M. (2019). What protects our professional caregivers from burning out? A longitudinal analysis of individual resilience. 16th European Society of Traumatic Stress Studies (ESTSS) Conference, Rotterdam, Netherlands.

Gaab J., **Bürgin D.** & Bentz D. (2017). Do endogenous cortisol levels influence the placebo effect? 1st official SIPS Conference on Placebo Studies (SIPS), Leiden, Netherlands.

Invited Presentations

Bürgin D. (January 2020). Childhood Adversity and Adulthood Trauma in the U.S. population-based Health and Retirement Study. Invited presentation at THRIVE Lab (PI: Aoife O'Donovan, PhD), UCSF, San Francisco, CA, USA.

Reviews for Peer-Reviewed Journals

2021	Biological Psychiatry (BPS)
2020	Journal of Traumatic Stress (JTS); International Journal of Behavioral Medicine (JBME); Psychoneuroendocrinology (PNE)

Membership in Scientific Societies

2019 -	Deutschsprachige Gesellschaft für Psychotraumatologie (DeGPT) European Society for Traumatic Stress Studies (ESTSS)

Organization of Scientific Meetings

2020 **LOCO Think Tank**
Organization and preparation of international Think Tank meeting to discuss and elaborate on the LOCO project and possibilities for future collaboration

Grants and Awards

Total Sum of acquired Third-Party Funds: **CHF 350'074**

2018 – 2021 **Associations of Adverse Childhood Experiences and Affective Disorders with Telomere Length and Peripheral Inflammation.**
Gertrude Thalmann Foundation; University Psychiatric Hospitals Basel
Funding: **CHF 337`008**
Role: Co-Investigator (PI: Marc Schmid)

2020 **Funding for Open-Access Publication at University of Basel**
Fact or Artifact? Childhood Adversity and Adulthood Trauma in the U.S. population-based Health and Retirement Study. European Journal of Psychotraumatology.
The Stress of Caring – Resilience and HPA-axis activity in hair samples of youth residential caregivers" Frontiers in Psychiatry
Funding: **USD 3'265**
Role: Applicant

Funding program: "Invite your expert"
PhD Program Health Sciences (PPHS), University of Basel
Funding: **CHF 1'800**
Role: Applicant

2019 **Support of Scientific Collaboration with Prof. O'Donovan (UCSF, THRIVE Lab) within the PhD project "The Effect of Early Adversity on Telomere Maintenance and Inflammation"**
Freie Akademische Gesellschaft (FAG) Basel
Dr. Betond Bonde Fundation
Funding: **CHF 5'290**
Role: Applicant

2018 – 2019 **Funding for external courses during PhD program in Clinical Research at University of Basel, Medical Faculty**
PhD Program Health Sciences (PPHS), University of Basel
Funding: **CHF 1'800**
Role: Applicant

David Bürgin
Basel, March 19th, 2021

Chapter 7: References

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