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PRÓ-REITORIA DE PESQUISA E PÓS-GRADUAÇÃO
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE

LUCIANA CRISTINA MANCIO BALICO

TRADUÇÃO, ADAPTAÇÃO TRANSCULTURAL E VALIDAÇÃO DO PEDIATRICS ACES AND RELATED LIFE EVENT SCREENER – PEARLS - PARA USO NO BRASIL

CAXIAS DO SUL
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Tese apresentada à Universidade de Caxias do Sul, para obtenção do título de doutora em Ciências da Saúde.
Orientadora: Profa. Dra Vandrea Carla de Souza
Coorientador: Prof. Dr. Emerson Rodrigues da Silva

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PROF. DR. JOSÉ MAURO MADI

TRADUÇÃO, ADAPTAÇÃO TRANSCULTURAL E VALIDAÇÃO DO PEDIATRICS ACES AND RELATED LIFE EVENT SCREENER – PEARLS - PARA USO NO BRASIL

Tese de Doutorado submetida à Banca Examinadora designada pelo Colegiado do Programa de Pós- Graduação em Ciências da Saúde da Universidade de Caxias do Sul, como parte dos requisitos necessários para a obtenção do título de doutora em Ciências da Saúde, Linha de Pesquisa: Saúde Materno-Infantil

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Dedicatória

Aos meus filhos, fontes de inspiração para tornar o mundo melhor.

Ao meu esposo, pelo apoio incansável e por me impulsionar na busca dos meus sonhos.

Ao meu pai e irmãos, pelo incentivo e confiança em meu potencial.

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RESUMO

Introdução e justificativa: As Experiências Adversas na Infância (ACEs) têm sido associadas a um impacto significativo na saúde física e mental ao longo da vida, evidenciado por uma relação de dose-resposta entre o escore de ACEs e diversas doenças. No entanto, a ausência de uma ferramenta validada para rastrear ACEs em crianças menores de 12 anos no Brasil ressalta a necessidade de estudos que abordem esse contexto específico.

Objetivos: Este trabalho visou traduzir, adaptar e validar o "*Pediatrics ACEs and Related Life Event Screener (PEARLS)*" para ser aplicado na população brasileira, investigando a associação das ACEs com desfechos em saúde em uma população brasileira além de avaliar o impacto dos níveis de ACEs e identificar os eventos adversos mais relevantes em uma população brasileira.

Metodologia: A metodologia desta tese foi dividida em três etapas principais. Primeiro, realizou-se a tradução, adaptação transcultural e validação do instrumento PEARLS para o português brasileiro (PEARLS-BR), que incluiu tradução, síntese, avaliação por um comitê de especialistas, avaliação pela população-alvo, retrotradução, estudo piloto e análise de algumas propriedades psicométricas (consistência interna, validade de conteúdo e confiabilidade teste-reteste). Na segunda etapa, foi realizado um estudo transversal em um Centro Clínico de Saúde Multidisciplinar e em um Centro de Referência em Atendimento Infantojuvenil de um Hospital Geral, especializado no atendimento a vítimas de violência. Com os dados coletados, realizou-se uma análise fatorial confirmatória (CFA) para identificar os domínios latentes do PEARLS-BR. Por fim, na terceira e última etapa, identificaram-se as associações entre altos escores no PEARLS-BR e problemas de saúde.

Resultados: PEARLS-BR foi testada com 202 participantes, demonstrando excelente compreensão e alta consistência interna (α=0,78-0,81). A validade de conteúdo variou de leve a quase perfeita, e a confiabilidade teste-reteste foi alta (ρ=0,89-0,94). A CFA apoiou um modelo de três fatores: maus-tratos, desafios domésticos e contexto social. O PEARLS-BR mostrou boa consistência e confiabilidade, com invariância de medida para idade e gênero. Escores mais altos em maus-tratos foram associados a aumentos não significativos nas chances de diversos problemas de saúde, enquanto o contexto social aumentou significativamente as chances de pior estado de saúde global. Os resultados indicam uma alta prevalência de ACEs na população estudada, com 78,2% dos cuidadores e 91,3% dos adolescentes relatando uma ou mais adversidades. Pontuações mais altas no PEARLS-BR foram significativamente associadas com pior saúde física, saúde mental, sintomas de TDAH, infecções, distúrbios gastrointestinais e dores de cabeça/enxaquecas. Eventos de vida relacionados foram associados a maiores chances de obesidade e condições atópicas.

Conclusões: A validação do PEARLS-BR representa um avanço significativo na identificação precoce e intervenção em ACEs na população pediátrica do Brasil. A ferramenta demonstrou

aplicabilidade e eficácia, permitindo a comparação com dados internacionais. Isso possibilita a geração de dados que podem informar políticas públicas futuras direcionadas à mitigação dos impactos das adversidades na infância. Além disso, a ferramenta validada no Brasil pode ser adaptada e validada para uso em outros países de língua portuguesa, ampliando seu escopo e utilidade. Pesquisas futuras devem focar na implementação de estratégias de intervenção e na exploração dos determinantes sociais da saúde para reduzir o impacto das ACEs na saúde infantil.

Palavras-chaves: Experiências Adversas da Infância; Tradução e Adaptação Transcultural; Estudos de Validação; Saúde Infantil; Psicometria.

ABSTRACT

Introduction and Justification: Adverse Childhood Experiences (ACEs) have been associated with a significant impact on physical and mental health throughout life, evidenced by a dose-response relationship between the ACE score and various diseases. However, the absence of a validated tool to screen for ACEs in children under 12 years old in Brazil highlights the need for studies that address this specific context.

Objectives: This study aimed to translate, adapt, and validate the “Pediatrics ACEs and Related Life Event Screener (PEARLS)” for use in Brazil. It investigated the association of ACEs with health outcomes in a Brazilian population and evaluated the impact of ACE levels, identifying the most relevant adverse events within this context.

Methodology: The methodology of this thesis was divided into three main stages. First, the translation, transcultural adaptation, and validation of the PEARLS instrument to Brazilian Portuguese (PEARLS-BR) were conducted, including translation, synthesis, expert committee evaluation, target population assessment, back-translation, pilot study, and analysis of psychometric properties (internal consistency, content validity, and test-retest reliability). In the second stage, a cross-sectional study was conducted at a Multidisciplinary Health Clinic and a Reference Center for Child and Adolescent Care at a General Hospital, specialized in the care of violence victims. With the collected data, a confirmatory factor analysis (CFA) was performed to identify the latent domains of PEARLS-BR. Finally, the third stage identified associations between high PEARLS-BR scores and health problems.

Results: The PEARLS-BR was tested with 202 participants, demonstrating excellent comprehension and high internal consistency (α=0.78-0.81). Content validity ranged from slight to almost perfect, and test-retest reliability was high (ρ=0.89-0.94). The CFA supported a three-factor model: maltreatment, household challenges, and social context. PEARLS-BR has shown good consistency and reliability, with measurement invariance for age and gender.

Higher maltreatment scores were non-significantly associated with increased odds of various health issues, while social context significantly increased the odds of poorer global health. Results indicate a high prevalence of ACEs, with 78.2% of caregivers and 91.3% of adolescents reporting one or more adversities. Higher PEARLS-BR scores were significantly associated with poorer physical health, mental health, ADHD symptoms, infections, gastrointestinal disorders, and headaches/migraines. Related life events were linked to higher odds of obesity and atopic conditions.

Conclusions: The validation of PEARLS-BR represents a significant advance in the early identification and intervention in ACEs in the pediatric population of Brazil. The tool demonstrated applicability and effectiveness, allowing for comparison with international data. This enables the generation of data that can inform future public policies aimed at mitigating the impacts of childhood adversities. Additionally, the validated tool in Brazil can be adapted and validated for use in other Portuguese-speaking countries, expanding its scope and utility. Future research should focus on the implementation of intervention strategies and the exploration of social determinants of health to reduce the impact of ACEs on child health.

Keywords: Adverse Childhood Experiences; Translation and Cross-Cultural Adaptation; Validation Studies; Child Health; Psychometrics.

SUMÁRIO

Esta Tese de Doutorado Acadêmico *Stricto Sensu* é apresentada no formato exigido pelo Programa de Pós-Graduação em Ciências da Saúde da Universidade de Caxias do Sul. A mesma é constituída da seção de introdução, limitações do estudo, perspectivas futuras, considerações finais, referências bibliográficas, e, inclusão de artigos originais submetido/publicado em periódico Qualis A na classificação da Coordenação de Aperfeiçoamento de Pessoal em Nível Superior (CAPES).

1 INTRODUÇÃO

Os efeitos das experiências adversas na infância (Adverse Childhood Experiences - ACEs) têm sido amplamente estudados, revelando um impacto significativo na saúde física e mental ao longo da vida. (1-4) Apesar dos avanços na compreensão desses efeitos, muitos aspectos ainda necessitam de investigação mais aprofundada. Segundo dados recentes, a prevalência de ACEs continua alta em diversas populações, inclusive no Brasil (5,6). Estes dados indicam que ainda há muito a ser explorado sobre como esses eventos impactam diferentes grupos e contextos específicos.

Estudos recentes têm demonstrado que as ACEs estão associadas a uma série de problemas de saúde, incluindo distúrbios mentais, comportamentais e doenças crônicas. Por exemplo, Bevilacqua et al. observa que a exposição a ACEs pode levar a uma maior incidência de transtornos de ansiedade e depressão. (7) Hughes et al. relatam que ACEs estão associadas a comportamentos de risco e problemas psicossomáticos. (8) Além disso, pesquisas indicam que as ACEs estão ligadas a vários desfechos físicos, como doenças hepáticas, isquemia cardíaca, câncer de pulmão, doença pulmonar obstrutiva crônica (DPOC), dermatites e infecções. (1,2,9,10) Esses achados ressaltam a importância de intervenções precoces na mitigação dos efeitos negativos das ACEs, abrangendo tanto afcções agudas quanto doenças psicossomáticas.

Apesar do conhecimento existente sobre os efeitos das experiências adversas na infância (ACEs), ainda não está claro como essas experiências influenciam populações específicas e em que medida variáveis contextuais e culturais podem moderar esses efeitos. Até o momento, não existe uma ferramenta validada para rastrear ACEs em crianças menores de 12 anos no Brasil. Este estudo se propos a traduzir, adaptar e validar o “Pediatrics ACEs and Related Life Event Screener (PEARLS)” para que possa ser utilizado na população brasileira de 0 a 18 anos. Dessa forma, será possível investigar a prevalência e os impactos das ACEs em uma amostra brasileira, buscando entender as particularidades desse contexto.

Para facilitar a compreensão, é essencial definir alguns conceitos-chave utilizados ao longo do estudo. Experiências Adversas na Infância (ACEs) referem-se a eventos potencialmente traumáticos ocorridos antes dos 18 anos, incluindo abuso, negligência e disfunção familiar. (1,11) PEARLS é uma ferramenta de rastreio de ACEs, cujo acrônimo significa “*Pediatric ACEs and Related Life Event Screening*”. (12) Essa ferramenta foi traduzida para o português brasileiro como “Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados”. No entanto, optou-se por manter o acrônimo

original em inglês, acrescentando um "Br" ao final para indicar a versão brasileira, a fim de preservar a nomenclatura reconhecida mundialmente e facilitar o reconhecimento e a comparabilidade dos resultados em contextos internacionais. Resiliência descreve a capacidade de se recuperar de dificuldades e adversidades, minimizando seus efeitos negativos. Suporte social, por sua vez, diz respeito à rede de apoio disponível ao indivíduo, que pode ser composta por familiares, amigos e membros da comunidade. (13)

O PEARLS foi inicialmente desenvolvido e validado nos Estados Unidos, em inglês e espanhol, como uma ferramenta abrangente para avaliar ACEs e eventos de vida relacionados, incluindo abuso, negligência, desafios familiares, discriminação, insegurança alimentar e violência comunitária. Criado sob a orientação do *Benioff Children's Hospital Research Center em Oakland* e da *University of California São Francisco*, o PEARLS foi concebido para abordar os fatores de risco associados ao estresse tóxico em crianças e adolescentes. Seu desenvolvimento faz parte de uma iniciativa mais ampla na Califórnia, alinhada ao movimento ACEs Aware, que visa reduzir os impactos das ACEs e do estresse tóxico por meio de uma abordagem colaborativa e interdisciplinar, envolvendo comunidades e profissionais de saúde para transformar os resultados de saúde pública a longo prazo. (14)

A versão original do PEARLS desenvolvida nos Estado Unidos apresentou excelentes propriedades psicométricas, com o alfa de Cronbach variando de 0,61 a 0,81 e de 0,70 a 0,87 na análise fatorial confirmatória (CFA). O ômega de McDonald, que variou de 0,55 a 0,73, reforçou a confiabilidade dos fatores. A CFA sustentou um modelo de três fatores, com índices de ajuste adequados ($X^2(116) = 139,68$, $p = .07$; RMSEA = 0,03 [90% CI: 0,00, 0,04]; CFI = 0,99; TLI = 0,99), além de evidenciar a invariância de medida em termos de idade, gênero e formato de triagem, garantindo que o instrumento mede consistentemente os mesmos construtos entre diferentes grupos. A estrutura de três domínios (Maltreatment, Household Challenges, Social Context) apresentou cargas fatoriais entre 0,44 e 0,83, reforçando a validade de construto do PEARLS. No estudo original, as ferramentas utilizadas para avaliação do constructo incluíram o PEARLS para avaliar ACES e eventos de vida relacionados, o Patient-Reported Outcomes Measurement Information System (PROMIS) para a saúde geral e o Behavior Rating Inventory of Executive Function (BRIEF) para função executiva. O diagnóstico de TDAH foi realizado utilizando códigos da Classificação Internacional de Doenças (CID-10), enquanto o International Study of Asthma and Allergies in Childhood (ISAAC) foi empregado para doenças atópicas. A saúde geral também foi avaliada com códigos da CID-10 extraídos dos registros eletrônicos de saúde e por meio de um questionário. (1,2)

Este estudo do PEARLS-BR é pioneiro ao traduzir, adaptar transculturalmente e validar o instrumento fora dos Estados Unidos, incluindo a avaliação de suas propriedades psicométricas no contexto brasileiro. A validação visa replicar e expandir os achados do

PEARLS original, assegurando que o instrumento seja culturalmente adequado e eficaz na detecção precoce de ACEs na população pediátrica brasileira. As etapas para a validação do PEARLS-BR estão detalhadas no artigo 1, figura 1, página 37 desta tese.

Os objetivos de pesquisa desta tese são diversos. O objetivo geral é traduzir, adaptar e validar o “Pediatrics ACEs and Related Life Event Screener (PEARLS)” para ser aplicado na população brasileira. Entre os objetivos específicos, estão (1) verificar a associação das ACEs com doenças físicas, psíquicas e sociais em uma população brasileira e comparar esses dados com os de outros países; (2) avaliar o impacto dos níveis de ACEs e investigar quais eventos adversos são mais relevantes em uma população brasileira; e (3) examinar as propriedades psicométricas do PEARLS-BR, incluindo a consistência interna (alfa de Cronbach e ômega de McDonald), validade de construto (CFA) e validade convergente (AVE).

Este estudo possui importância prática ao potencialmente informar pediatras e gestores em saúde sobre os dados epidemiológicos relativos às ACEs, possibilitando a implementação de políticas públicas e intervenções que visem reduzir os impactos de ACEs na população brasileira, promovendo saúde e bem-estar. O cérebro infantil é vulnerável às adversidades e, consequentemente, à desregulação do sistema de resposta ao estresse. Detectar precocemente as ACEs é crucial para evitar que o estresse tóxico se torne crônico. Portanto, é necessária uma ferramenta adequada de rastreamento de ACEs, aplicável na prática pediátrica brasileira, para identificar precocemente crianças e adolescentes com altos escores e, consequentemente, com risco aumentado. Isso poderá melhorar as chances de detecção precoce de doenças associadas às ACEs, aumentar as taxas de cura e, principalmente, prevenir o desenvolvimento de doenças. (15)

Do ponto de vista teórico, esta pesquisa contribuirá significativamente para a literatura existente, oferecendo uma visão mais detalhada das ACEs no contexto brasileiro e comparando esses dados com estudos internacionais. Com a validação da ferramenta PEARLS para a população pediátrica brasileira, outros pesquisadores poderão conduzir suas investigações utilizando este instrumento, permitindo a exploração de diversas questões relacionadas às ACEs. Isso promoverá um melhor entendimento dos fatores de risco e proteção e contribuirá para o desenvolvimento de intervenções mais eficazes e específicas para essa população. Além disso, este é o primeiro estudo de validação da PEARLS, além do original, para outra língua, estabelecendo um parâmetro valioso para que outros países possam validar o instrumento em seus próprios contextos linguísticos e culturais. Esta pesquisa servirá como referência metodológica e prática, facilitando a adaptação da PEARLS e promovendo a comparabilidade dos resultados em diferentes populações ao redor do mundo.

A viabilidade da realização deste estudo foi assegurada pela coleta de dados realizada no Centro Clínico de Atenção Multidisciplinar à Saúde e no Centro de Referência em

Atendimento Infantojuvenil do Hospital Geral, ambos reconhecidos como centros especializados no atendimento infantil e adolescente, sendo o Hospital Geral parte da 5ª Coordenadoria Regional de Saúde do Rio Grande do Sul, abrangendo 49 municípios com uma população estimada em aproximadamente 1.200.000 habitantes. (16) Durante a pesquisa, foram empregadas metodologias validadas e um rigoroso controle de qualidade, garantindo a relevância e aplicabilidade dos resultados obtidos.

Esta tese está estruturada para investigar as experiências adversas na infância no contexto brasileiro, a partir da validação da PEARLS-BR. A "Introdução" contextualiza o estudo, definindo conceitos essenciais e enfatizando a relevância de examinar as ACEs neste cenário específico.

Após a Introdução, como resultado da tese, estão incluídos, em forma de capítulos, o primeiro artigo, que já foi submetido e está no prelo, além dos artigos dois e três que serão submetidos para publicação. Também está incluído um capítulo de livro já publicado. O primeiro artigo escrito foi intitulado "*Pediatrics ACES and Related Life Event Screener (PEARLS): Translation, transcultural Adaptation, and Validation to Brazilian Portuguese*". Este artigo, que está no prelo, aborda a tradução, adaptação e validação do "*Pediatrics ACEs and Related Life Event Screener (PEARLS)*" para a população brasileira. O estudo detalha o processo metodológico de tradução e adpatação cultural e apresenta os resultados iniciais da validação do instrumento.

O segundo artigo intitulado "*Pediatric ACEs and Related Life Event Screener (PEARLS-BR) latent domains and child health in a Brazilian sample: A Confirmatory Factor Analysis and Correlation Study*" está em processo de submissão para publicação. Este estudo utilizou a análise fatorial confirmatória para identificar os domínios latentes e correlacioná-los com diversos desfechos de saúde. O estudo compara esses dados com os resultados de pesquisas internacionais, destacando as particularidades do contexto brasileiro.

O terceiro artigo, intitulado "*Adverse Childhood Experiences and Related Life Events Screener (PEARLS-BR), Prevalence and Health Outcomes in a Brazilian Context*", explora a relação entre as ACEs e a saúde das crianças brasileiras. Este estudo transversal analisou dados de crianças e adolescentes, revelando associações significativas entre altos escores no PEARLS-BR e problemas de saúde, como asma e dermatite atópica. O artigo, que está em processo de submissão para publicação, contribui para a literatura ao fornecer evidências sobre a prevalência de ACEs e seus impactos na saúde em uma população pediátrica brasileira, destacando a necessidade de intervenções precoces.

O capítulo intitulado "*Experiências adversas na infância: estresse tóxico e o impacto na saúde da criança*" foi publicado no e-book "*Psicologia e contemporaneidade: fatores psicossociais em diferentes contextos*", no ano de 2021, pela editora EDUCS. O texto examina os efeitos do estresse tóxico na saúde mental e nos desfechos orgânicos durante a infância.

Neste capítulo é destacado que a identificação precoce e ativa das experiências adversas na infância por profissionais de saúde pode fornecer orientações valiosas para as famílias, ajudando a mitigar os danos e impactos na saúde a longo prazo.

As "Limitações do Estudo" abordam as restrições encontradas durante a pesquisa, baseando-se nas análises e discussões presentes nos artigos desenvolvidos ao longo deste doutorado. Entre as principais limitações, destacam-se a ausência de análises de invariância configural, métrica e escalar, devido ao tamanho reduzido e desproporcional das amostras e a limitação geográfica da coleta de dados, que se concentrou na região sul do Brasil.

Em "Perspectivas Futuras", são discutidas as direções futuras da pesquisa, utilizando as informações dos artigos desenvolvidos neste estudo. Entre as principais perspectivas, estão a adaptação e validação do instrumento PEARLS-BR em diferentes contextos regionais, o desenvolvimento de tratamentos e intervenções eficazes para mitigar o impacto das adversidades na infância e a necessidade de estudos longitudinais e amostras maiores para validar as descobertas iniciais.

As "Considerações Finais" baseiam-se nas análises e discussões realizadas ao longo dos três artigos desenvolvidos durante o doutorado. Esta seção sintetiza os principais achados, reforça a importância da investigação das ACEs no Brasil e propõe recomendações para futuras pesquisas e políticas públicas.

Após as referências, a tese inclui como apêndices o PEARLS-BR Criança, o PEARLS-BR Adolescente e o PEARLS-BR Autorrelato, que são versões traduzidas, adaptadas e validadas do questionário original para uso na populaçao brasileira. Além desses, outros documentos anexos são disponibilizados, como o acordo assinado entre a UCS e a detentora dos direitos autorais do PEARLS, a aprovação da tradução reversa pelos detentores dos direitos autorais, e a autorização dos detentores dos direitos autorais do PROMIS para a utilização da ferramenta neste estudo.

Ao considerar a abrangência das experiências adversas na infância e seu impacto significativo na saúde das crianças e adolescentes, este estudo visa fornecer insights valiosos para intervenções futuras e políticas públicas no Brasil. Com a validação do instrumento PEARLS-BR, espera-se aprimorar a detecção precoce das ACEs e suas consequências, contribuindo para a literatura internacional e promovendo a saúde e o bem-estar da população pediátrica brasileira. Além disso, uma importante contribuição deste estudo é deixar à disposição dos pesquisadores brasileiros uma ferramenta de triagem validada especificamente para a população pediátrica.

2 **CAPÍTULO 1** – ARTIGO 1: PEDIATRICS ACES AND RELATED LIFE EVENT SCREENER (PEARLS): TRANSLATION, TRANSCULTURAL ADAPTATION, AND VALIDATION TO BRAZILIAN PORTUGUESE

Full title: Pediatrics ACES and Related Life Event Screener (PEARLS): Translation, transcultural Adaptation, and Validation to Brazilian Portuguese

Short title: PEARLS Validation to Brazilian Portuguese

Abstract:

Objective: Adverse Childhood Experiences (ACEs) have been associated with negative health outcomes. Screening for ACEs is crucial for improving health results, however, there is a shortage of standardized tools designed for children in Brazilian Portuguese. This study aimed to translate, culturally adapt, and validate the Pediatrics ACES and Related Life Event Screener (PEARLS) for use in Brazil.

Method: A cross-sectional study was conducted at a Multidisciplinary Health Care Clinical Center and a General Hospital-Reference Center for Child and Adolescent Care. PEARLS was translated and culturally adapted following a methodology that includes translation, synthesis, expert committee evaluation, target audience evaluation, back translation, and pilot study. Internal consistency, content validity, and test-retest reliability were assessed.

Results: The PEARLS-BR versions for Children, Teen, and Teen Self-Report were developed and subjected to pilot testing with 202 subjects. Participants demonstrated excellent comprehension, with Verbal Rating Scale median scores of 4 (IQR 4-5). Internal consistency was high, with Cronbach's alpha coefficients ranging from 0.78 to 0.81. Content validity, assessed by Kappa, indicated slight to almost perfect agreement across constructs. Test-retest reliability, assessed by Spearman's correlation coefficient, ranged from 0.89 to 0.94.

Conclusions: PEARLS-BR (Child, Teen, and Teen Self-Report versions) were successfully translated, culturally adapted, and validated for assessing ACEs in Brazilian children and adolescents. This tool fills a crucial gap in ACE assessment in the Brazilian context, aligning with global recommendations for screening ACEs to improve overall health outcomes.

Keywords: Adverse Childhood Experiences; Translation; Validation Studies; Screening

Introduction

Adverse Childhood Experiences (ACEs) are defined as stressful or traumatic events that children experience before age 18 years. (1) These adversities are associated with the development of long-term health conditions and immediate adverse health outcomes that extend from childhood/adolescence into adulthood. (2-4) The landmark ACE Study conducted in adults revealed a clear dose-response relationship between ACE scores and their impact on health, indicating that ACE scores are associated with an increased likelihood of developing severe psychological issues such as substance dependency, depression, and suicide, as well as physical conditions including hepatitis, cardiac ischemia, lung cancer, and chronic obstructive pulmonary disease in adulthood. (2)

The groundbreaking ACE Study catalyzed the development of the "Pediatrics ACEs and Related Life Event Screener (PEARLS)," designed to screen for ACEs in pediatric population, thus enabling early identification and intervention. Recent investigations into the impact of ACEs in children have revealed associations with adverse health outcomes, including compromised executive functioning, (3,5) increased susceptibility to respiratory (3) and dermatological conditions, (3,6) and harms for the immune and endocrine systems. (3,4) Notably, high ACE scores are associated with a higher prevalence of asthma, (3,7) respiratory tract infections, (3,7) and learning difficulties in schoolchildren, (3,8) as well as with sleep disturbance, (9) development delay, and cognitive impairment (1,10) in infants. Adolescents exposed to ACEs are at risk for obesity, (11) bullying, violence, (12) smoking, (13) early pregnancy, and parenthood. (14) These findings underscore the importance of early identification and intervention.

It is hypothesized that the link between ACEs and poor health is due to abnormal functioning of the hypothalamic-pituitary-adrenal (HPA) axis, often assessed through cortisol patterning, and inflammation, typically measured via C-reactive protein (CRP). (15) This chronic stress response leads to heightened inflammation, increasing susceptibility to infections and autoimmune conditions. (16) Inflammatory and epigenetic markers, such as C-reactive protein and telomeres, (17) are implicated in the long-lasting impact of ACEs, potentially influencing intergenerational transmission. Timely identification of ACEs is crucial to break the cycle of toxic stress.

While screening for ACEs is recommended by prominent health organizations, including the Center for Disease Control and Prevention (CDC), (18) the American Academy of Pediatrics (AAP), (4) and the World Health Organization (WHO), (1) there is currently a gap in research regarding prevalence and associations of ACEs with physical and psychological diseases in Brazilian children. Additionally, the absence of validated and standardized instruments in Brazilian Portuguese for ACE assessment highlights the need for validated tools that are culturally and contextually appropriate. The use of non-validated instruments can result in inaccurate assessments, leading to inappropriate interventions, which ultimately compromise the quality of care.

Given the vulnerability of the developing brain to adversities, early detection of ACEs is essential to prevent chronic toxic stress. Therefore, this pioneering study, the first outside the United States, aims to translate, culturally adapt, and validate the PEARLS-BR questionnaire through the process of reliability testing, face validity, and gathering evidence based on content and internal structure. The goal is to establish the PEARLS-BR as a reliable tool for use in Brazilian pediatric practice, supporting the early identification of ACE-related diseases.

Materials and Methods

The cultural adaptation of the PEARLS (Child, Teen, and Teen self-report versions) was conducted with authorization from the developers under a licensing agreement signed between the University of California San Francisco (UCSF), the copyright holder of the instrument in question, and the Universidade de Caxias do Sul (UCS). This research received approval from the UCS Research Ethics Committee (number 6.090.525).

Instruments

PEARLS. PEARLS is a self-applicable questionnaire designed to screen for ACEs in individuals from birth to eighteen years old. Both the PEARLS Child and PEARLS Teen versions consist of 17 questions, with PEARLS Teen including an additional two questions. These items assess the occurrence of sexual, physical, or emotional violence; neglect; parental mental illness, substance abuse, or incarceration; parental separation or divorce; and domestic violence, as well as explore food insecurity, housing instability, community violence, and discrimination. PEARLS Child and PEARLS Teen are completed by a caregiver, while PEARLS Teen Self-Report is completed by the adolescent. Scoring involves summing the affirmative responses on the questionnaire. The resulting PEARLS score can be interpreted as either continuous or categorical. When considered continuously, it allows for an assessment of ACEs, Related Life Events, or the total PEARLS score, providing a nuanced view of the

individual's experiences. Alternatively, it can be categorized, particularly for ACEs, into groups such as 0, 1-3, and 4+, which helps in identifying different levels of exposure to adverse experiences. (3)

The PEARLS instrument was initially developed and validated in the United States, demonstrating good psychometric properties. The original version showed adequate reliability and validity, with Cronbach's alpha ranging from 0.61 to 0.87 and factor loadings between 0.44 and 0.83. Confirmatory Factor Analysis (CFA) supported a three-factor model (Maltreatment, Household Challenges, Social Context), with satisfactory fit indices ($X^2(116) = 139.68$, $p = .07$; RMSEA = 0.03; CFI = 0.99; TLI = 0.99), and also demonstrated measurement invariance across age, gender, and screening format. (3,4)

QUESI. The Childhood Trauma Questionnaire (CTQ) is a validated version for use in the Brazilian population known as the “Questionário sobre Traumas na Infância” (QUESI). (19,20) It is designed for adolescents (from 12 years old) and adults, where respondents rate the frequency of 28 statements related to childhood trauma experiences on a five-point Likert scale. The QUESI assesses occurrences of sexual, physical, or emotional abuse, as well as emotional and physical neglect. In this study, the QUESI was employed to calculate the convergent validity of the PEARL-BR. Both caregivers and teenagers over 13 years old completed the QUESI for this purpose.

Procedure

International procedures recommended by the literature and based on the best available methodological practices (21,22) were followed in this cross-sectional study. The process of translation and transcultural adaptation followed the model used by Borsa et al (23) composed of 6 stages (Figure 1).

Evidence Based on Content

The PEARLS was translated from the original language, English, to Brazilian Portuguese by two bilingual English professors, whose native language is Portuguese, resulting in two translated versions of the instrument (T1 and T2). Following the translation process, the two versions were discussed and merged into the Synthesis 1 (S1). The S1 was submitted to the appraisal of an expert committee composed of a pharmacist, a social worker, and a pediatrician, experts in the fields of health sciences and public and social policies and fluent in English language. Each expert judge analyzed the content validity, considering the four dimensions suggested by the literature: semantic, idiomatic, experimental, and conceptual. (21,22) Additionally, aspects such as structure, layout, instrument instructions, comprehensiveness, and adequacy of expressions in each item were also evaluated. (23)

They also compared the original instrument and the S1, ensuring the best fit with the context and experiences of Brazilian children and teens. The committee collectively discussed each suggestion for each item, arriving at a conclusion together, successfully consolidating and obtaining synthesis 2 (S2).

The face validity was conducted with the target population to assess content validation and the overall meaning of the S2. The instrument was evaluated by healthcare professionals (nutritionist, pediatrician, pediatric resident, nephrology resident, Pediatric Neurologist, Physical Therapist, social worker, Nurse Technician, psychologist and nurse), and academics from health sciences fields (medicine, nutrition and physiotherapy), as well as by a convenience sample of individuals treated at a Multidisciplinary Health Care Center. A total of 30 participants were individually interviewed after signing the informed consent form. They evaluated the clarity, comprehensibility, and adequacy of S2 using a structured feedback form. This form allowed participants to assess each item of the instrument and suggest modifications, including potential synonyms or changes in wording to enhance the instrument's clarity and relevance. Based on the received suggestions and the analysis of the interviewees' feedback, the expert committee decided to maintain version S2 without significant alterations.

The version S2 of the instrument was translated back into English by two different translators. One translator is a bilingual professor whose native language is English (TR1), while the other is a bilingual professor whose native language is Portuguese (TR2). This stage aimed to assess how well the translated version (S2) reflected the content of the original version. Two back translations of the instrument (TR1 and TR2) were obtained, and a third bilingual individual synthesized them into a document named S1TR. Thus, PEARLS-BR was obtained and had the approval of the developer.

Evidence Based on Relationships with External Variables

The pilot study of PEARL-BR was carried out from June 2023 to January 2024. It was conducted at both a Multidisciplinary Health Care Center and a General Hospital-Reference Center for Child and Adolescent Care. The General Hospital is part of the 5th Regional Health Coordination of Rio Grande do Sul, covering 49 cities with a population of approximately 1.200.000 inhabitants. Families participating in the pilot study were recruited from a convenience sample in the waiting room, where they signed the consent form, and adolescents additionally signed the assent form. It was aimed to recruit 200 caregivers. Specifically, caregivers were included if they met the following criteria: aged over 18, primary caregiver of a child aged 18 or younger, Brazilian Portuguese speaker, and not having another child included in the same study.

During the pilot study phase, participants completed the PEARL-BR questionnaire, the QUESI, and answered sociodemographic information. Following this, they responded to a five-

point verbal rating scale (VRS) aimed to assessing the overall clarity of the instrument. The pivotal query of this scale was: "Did you understand what was asked in the PEARLS-BR questionnaire?" Scores ranged from a minimum of "1" ("no comprehension") to a maximum of "5" ("complete comprehension"). A score of three or below denoted inadequate understanding. Moreover, alongside caregivers, 10 healthcare professionals recruited by a convenience sample from the Multidisciplinary Health Care Center also provided feedback through the VRS after signing the informed consent form. The test-retest reliability assessment, a key measure of reliability, was conducted 30 days after caregivers completed the PEARLS-BR in the pilot study, with the aim of obtaining a minimum of 50 retests.

Statistical analysis

All the study data were collected and managed using REDCap (Research Electronic Data Capture), hosted at UCS (24,25). REDCap is a secure web-based software platform designed to support data capture for research studies. Statistical analysis was conducted using the R software version 3.5.2. Continuous variables were expressed as median and interquartile range. Histograms and the Shapiro-Wilk test were used to test quantitative data for normality of distribution. Internal consistency of the instrument was assessed using Cronbach's alpha coefficient, with values above 0.75 indicating satisfactory consistency. The 95% confidence intervals for the Cronbach's alpha were computed employing the Duhachek method (PSYCH package). Comprehension and semantic equivalence were evaluated using the verbal rating scale (VRS), where a score above three signified adequate understanding. The Kappa concordance coefficient was employed to assess the content validity index of the instrument, with values exceeding 0.60 considered satisfactory. Test-retest reliability was determined using the Spearman correlation coefficient, with values above 0.75 indicating reliable consistency.

Results

The stages and procedures for translation, transcultural adaptation, and validation followed the flow outlined in Figure 1. Table 1 presents all items of the instrument in their original versions, progressing through each phase until the final version.

To enhance clarity in the title, the term “adverse childhood experiences” was chosen instead of the acronym “ACE's”. In the original PEARLS, questions were presented in the present perfect tense, indicating actions in the past with relevance to the present. However, since the present perfect tense does not exist in Brazilian Portuguese, the decision was made to employ the past perfect indicative, indicating that if an action occurred at any point in the past, it should already be considered as positive in the response.

During the synthesis evaluation by the expert committee, eight points were raised: seven concerning semantic, idiomatic, experiential, or conceptual equivalence, and one regarding the layout and formatting of the instrument. Four of these points were modified resulting in S2 (final version). Changes included adjusting the layout with increased line spacing while maintaining the original PEARLS structure. Additionally, question 6 of part 1 was revised to ensure semantic equivalence, and question 2 of part 1 was expanded to include examples of mental illnesses. Question 9 of part 2 was also revised to align with the original text. The remaining four points were retained the same after analysis by the experts committee.

During the evaluation phase of the PEARLS-BR by a diverse target audience of 30 individuals, including healthcare professionals, caregivers, and academics, each component was meticulously reviewed. Among these participants, 80% (n=24) found the version to be clear, comprehensible, and well-suited to the Brazilian context, while the remaining 20% (n=6) provided feedback prompting a detailed item-by-item review. Following consultations with the expert committee, it was decided to maintain version S2 without alterations. Additionally, after understanding the nuances of Brazilian grammar and the use of gender-specific endings such as "o" and "a" in words like "filho/filha", the original PEARLS authors approved the PEARLS-BR version.

To ensure the validity of the study, a pilot study was conducted involving the preliminary application of the instrument in a sample representing the target population. A total of 202 caregivers participated: 133 responded to the PEARLS-BR Child, 69 to the PEARLS-BR Teen, and adolescents over 13 years old completed the PEARLS-BR Teen Self-Report. Throughout this process, the appropriateness of the items in terms of their meaning and comprehensibility, as well as the instructions for test administration, was assessed. No adjustments were deemed necessary, indicating the readiness of the instrument for use. The characteristics of the children, adolescents, and their respective caregivers involved in this phase are shown in Table 2.

The VRS within the PEARLS-BR Child and Teen, as evaluated by caregivers, demonstrated strong comprehension and semantic equivalence, achieving a median score of 4 (IQR: 4-5). Similarly, adolescents completing the PEARLS-BR Teen Self-Report rated the instrument similarly, with a median score of 4 (IQR: 4-5). Additionally, ten healthcare professionals assessed comprehension and semantic equivalence, yielding a median score of 5 (IQR: 4-5).

A measurement of internal consistency, as assessed through Cronbach's alpha, revealed high reliability across all versions of PEARLS-BR. Specifically, the Child version exhibited an alpha coefficient of 0.81 (95% CI: 0.77-0.86), the Teen version 0.79 (95% CI: 0.72-0.85), and the Teen Self-Report version 0.78 (95% CI: 0.71-0.85).

At the outset of this analysis, it is pertinent to clarify that the levels of agreement are

being assessed in accordance with the QUESI. The evidence of convergent validity, assessed using Kappa, indicated varying degrees of agreement for the emotional abuse construct across different versions of the instrument: moderate agreement (0.50) for the Child version, fair agreement (0.33) for the Teen version, and moderate agreement (0.51) for the Teen Self-Report version. Similarly, moderate agreement was observed for the physical abuse construct across all versions, with values of 0.52, 0.47, and 0.49 for the Child, Teen, and Teen Self-Report versions, respectively. Regarding the sexual abuse construct, substantial agreement (0.67, 0.79) and almost perfect agreement (0.83) were noted across the same versions. Furthermore, the physical neglect construct showed slight agreement (0.17, 0.15) for the Child and Teen versions, and fair agreement (0.26) for the Teen Self-Report version. The instrument used to make these comparisons measures slightly different outcomes, thereby providing additional context for interpreting the agreement levels.

The test-retest reliability results from the Spearman test demonstrated a strong positive and statistically significant agreement between the initial and subsequent responses, obtained after a 30-day interval. Specifically, for the PEARLS-BR Child version, $\rho = .91$; for the PEARLS-BR Teen version, $\rho = .90$; and for the PEARLS-BR Teen self-report version, $\rho = .94$. In this phase, a total of 61 participants were involved, with 43 responding to the Child version and 18 to the Teen and Teen Self-Report versions, respectively.

The final version of PEARL-BR Child is available in Supplementary Material 1 (Apendice A), while PEARLS-BR Teen can be found in Supplementary Material 2 (Apêndice B), and PEARLS-BR Teen Self-Report is available in Supplementary Material 3 (Apêndice C).

Discussion

This study presents the Brazilian Portuguese version of the PEARLS instrument, tailored for screening ACEs in individuals from birth to eighteen years old within the Brazilian context. The development of PEARLS-BR followed a comprehensive process involving translation, cultural adaptation, and validation, complying the existing literature. (21,22) The methodology adhered to guidelines proposed by Borsa et al, (23) previously successful in Brazil for translating and validating several instruments. (26-28)

The translation and back-translation process, along with their syntheses, were meticulously conducted, facilitated by the structured and high-quality services provided by the academic language center. The expert committee identified 8 discussion points, resulting in modifications to 4 items while preserving the essence of the original instrument. The committee, comprising esteemed faculty members holding doctoral degrees, ensured the reliability of their work, given their active engagement in health sciences, public policies, and social sciences.

The PEARLS-BR addresses a critical gap in screening ACEs within the Brazilian population, focusing specifically on individuals aged from birth to eighteen years old, unlike other tools limited to those above 12 years. Active involvement of caregivers and healthcare professionals was crucial for refining the screener, enhancing item clarity and comprehension. Engaging with diverse stakeholders ensured semantic, idiomatic, and conceptual equivalence, making the tool comprehensible and applicable to the target population. The VRS, which measured comprehension and semantic equivalence, was also adequate for the tool's face validity.

The PEARLS-BR demonstrated satisfactory internal consistency across all three versions. Additionally, the Spearman test showed strong and statistically significant agreement between initial and subsequent responses for all PEARLS-BR versions, indicating robust test-retest reliability. The results confirm the content validity of PEARLS-BR in identifying traumatic experiences during childhood and adolescence, especially concerning sexual abuse in the Teen self-report version. Notably, while the QUESI (19,20) was utilized for comparison, it evaluates different components. Whereas the PEARLS (1,4) assess ACEs from birth to eighteen years across maltreatment, household challenges, and social context domains, the QUESI examines the frequency of five components (sexual, physical, and emotional abuse, emotional and physical neglect), in individuals aged 12 and older. (20) Furthermore, all QUESI components fall within the maltreatment domain of the PEARLS. Nonetheless, content validity was confirmed through healthcare professional assessments, content analysis during face validity, pilot study, and QUESI comparison.

Despite data collection being limited to a sample from the southern region of Brazil utilizing public health services, the PEARLS-BR can be utilized nationwide due to its adherence to rigorous scientific processes, proposed by the literature, similar to other questionnaires and scales also validated in Brazil using the same methodology. (23,26-28) The tool's reliability and applicability in diverse healthcare settings facilitates open communication and comfortable disclosure of sensitive information.

The PEARLS-BR serves as a practical tool for healthcare professionals in primary care settings, aiming to screen ACEs for children and adolescents. This instrument, similar to the original PEARLS, is not intended for psychodiagnostics but rather as a valuable resource for professionals who may lack access to specialized psychology or social services. (1) It also serves as a valuable research instrument, facilitating studies aimed at understanding and addressing ACEs in diverse populations.

Further research is necessary to develop effective treatments and interventions to mitigate the impact of ACEs on individuals' well-being. Routine screening can provide crucial data to assess the economic burden of ACEs, (29) and guide investment in strategies to improve population health. However, a limitation of this study was the absence of confirmatory

factor analysis and assess measurement invariance. Future studies should focus on conducting confirmatory factor analysis and assessing measurement invariance across diverse populations to validate construct validity. Ongoing efforts to standardize the PEARLS underscore the importance of additional research to establish its psychometric properties in the Brazilian context.

PEARLS-BR underwent a successful translation into Brazilian Portuguese, along with cultural adaptation and validation, enabling its utilization for assessing ACEs within the pediatric Brazilian population.

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Table 1: Adaptations of the Pediatric ACEs and Relevant Life Events Screener (PEARLS) in the translation and transcultural adaptation to Brazilian Portuguese process[a].

Item	Original	S1	S2	S1TR	Final Version
Title on the cover	PEARLS Pediatrics ACEs and Related Life Events Screener Teen	PEARLS Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados ADOLESCENTE	PEARLS Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados ADOLESCENTE	PEARLS Pediatrics Adverse Childhood Experiences and Related Life Events Screener Teen	PEARLS-BR Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados ADOLESCENTE
Instruction on the cover	Many families experience stressful events in their lives. Over time these experiences may affect your child's health and wellbeing. There are many things you can do and may already be doing to help. Because these events are so common, we are offering resources to all caregivers in our clinic on how to support your child and yourself. We are asking everyone these questions. Some people find that answering the questions gives you time to think about how certain experiences may be impacting your child's health and what you can do to help. Your answers help us to support you and your child to be as healthy as possible. The survey is confidential and optional*****. Your experiences are your own and no matter	Muitas famílias experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a saúde e o bem estar do seu filho(a). Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar seu filho(a) e você mesmo. Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a saúde do seu filho(a) e o que você pode fazer para ajudar. Suas respostas nos ajudam a apoiar você e seu filho a serem o mais saudáveis	Muitas famílias experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a saúde e o bem estar do seu filho(a). Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar seu filho(a) e você mesmo. Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a saúde do seu filho(a) e o que você pode fazer para ajudar. Suas respostas nos ajudam a apoiar você e seu filho a serem o mais saudáveis	Many families experience stressful events throught their lives. Over time, these experiences can affect your health and well-being. There are many things that you can do or that may you are already doing to help. As these events are very common, we are offering resources to all the caregivers in our clinic about how to support you. We are asking everyone these questions. For some people, answering the questions helps them to think about how certain experiences might impact your health. Your answers help us to support you to be as healthy as possible. The survey is confidential and optional*. The experiences are yours and no matter what you choose to share, we're here	Muitas famílias experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a saúde e o bem estar do seu filho(a). Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar seu filho(a) e você mesmo. Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a saúde do seu filho(a) e o que você pode fazer para ajudar. Suas respostas nos ajudam a apoiar você e seu filho a serem o mais saudáveis

	what you choose to share, we are here to help. *It is important for you to know though that if you tell us that your child is currently unsafe or being physically, verbally, or sexually hurt or neglected we may need to share this with other authorities.	possível. A pesquisa é confidencial e opcional*. As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar. *Porém, é importante saber que caso você nos conte que no momento seu filho não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.	possível. A pesquisa é confidencial e opcional*. As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar. *Porém, é importante saber que caso você nos conte que no momento seu filho não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.	to help. *It is important that you know that, if at this time you are not safe, or is being physically, verbally, or sexually abused or neglected, we will possibly have to share this information with the authorities.	possível. A pesquisa é confidencial e opcional*. As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar. *Porém, é importante saber que caso você nos conte que no momento seu filho não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.
Page 1 Title	Pediatric ACEs and Related Life Events Screener (PEARLS)	Experiências Adversas Na Infância Pediátrico e Rastreador De Eventos De Vida Relacionados (PEARLS)	Experiências Adversas na Infância Pediátrico e Rastreador De Eventos De Vida Relacionados (PEARLS)	Pediatric Adverse Childhood Experiences and Related Life Events Screener (PEARLS-BR)	Experiências Adversas na Infância Pediátrico e Rastreador De Eventos De Vida Relacionados (PEARLS-BR)
Page 1 Sentence under the title	TEEN - To be completed by: Caregiver	ADOLESCENTE – deve ser preenchido pelo: PAI/MÃE/RESPONSÁVEL	ADOLESCENTE – deve ser preenchido pelo: PAI/MÃE/RESPONSÁVEL	ADOLESCENT – must be filled out by: father/mother/guardian	ADOLESCENTE – deve ser preenchido pelo: PAI/MÃE/RESPONSÁVEL
Page 1 Instruction	At any point in time since your child was born, has your child seen or been present when the following experiences happened? Please include past and present experiences. Please note, some questions have more than one part separated by “OR.” If any part of the question is answered “Yes,” then the answer to the entire question is “Yes.”	Em algum momento desde o nascimento de seu filho(a), ele/ela viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes. Observe que algumas perguntas têm mais de uma parte separada por “OU”. Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".	Em algum momento desde o nascimento de seu filho(a), ele/ela viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes. Observe que algumas perguntas têm mais de uma parte separada por “OU”. Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".	At any point since the birth of your child, has your son or daughter been present when the following experiences happened? Include past and present experiences. Note that some questions have more than one part separated by “OR”. If the answer to any part of the question is "Yes”, the answer to the whole question is "Yes".	Em algum momento desde o nascimento de seu filho(a), ele/ela viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes. Por favor, observe que algumas perguntas têm mais de uma parte separada por “OU”. Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".

Page 1 **Part 1** **Item 1**	Do you think your child ever felt unsupported, unloved and/or unprotected?	Você acha que seu filho(a) já se sentiu sem apoio, sem amor e / ou desprotegido?	Você acha que seu filho(a) já se sentiu sem apoio, sem amor e / ou desprotegido?	Do you think that your child has ever felt a lack of support, unloved, and/or unprotected?	Você acha que seu filho(a) já se sentiu sem apoio, sem amor e / ou desprotegido?
Page 1 **Part 1** **Item 2**	Has your child ever lived with a parent/caregiver who had mental health issues? (For example, depression, schizophrenia, bipolar disorder, PTSD, or an anxiety disorder)	Seu filho(a) já morou com um dos pais/ responsável que apresentava problemas de saúde mental?	Seu filho(a) já morou com um dos pais/responsável que apresentava problemas de saúde mental? (Por exemplo, depressão, esquizofrenia, transtorno bipolar, transtorno de estresse pós-traumático e/ou transtorno de ansiedade.)	Has your child ever lived with a parent/guardians that experienced mental health problems? (for example, depression, schizophrenia, bipolar disorder, post-traumatic stress disorder and/or anxiety disorder).	Seu filho(a) já morou com um dos pais/responsável que apresentava problemas de saúde mental? (Por exemplo, depressão, esquizofrenia, transtorno bipolar, transtorno de estresse pós-traumático e/ou transtorno de ansiedade.)
Page 1 **Part 1** **Item 3**	Has a parent/caregiver ever insulted, humiliated, or put down your child?	Algum dos pais/responsável já insultou, humilhou ou rebaixou seu filho(a)?	Algum dos pais/responsável já insultou, humilhou ou rebaixou seu filho(a)?	Has any parent/guardian ever insulted, humiliated or demeaned your child?	Algum dos pais/responsável já insultou, humilhou ou rebaixou seu filho(a)?
Page 1 **Part 1** **Item 4**	Has the child's biological parent or any caregiver ever had, or currently has a problem with too much alcohol, street drugs or prescription medications use?	Um dos pais biológicos da criança ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?	Um dos pais biológicos da criança ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?	Has a biological parent or guardian ever had, or currently has any problem with excessive use of alcohol, drugs, or prescription medications?	Um dos pais biológicos da criança ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?
Page 1 **Part 1** **Item 5**	Has your child ever lacked appropriate care by any caregiver? (For example, not being protected from unsafe situations, or not cared for when sick or injured even when the resources were available)	Seu filho(a) já teve falta de cuidados adequados por parte de algum responsável? (por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis).	Seu filho(a) já teve falta de cuidados adequados por parte de algum responsável? (por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis).	Has your child ever experienced a lack of adequate care on the part of a parent/guardian? (for example, not being protected in unsafe situations, or not being taken care of when sick or injured, even when the resources were available).	Seu filho(a) já teve falta de cuidados adequados por parte de algum responsável? (por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis).

Page 1 **Part 1** **Item 6**	Has your child seen or heard a parent/caregiver: (Mark yes, if any are true for you or your family) screamed at, sworn at, insulted, or humiliated by someone they know? ever slapped, kicked, punched, beaten up or hurt with a weapon?	Seu filho já viu ou ouviu um dos pais/responsável: (assinale sim, se qualquer um for verdadeiro para você ou sua família). sendo gritado(a), xingado(a), insultado(a) ou humilhado(a) por outro adulto? sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?	Seu filho(a) já viu ou ouviu um dos pais/responsável: (Assinale sim, se qualquer um for verdadeiro para você ou sua família). Sendo tratado a gritos ou xingado(a), insultado(a) ou humilhado(a) por outro adulto? OU sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?	Has your child ever seen/heard a parent/guardian: (Mark “yes”, if any are true for you or your family). Being screamed or sworn at, insulted, or humiliated by another adult? OR being slapped, kicked, punched, beaten, or injured with a weapon?	Seu filho(a) já viu ou ouviu um dos pais/responsável: (Assinale sim, se qualquer um for verdadeiro para você ou sua família). Sendo tratado a gritos ou xingado(a), insultado(a) ou humilhado(a) por outro adulto? OU sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?
Page 1 **Part 1** **Item 7**	Has any adult in the household: (Mark yes, if any are true for you or your family) often or very often pushed, grabbed, slapped, or thrown something at your child? ever hit your child so hard that your child had marks or was injured? ever threatened your child or acted in a way that made your child afraid that they might be hurt?	Algum adulto na casa (assinale sim, se qualquer um for verdadeiro para você ou sua família). frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em seu filho(a)? já bateu em seu filho(a) com tanta força que deixou marcas ou o/a machucou? já ameaçou seu filho(a) ou agiu de maneira que o/a fez ficar com medo de se machucar?	Algum adulto na casa (assinale sim, se qualquer um for verdadeiro para você ou sua família). frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em seu filho(a)? OU já bateu em seu filho(a) com tanta força que deixou marcas ou o/a machucou? OU já ameaçou seu filho(a) ou agiu de maneira que o/a fez ficar com medo de se machucar?	Has any adult at household: (Mark “yes” if any are true for you or your family). Frequently or very frequently pushed, grabbed, spanked, or thrown something at your child? OR ever hit your child with such force that it left marks or hurt your child? OR ever threatened your child or acted in such a way that it made your child afraid of being hurt?	Algum adulto na casa (assinale sim, se qualquer um for verdadeiro para você ou sua família). frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em seu filho(a)? OU já bateu em seu filho(a) com tanta força que deixou marcas ou o/a machucou? OU já ameaçou seu filho(a) ou agiu de maneira que o/a fez ficar com medo de se machucar?
Page 1 **Part 1** **Item 8**	Has your child ever experienced sexual abuse? (For example, anyone touched your child or asked your child to touch that person in a way that was unwanted, or made your child feel uncomfortable, or anyone ever attempted or actually had oral, anal, or vaginal sex with your child)	Seu filho(a) já sofreu abuso sexual? (por exemplo, alguém tocou em seu filho(a) ou pediu a ele/ela que tocasse essa pessoa de uma forma indesejada ou fez seu filho(a) se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com seu/sua filho(a))	Seu filho(a) já sofreu abuso sexual? (por exemplo, alguém tocou em seu filho(a) ou pediu a ele/ela que tocasse essa pessoa de uma forma indesejada ou fez seu filho(a) se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com seu/sua filho(a))	Has your child ever experienced sexual abuse? (Por example, anybody touched your child or asked him/her to touch that person in an unwanted way or made your child feel uncomfortable, or someone attempted or actually performed oral, anal or vaginal sex with your child.)	Seu filho(a) já sofreu abuso sexual? (por exemplo, alguém tocou em seu filho(a) ou pediu a ele/ela que tocasse essa pessoa de uma forma indesejada ou fez seu filho(a) se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com seu/sua filho(a))

Page 1 Part 1 Item 9	Has your child ever lived with a parent/caregiver who went to jail/prison?	Seu filho(a) já morou com um dos pais/responsável que foi para a cadeia/ prisão?	Seu filho(a) já morou com um dos pais/responsável que foi para a cadeia/ prisão?	Has your child ever lived with parents/guardians that went to jail/prison?	Seu filho(a) já morou com um dos pais/responsável que foi para a cadeia/ prisão?
Page 1 Part 1 Item 10	Have there ever been big changes in the relationship status of the child's caregiver(s)? (for example, a parent/caregiver got a divorce or separated, or a romantic partner moved in or out)	Já houve mudanças significativas no status de relacionamento do(s) responsável(eis) da criança? (por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma?)	Já houve mudanças significativas no status de relacionamento do(s) responsável(eis) da criança? (por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma?)	Have there been significant changes in the relationship status of the child's parents/guardians? (for example, parents/guardians got divorced or separated, or a romantic partner moved into or out of the same residence?)	Já houve mudanças significativas no status de relacionamento do(s) responsável(eis) da criança? (por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma?)
Page 1 Footer	How many "Yes" did you answer in Part 1? Please continue to the other side for the rest of questionnaire.	Quantos "Sim" você respondeu na Parte 1? Por favor continue respondendo o restante do questionário do outro lado da página.	Quantos "Sim" você respondeu na Parte 1? Por favor continue respondendo o restante do questionário do outro lado da página.	How many times have you marked "Yes" in Part 1? Please continue answering the resto f the questionnaire on the other side of the page.	Quantos "Sim" você respondeu na Parte 1? Por favor continue respondendo o restante do questionário do outro lado da página.
Page 2 Part 2 Item 1	Has your child ever seen, heard, or been a victim of violence in your neighborhood, community, or school? (For example, targeted bullying, assault, or other violent actions, war or terrorism).	Seu filho(a) já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).	Seu filho(a) já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (Por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).	Has your child ever seen, heard or been a victim of violence in your neighborhood, community, or school? (For example, targeted bullying, aggression or other violent acts, war or terrorism).	Seu filho(a) já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (Por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).
Page 2 Part 2 Item 2	Has your child experienced discrimination? (for example, being hassled or made to feel inferior or excluded because of their race, ethnicity, gender identity, sexual orientation, religion, learning differences, or disabilities).	Seu filho(a) já experienciou discriminação? (por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências).	Seu filho(a) já experienciou discriminação? (Por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências.)	Has your child ever experienced discrimination? (for example, being disturbed or made to feel inferior or excluded due to your child's race, ethnicity, gender identity, sexual orientation, religion, learning difficulties or disabilities.)	Seu filho(a) já experienciou discriminação? (Por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências.)

Page 2 **Part 2** **Item 3**	Has your child ever had problems with housing? (For example, being homeless, not having a stable place to live, moved more than two times in a six-month period, faced eviction or foreclosure, or had to live with multiple families or family members).	Seu filho(a) já teve problemas de moradia? (por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família)	Seu filho(a) já teve problemas de moradia? (Por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família.)	Has your child ever had problems with housing? (for example, being homeless, not having a stable place to live, having to move more than twice during a period of six months, facing eviction or foreclosure or having to live with various families or family members).	Seu filho(a) já teve problemas de moradia? (Por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família.)
Page 2 **Part 2** **Item 4**	Are you currently or have you ever: (Mark yes, if any apply): worried that the food for your child would run out before you got money to buy more? had the food you bought for your child not last and did not have money to buy more?	Você atualmente ou alguma vez: (assinale sim, se qualquer um for verdadeiro para você ou sua família): Ficou preocupado que a comida para seu filho(a) acabasse antes de você tivesse dinheiro para comprar mais? Que a comida que você comprou para seu filho(a) não durou e não teve dinheiro para comprar mais?	Você atualmente ou alguma vez: (assinale sim, se qualquer um for verdadeiro para você ou sua família): Ficou preocupado que a comida para seu filho(a) acabasse antes de você tivesse dinheiro para comprar mais? OU que a comida que você comprou para seu filho(a) não durou e não teve dinheiro para comprar mais?	Are you currently or have you ever: (Mark yes, if any apply): Been worried that the food for your child would run out before you could buy more? OR had the food you bought for your child not last and did not have money to buy more?	Você atualmente ou alguma vez: (assinale sim, se qualquer um for verdadeiro para você ou sua família): Ficou preocupado que a comida para seu filho(a) acabasse antes de você tivesse dinheiro para comprar mais? OU que a comida que você comprou para seu filho(a) não durou e não teve dinheiro para comprar mais?
Page 2 **Part 2** **Item 5**	Has your child ever been separated from their parent or caregiver due to foster care, or immigration?	Seu filho(a) já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?	Seu filho(a) já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?	Has your child ever been separated from their parents or guardians due to foster care or immigration situations?	Seu filho(a) já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?
Page 2 **Part 2** **Item 6**	Has your child ever lived with a parent/caregiver who had a serious physical illness or disability?	O seu filho(a) já morou com um dos pais / responsável que sofre de uma doença física grave ou deficiência?	O seu filho(a) já morou com um dos pais / responsável que sofre de uma doença física grave ou deficiência?	Has your child ever lived with any of their parents/guardians that suffers from a serious physical illness or disability?	O seu filho(a) já morou com um dos pais / responsável que sofre de uma doença física grave ou deficiência?
Page 2 **Part 2** **Item 7**	Has your child ever lived with a parent or caregiver who died?	Seu filho(a) já morou com um dos pais ou responsável que tenha falecido?	Seu filho(a) já morou com um dos pais ou responsável que tenha falecido?	Has your child ever lived with a parent or guardian who died?	Seu filho(a) já morou com um dos pais ou responsável que tenha falecido?
Page 2 **Part 2** **Item 8**	Has your child ever been detained, arrested or incarcerated?	Seu filho(a) já foi detido(a), preso(a) ou encarcerado(a)?	Seu filho(a) já foi detido(a), preso(a) ou encarcerado(a)?	Has your child ever been detained, arrested, or incarcerated?	Seu filho(a) já foi detido(a), preso(a) ou encarcerado(a)?

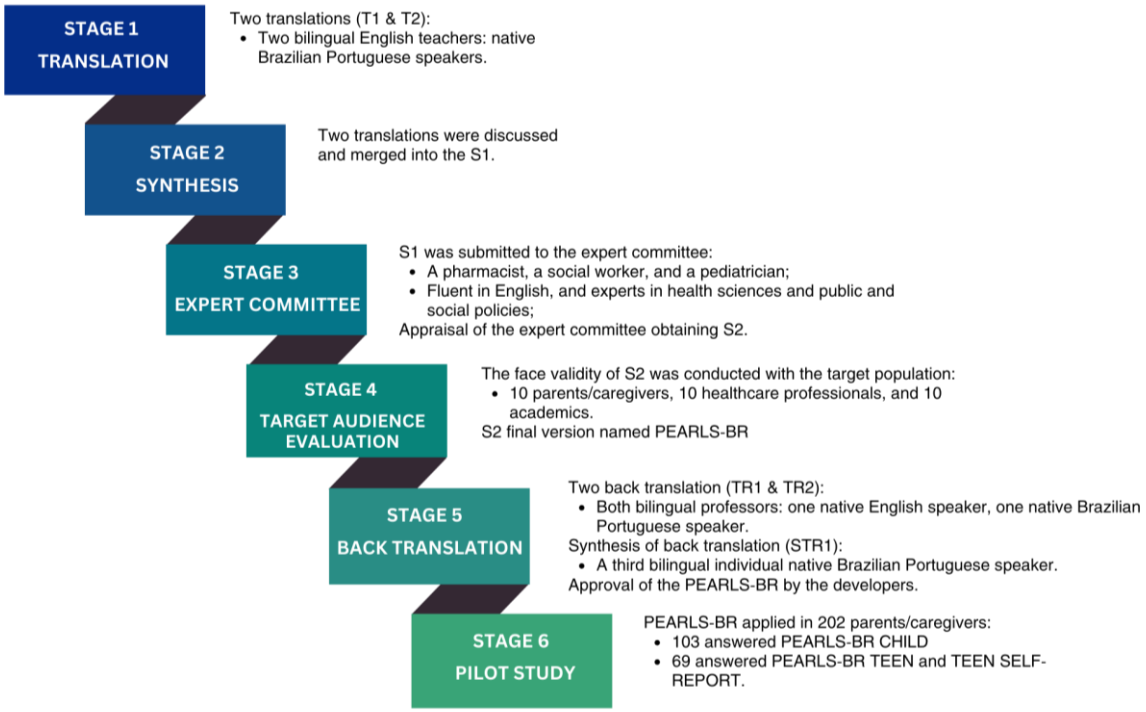
Page 2 Part 2 Item 9	Has your child ever experienced verbal or physical abuse or threats from a romantic partners? (for example, a boyfriend or girlfriend)	Seu filho(a) já sofreu abuso verbal ou físico ou ameaças de um parceiro romântico de um de seus pais/responsável? (por exemplo, um namorado ou namorada de um de seus pais / responsável).	Seu filho(a) já sofreu abuso verbal ou físico ou ameaças de um parceiro romântico? (Por exemplo, um namorado ou namorada.)	Has your child ever suffered verbal or physical abuse or threats from a romantic partner? (For example, a boyfriend or girlfriend).	Seu filho(a) já sofreu abuso verbal ou físico ou ameaças de um parceiro romântico? (Por exemplo, um namorado ou namorada.)
Page 3 Instruction	We would like to understand more about your child's and your family's strengths and resources.	PARTE 3: Gostaríamos de entender mais sobre os pontos fortes do seu filho(a) e da sua família.	PARTE 3: Gostaríamos de entender mais sobre os pontos fortes do seu filho(a) e da sua família.	Part 3: We would like to understand more about the resources and strengths of your child and of your family.	PARTE 3: Gostaríamos de entender mais sobre os pontos fortes do seu filho(a) e da sua família.
Page 3 Item 1	What are your child's best qualities?	Quais são as melhores qualidades do seu filho(a)?	Quais são as melhores qualidades do seu filho(a)?	What are your child's best qualities?	Quais são as melhores qualidades do seu filho(a)?
Page 3 item 2	What are things that help you (or your family) get through hard times (or cope with stress)?	Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?	Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?	What are the things that help you (or your family) to overcome difficult moments (or deal with stress)?	Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?

[a] The PEARLS TEEN and PEARLS TEEN SELF-REPORT instruments comprise nine questions in part 2, while the PEARLS CHILD version concludes at question 7 in the same section.

Table 2: Sociodemographic characteristics of the pilot study participants.

Characteristics	PEARLS CHILD (n = 133)		PEARLS TEEN (n = 69)	
	Caregivers	Children	Caregivers	Teens
Age, median (IQR)	36 (28-42)	7 (4-10)	40 (34-47)	14 (13-14)
Sex, n (%)				
Male	27 (20.3)	54 (40.6)	6 (8.7)	13 (18.8)
Female	106 (79.7)	79 (59.4)	63 (91.3)	56 (81.2)
Ethnic-racial classification, n (%)				
White	82 (61.7)	88 (66.2)	41 (59.4)	46 (66.7)
Black	6 (4.6)	3 (2.3)	5 (7.2)	6 (8.7)
Brown/Mixed-race	42 (31.5)	40 (30.1)	22 (31.9)	16 (23.1)
Indigenous	3 (2.2)	1 (0.7)	1 (1.5)	0
Asian	0	1 (0.7)	0	1 (1.5)
Educational level, n (%)				
No formal education	0	20 (15.0)	0	0
kindergarten	1 (0.7)	34 (25.6)	0	0
Elementary School	7 (5.3)	58 (43.6)	15 (21.7)	1 (1.5)
Middle School	31 (23.3)	21 (15.8)	19 (27.5)	46 (66.7)
High School	81 (60.9)	0	32 (46.4)	21 (30.3)
College/underdegree	11 (8.3)	0	3 (4.4)	1 (1.5)
Degree	2 (1.5)	0	0	0
Caregiver-child relationship, n (%)				
Father	23 (17.3)		5 (7.2)	
Mother	95 (71.4)		51 (73.9)	
Grandfather	3 (2.2)		1 (1.5)	
Grandmother	5 (3.8)		9 (13.0)	
Aunt	5 (3.8)		1 (1.5)	
Others	2 (1.5)		2 (2.9)	
Marital Status, n (%)				
Single	51 (38.4)		26 (37.7)	
Married	42 (31.5)		19 (27.5)	
Civil Union	21 (15.8)		15 (21.7)	
Separated	15 (11.3)		5 (7.2)	
Widowed	4 (3.0)		4 (5.9)	
Income (in R$/per month)				
2,589.00 or less	76 (57.1)		41 (59.4)	
Greater than 2,589.00	57 (42.9)		28 (40.6)	
Housing Type, n (%)				
House	112 (84.2)		65 (94.1)	
Apartment	19 (14.3)		4 (5.9)	
Shared housing	2 (1.5)		0	
Number of rooms, median (IQR)	5 (4-6)		6 (5-7)	
Number of cohabitants, median (IQR)	4 (3-5)		4 (3-5)	

Figure 1: The graphical representation of stages for transcultural adaptation of PEARLS, adapted from Borsa et al. (23)[a]



[a] Modified drawing from Pereira et al. (30)

3 **CAPÍTULO 2** – ARTIGO 2: PEDIATRIC ACES AND RELATED LIFE EVENT SCREENER (PEARLS-BR) LATENT DOMAINS, AND CHILD HEALTH IN A BRAZILIAN SAMPLE: A CONFIRMATORY FACTOR ANALYSIS AND CORRELATION STUDY

Full title: Pediatric ACEs and related life event screener (PEARLS-BR) latent domains, and child health in a Brazilian sample: A Confirmatory Factor Analysis and Correlation Study

Short title: PEARLS-BR Study: Brazilian Factor Analysis

Abstract:

Introduction: Adverse Childhood Experiences (ACEs) significantly affect health outcomes. This study aims to evaluate the psychometric properties of the Pediatric ACEs and Related Life Events Screener (PEARLS-BR) in Brazil, identify latent domains, and explore their associations with pediatric health outcomes.

Methods: A cross-sectional study was conducted at a Multidisciplinary Health Care Clinical Center and a General Hospital-Reference Center for Children and Adolescents, involving 202 caregivers of children and teens aged 0-18. Caregivers completed the PEARLS-BR to assess adverse childhood experiences, along with additional questions regarding the health of the children in their care. Confirmatory Factor Analysis (CFA) was performed to identify latent domains, and measurement invariance was evaluated across age and gender. Logistic regression models were used to examine associations between ACEs domains and health outcomes.

Results: The CFA supported a three-factor model encompassing maltreatment, household challenges, and social context. The PEARLS-BR demonstrated good internal consistency and reliability. Measurement invariance was confirmed across age and gender. Higher scores in the maltreatment domain were associated with non-significant increases in the odds of obesity, atopy, ADHD symptoms, infections, and mental health issues. Household challenges showed non-significant associations with most health outcomes, whereas the social context domain significantly increased the odds of reporting worse global health status.

Conclusions: The PEARLS-BR is a valid and reliable instrument for assessing childhood adversities in Brazilian children. The findings highlight its potential for early identification and intervention, supporting the development of targeted public health initiatives to mitigate the long-term effects of ACEs on health outcomes in Brazil.

Keywords: Adverse Childhood Experiences; Psychometrics; Child Health; Factor Analysis, Statistical; PEARLS-BR

Introduction

Adverse Childhood Experiences (ACEs) refer to stressful or traumatic events, including abuse and household dysfunction, experienced during childhood and have been extensively linked to a wide range of long-term health outcomes. (1,2) These early adversities can significantly impact neuro-endocrine-immune functions and genetic regulation, increasing the risk of physical and mental health problems across the lifespan. (3,4) The toxic stress response, involving alterations in neuro-endocrine-immune and genetic regulatory mechanisms, is considered a critical pathway through which cumulative exposures to early adversities elevate the risk of morbidity and mortality. (4,5) However, in Brazil, research on the burden of ACEs and their public health impact remains limited, underscoring the importance of understanding their prevalence and effects within this specific context.

Despite the global recognition of ACEs' detrimental effects, research specifically addressing the Brazilian population remains sparse. Most studies have focused on high-income countries, potentially neglecting unique cultural and socio-economic factors that could influence the prevalence and impact of ACEs. (6) Consequently, there is a significant gap in the literature regarding the multidimensional impact of ACEs on Brazilian children, including their association with health outcomes and the effectiveness of tailored interventions. Addressing this gap requires studies that validate and adapt ACE assessment tools for children in the Brazilian context, ensuring their relevance and efficacy in capturing local experiences of adversity.

Existing studies on ACEs in Brazil have predominantly focused on adolescents, primarily using tools validated for older age groups such as the Childhood Trauma Questionnaire (CTQ), which is designed for individuals aged 12 and above. (7-9) Research involving Brazilian younger children are rare, and employs ACE assessment tools originally developed for adults, which may not fully capture the nuances of childhood adversity in this demographic, or even tools that are not validated in Brazil. (10) This reliance on adult-oriented tools highlights a critical need for age-appropriate instruments that are validated for use with the Brazilian population to accurately assess ACEs among younger children, ensuring that their unique experiences and developmental stages are adequately considered.

To address these gaps and facilitate the application and alignment of the Pediatric ACEs and Related Life Events Screener (PEARLS), known locally as "*Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados*" (PEARLS-BR), toxic stress mitigation, and resource linkage in primary care, this study aims to: (1) conduct a psychometric analysis to derive a set of latent domains from the PEARLS-BR, providing evidence based on internal structure (construct validity); (2) demonstrate that these domains maintain measurement invariance across key factors relevant to pediatric care, such as age

groups and gender; and (3) assess the association between these latent domains and various pediatric clinical, mental, and behavioral health outcomes. By doing so, this research aims to contribute to a comprehensive understanding of the unique challenges faced by Brazilian children, confirm the validity of the instrument for clinical assessment, and provide valuable insights for the development of targeted interventions to mitigate the adverse effects of early childhood experiences.

Materials and Methods

Study population and design

This study used data from the PEARLS-BR Study, which was conducted as a cross-sectional analysis. The recruitment was carried out from June 2023 to January 2024, at both a Multidisciplinary Health Care Clinical Center and a General Hospital-Reference Center for Child and Adolescent Care. Families participating in the pilot study were recruited through a convenience sample in the waiting room, where they signed the consent form, and adolescents additionally signed the assent form. A total of 202 caregivers were included if they met specific criteria: aged over 18, primary caregiver of a child aged 18 or younger, Brazilian (Brazilian Portuguese speaker), and not having another child included in the study. Caregivers provided information on their children's ACEs using the PEARLS-BR instrument and completed surveys on sociodemographic and health data. The entire process took approximately 25 minutes per participant.

The study was conducted with the authorization of the original PEARLS developers under a licensing agreement between the University of California San Francisco (UCSF) and the Universidade de Caxias do Sul (UCS). The UCS Research Ethics Committee approved the research (approval number 6.090.525).

ACEs and related life events

ACEs and related life events were assessed using the "*Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados*" (PEARLS-BR) questionnaire. PEARLS-BR is a self-administered questionnaire designed to screen for ACEs and related life events in individuals from birth to eighteen years old. PEARLS-BR Child and PEARLS-BR Teen versions consist of seventeen questions, with PEARLS-BR Teen including an additional two questions. These items assess the occurrence of sexual, physical, or emotional violence; neglect; parental mental illness, substance abuse, or incarceration; parental separation or divorce; domestic violence; as well as explore food insecurity, housing instability, community violence, and discrimination. PEARLS-BR Child and PEARLS-BR Teen

are completed by a caregiver. Scoring involves summing the affirmative responses on the questionnaire (with each item dichotomized as yes or no). For the purposes of this study, only the 17 questions common to both versions were considered in the confirmatory factor analysis. A list of all 17 ACEs and related life events measured is provided in Figure 1.

Outcomes assessment

Child general health was measured using the Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health 10-item questionnaire, which evaluates various aspects of physical, mental, and social health, alongside pain, fatigue, and perceived quality of life as reported by caregivers. This instrument, validated in Brazil, was authorized for use in this study through an agreement signed between the copyright holder and UCS. (11) Responses were categorized on a scale from excellent to poor, with each question assigned a numeric code: 5 for excellent, 4 for very good, 3 for good, 2 for fair, and 1 for poor. Once responses were recoded, scores were summed for each item. Summed scores were then divided into three categories: Global Physical Health, Global Mental Health, and overall Global Health. The raw scores were analyzed as continuous variables and converted into t-scores for norm-referenced comparisons. (12,13) Lower t-scores indicated poorer health, with a range of 23.5 to 57.7 for physical health, 21.2 to 59 for mental health, and similar ranges for the overall Global Health score.

The Swanson, Nolan, and Pelham (SNAP-IV) questionnaire, a public domain instrument, validated for use in Brazil, was used to assess potential symptoms of Attention Deficit Hyperactivity Disorder (ADHD). (14) Comprising 18 items, each response is categorized as 'not at all' (unscored), 'just a little' (unscored), 'quite a bit' (scored as 1), and 'very much' (scored as 1). Total scores are then calculated across all items, with diagnostic criteria for ADHD established if the total attention or hyperactivity score reaches 6 or above.

Data on the presence of asthma, allergic rhinitis, and atopic dermatitis were gathered using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. This questionnaire has been validated and standardized for international use. (15-18) In order to utilize it in Brazil, an agreement was signed between the copyright holder of ISAAC and UCS, granting permission for its application. The individual pathologies (rhinitis, dermatitis, and asthma) were not evaluated separately; instead, the presence of any of these conditions was grouped under the variable "atopy”.

Height and weight data were extracted from the latest medical records, and sex - and age - specific body mass index (BMI) z-scores and percentiles were calculated using the World Health Organization BMI charts. (19-22) Children were classified as eutrophic, overweight, obese, and undernourished. For analysis, comparisons were made between obese and eutrophic children, excluding those classified as overweight or undernourished.

It was utilized caregiver-reported data to identify the presence of acute infections (including upper and lower respiratory infections, sinusitis, bronchiolitis, pneumonia, influenza and other viral infections, scarlet fever, otitis, and conjunctivitis), as well as gastrointestinal tract disorders (urinary tract infections, nausea, abdominal pain, epigastric pain, colic, and constipation) and headaches. The data collection spanned the 12 months preceding recruitment, with the presence or absence of each condition.

Covariates assessment

Socio-demographic covariates were identified *a priori* based on existing literature on childhood adversities and health outcomes. (23) They were child age (continuous), sex, race/ethnicity (categorized as White, Black, Brown, Indigenous, and Asian), caregiver education (categorized as never attended school, preschool, elementary school, high school, college or higher education), and family income per month, which was dichotomized as <R$2,589 vs. ≥R$2,590 based on the income threshold for personal income tax liability in Brazil and the criteria set by the *Cadastro Único* (Decree No. 6,135/2007) for defining low-income families.

Validation Process

Evidence Based on Internal Structure (Construct Validity): A confirmatory factor analysis (CFA) was employed to evaluate the internal structure of the PEARLS-BR, identifying three latent domains: "maltreatment," "household challenges," and "social context." These domains are supported by previous studies that have consistently demonstrated the theoretical validity of this factor structure.

Evidence Based on Relationships with External Variables (Criterion Validity): Criterion validity was assessed through binomial logistic regression analyses, examining the associations between the PEARLS-BR latent domains and various pediatric health outcomes. This analysis provided insight into how these domains relate to external health variables, further validating the instrument.

Statistical analysis

A three-factor model was tested to evaluate the latent structure of the PEARLS-BR items, informed by prior studies that support this structure, encompassing "maltreatment," "household dysfunction," and "social stressors". (23,24) The confirmatory factor analysis (CFA) was conducted using diagonally weighted least squares (DWLS) estimation in R (package “lavaan”).

Model fit was evaluated using several indices: the chi-square statistic to assess overall fit, the comparative fit index (CFI ≥ 0.95) and Tucker-Lewis index (TLI ≥ 0.95) for relative fit,

the root mean square error of approximation (RMSEA ≤ 0.05) for absolute fit, and the standardized root mean square residual (SRMR < 0.08) to measure the average discrepancy between observed and predicted correlations. (25,26)

These latent domains, namely “maltreatment”, “household challenges”, and “social context”, were derived from the 17 PEARLS items. A standardized factor loading cutoff of ≥ 0.30 was applied for inclusion. Cronbach's alpha (α) and McDonald's omega (ω) were calculated to assess internal consistency for the items within each factor and reliability of the latent domains, with values above 0.75 indicating satisfactory consistency. The 95% Confidence intervals for α and ω were computed using the Bias-Corrected and Accelerated (BCa) Bootstrap Interval.

Once the domains were established, composite scores for each PEARLS-BR domain were calculated for each participant by summing the number of affirmative responses within each domain. Additionally, a second-order factor structure was incorporated into the CFA to represent an overarching summary measure of adversity, acknowledging the intercorrelation of items and the aggregate scoring commonly found in the literature. (25,26)

To evaluate the invariance of the model across different groups, multigroup CFA analyses were conducted. These analyses examined the model's fit across different age ranges (<13 years vs. ≥13 years) and genders (male and female), using model fit indices such as chi-square, CFI, TLI, RMSEA, and SRMR.

The association between the latent domains and health outcomes were examined using a binomial logistic regression model, with the three risk factor domains and covariates as predictors. This analysis allowed for the estimation of the magnitude of the association between each risk factor and the probability of occurrence of the outcome, expressed as an Odds Ratio (OR). To assess the precision of these estimates, the Bootstrap technique was employed. This method involved creating multiple random samples from the original data and refitting the model in each sample. From these results, 95% confidence intervals (CIs) were calculated for the ORs, indicating the most plausible range of values for the true association between each risk factor and the outcome.

All the study data were collected and managed using REDCap (Research Electronic Data Capture), hosted at UCS. REDCap is a secure web-based software platform designed to support data capture for research studies. (27,28) Statistical analysis was conducted using R software version 3.5.2. Continuous variables were expressed as median and interquartile range. Histograms and the Shapiro-Wilk test were used to test quantitative data for normality of distribution.

Results

The sample of children and adolescents was predominantly female (n = 135, 66.8%), with a median age of 10 years (IQR = 5-13). Most participants were white (n = 134, 66.3%) and from low-income backgrounds (n = 117, 57.9%), with a total - or less than that - family income of 2,589 Brazilian Reais per month, equivalent to approximately 504 USD. A majority of the participants' caregivers had a high school education (n = 113, 55.9%). Participants reported experiencing an average of 3.4 ACEs and related life events (SD = 3.2). The characteristics of the children, adolescents, and their respective caregivers who participated in this study are detailed in Table 1.

Table 1: Sociodemographic characteristics of the study participants.

Characteristics	Caregivers (n = 202)	Children and teens (n = 202)
Age, median (IQR)	37 (31-45)	10 (5-13)
Sex, n (%)		
Male	33 (16.3)	67 (33.2)
Female	169 (83.7)	135 (66.8)
Ethnic-racial classification, n (%)		
White	123 (60.9)	134 (66.3)
Black	11 (5.4)	9 (4.5)
Brown/Mixed-race	64 (31.7)	56 (27.7)
Indigenous	4 (2)	1 (0.5)
Asian	0	2 (1)
Educational level, n (%)		
Never attended school	0	20 (9.9)
Preschool	1 (0.5)	34 (16.8)
Elementary School (1st to 9th grade)	72 (35.7)	126 (62.4)
High School (10th to 12th grade)	113 (55.9)	20 (9.9)
College or higher education	16 (7.9)	2 (1)
Caregiver-child relationship, n (%)		
Father	28 (13.9)	
Mother	146 (72.3)	
Grandfather	4 (2)	
Grandmother	14 (6.9)	
Aunt	6 (2.9)	
Others	4 (2)	
Marital Status, n (%)		
Single	77 (38.1)	
Married	61 (30.2)	
Civil Union	36 (17.8)	
Divorced	20 (9.9)	
Widowed	8 (4)	
Income (in R$/per month)		
2,589.00 or less	117 (57.9)	
Greater than 2,589.00	85 (42.1)	
Housing Type, n (%)		
House	177 (87.6)	
Apartment	23 (11.4)	
Shared housing	2 (1)	
Number of rooms, median (IQR)	5 (4-6)	
Number of cohabitants, median (IQR)	4 (3-5)	

Confirmatory Factor Analysis Structure

The CFA demonstrated an excellent fit for the three-factor model with a second-order summary factor, as indicated by fit indices (RMSEA = 0.000; CFI = 1.000; TLI = 1.001; SRMR = 0.130) (Table 2). The latent structure is depicted in Figure 1. The first domain, labeled "Maltreatment," comprised six items related to various forms of abuse and neglect, including emotional abuse, verbal abuse, physical neglect, domestic violence, physical abuse, and

sexual abuse (score range 0–6). The second domain, labeled "Household Challenges," included seven items representing disruptions in the child's household, such as caregiver mental illness, substance abuse, incarceration, divorce or separation, child separation from caregiver, caregiver physical illness, and death of a caregiver (score range 0–7). The third domain, labeled "Social Context," encompassed four items capturing environmental and social stressors like neighborhood violence, discrimination, housing insecurity, and food insecurity (score range 0–4). These domains and their corresponding items reflect the theoretical framework and empirical evidence supporting the multidimensional structure of the PEARLS-BR scale.

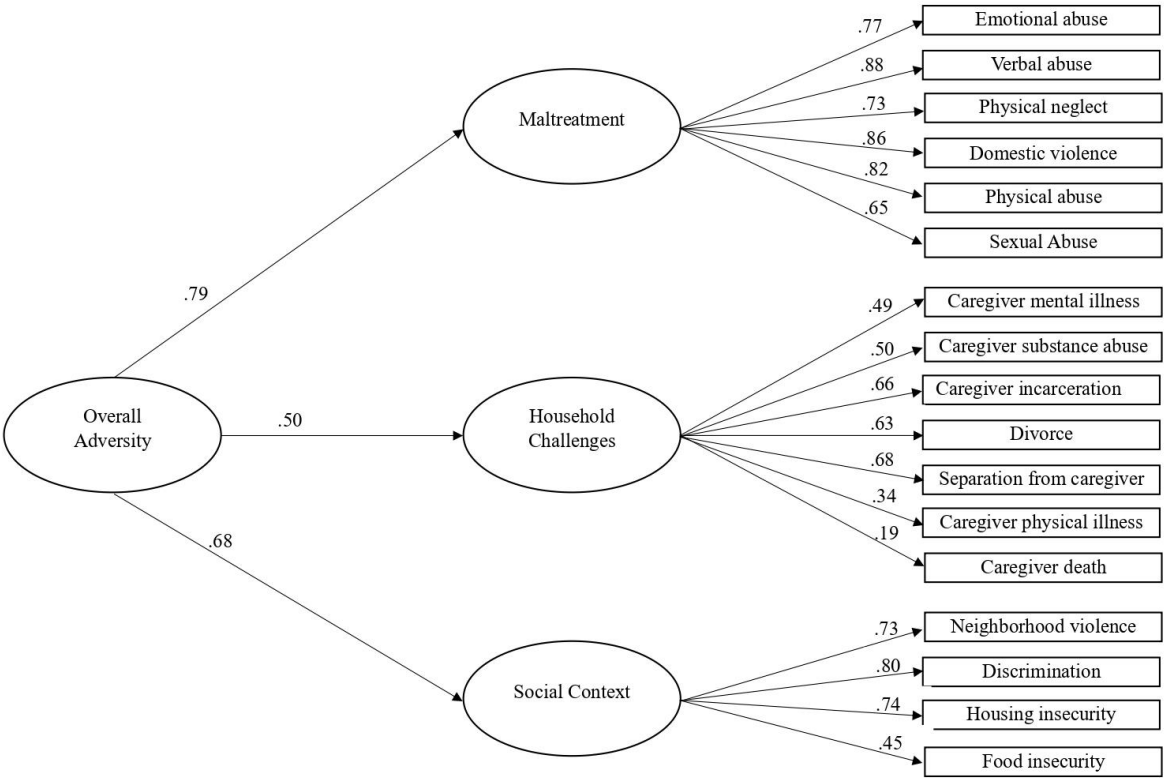


Fig.1 Diagram of Confirmatory Three-Factor Model of the "*Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados*" (PEARLS-BR)

The analysis indicated significant variances for each factor: 0.58 for "Maltreatment," 0.23 for "Household Challenges," and 0.54 for "Social Context." Covariances between the factors were also significant: 0.37 between "Maltreatment" and "Household Challenges," 0.43 between "Maltreatment" and "Social Context," and 0.30 between "Household Challenges" and "Social Context." These results suggest that the items are good indicators of their respective factors and that the factors are significantly related. All factor loadings and covariances were significant with p-values ≤ 0.007, except for the "caregiver death" item, which had a non-

significant factor loading (p = 0.130).

The regressions for "overall adversity" on "maltreatment," "household challenges," and "social context" demonstrated statistical significance. The standardized factor loadings (β) for “maltreatment”, “household challenges”, and “social context” indicate significant linear relationships between these domains and overall adversity (Table 2).

The reliability of the factors was evaluated using both Cronbach's alpha and McDonald's omega coefficients, along with their corresponding 95% confidence intervals (CI). For the "Maltreatment" factor, Cronbach's alpha was 0.89 (95% CI: 0.85 - 0.93) and McDonald's omega was 0.84 (95% CI: 0.77 - 0.90), both indicating high internal consistency. The "Household Challenges" factor had a Cronbach's alpha of 0.72 (95% CI: 0.53 - 0.85) and a McDonald's omega of 0.45 (95% CI: 0.28 - 0.62). In contrast, the "Social Context" factor showed a Cronbach's alpha of 0.60 (95% CI: 0.15 - 0.79) and a McDonald's omega of 0.56 (95% CI: 0.41 - 0.65), reflecting varying levels of internal consistency across the factors (see Table 2).

The average number of exposures for each domain was as follows: 1.2 for “Maltreatment" (SD = 1.6), 1.1 for "Household Challenges" (SD = 1.2), and 1.0 for "Social Context" (SD = 1.0). These exposure rates indicate the extent to which children in the sample experienced different types of adversities.

Table 2: Factor Loadings and Reliability Indices for the Second Order CFA Model[a]

			Est. Loading[b]			Reliability (95% CI)	
Factor	**Variable**	**% Exposed**	**(β± SE)**	**95% CI[c]**	***p*-value**	**α**	**ω**
First Order Maltreatment	Emotional Abuse	28	0.77 (0.05)	(0.67; 0.88)	<0.001	0.89 (0.85 a 0.93)	0.84 (0.77 a 0.90)
	Verbal Abuse	22	0.88 (0.03)	(0.82; 0.95)	<0.001		
	Physical Neglect	14	0.73 (0.06)	(0.62; 0.84)	<0.001		
	Domestic Violence	26	0.86 (0.04)	(0.77; 0.94)	<0.001		
	Physical Abuse	15	0.82 (0.05)	(0.72; 0.93)	<0.001		
	Sexual Abuse	20	0.65 (0.07)	(0.52; 0.78)	<0.001		
Household Challenges	Caregiver Mental Illness	22	0.49 (0.08)	(0.34; 0.65)	<0.001	0.72 (0.53 a 0.85)	0.45 (0.28 a 0.62)
	Caregiver Substance Abuse	20	0.50 (0.08)	(0.34; 0.67)	<0.001		
	Caregiver Incarceration	7	0.66 (0.09)	(0.48; 0.84)	<0.001		
	Caregiver Divorce	42	0.63 (0.08)	(0.48; 0.78)	<0.001		
	Separation from Caregiver	7	0.68 (0.07)	(0.55; 0.82)	<0.001		
	Caregiver Physical Illness	4	0.34 (0.13)	(0.10; 0.59)	=0.007		
	Caregiver Death	6	0.19 (0.12)	(-0.04; 0.43)	=0.130		
Social Context	Neighborhood Violence	28	0.73 (0.06)	(0.61; 0.86)	<0.001	0.60 (0.15 a 0.79)	0.56 (0.41 a 0.65)
	Discrimination	24	0.80 (0.06)	(0.69; 0.92)	<0.001		
	Housing Insecurity	4	0.74 (0.09)	(0.56; 0.92)	<0.001		
	Food Insecurity	44	0.45 (0.08)	(0.29; 0.62)	<0.001		
Second-order Overall Adversity	Maltreatment		0.79 (0.03)	(0.72; 0.85)	<0.001		
	Household Challenges		0.50 (0.06)	(0.37; 0.62)	<0.001		
	Social Context		0.68 (0.07)	(0.53; 0.79)	<0.001		

[a]Model fit indices: $X^2(130) = 127.575$, $p = .07$; RMSEA = 0.000 [90% CI: 0.000, 0.033]; CFI = 1.000; TLI = 1.001; SRMR = 0.130
[b]Est: Parameter estimate (the standardised factor loading of each item). SE: Standard error of the estimate.
[c]95% CI: 95% confidence interval

Assessment of Measurement Invariance Across Age Groups and Genders

The multigroup CFA demonstrated measurement invariance across different age groups and genders, ensuring the robustness of the PEARLS-BR instrument in diverse subpopulations. For children under 13 years old, the model fit indices were excellent, indicating a strong fit. Similarly, for adolescents aged 13 and older, the fit indices also showed a good model fit. Gender-specific analyses revealed that the model fit for females was particularly strong, with a CFI of 1.000 and a TLI of 1.005, indicating an excellent fit. For males, while the fit was slightly less precise, it still indicated a good fit overall. A summary of the fit statistics for the multiple group CFAs for age group and gender is shown in Table 3. These results confirm the suitability of the PEARLS-BR for use across different demographic groups in Brazil, supporting its validity and reliability in capturing ACEs consistently across varied contexts.

Table 3: Summary of fit Statistics of Measurement Invariance Models across Age and Gender.

Group	Chi-square	Degrees of freedom	CFI	TLI	RMSEA	SRMR
<13 years old	144.167	130.000	0.996	0.996	0.029	0.165
≥13 years old	136.843	130.000	0.996	0.995	0.028	0.184
Male	163.138	130.000	0.991	0.989	0.062	0.199
Female	117.741	130.000	1.000	1.005	0.000	0.145

Associations between PEARLS domains and child outcomes

In a multivariable analysis adjusting for age, sex, family income, and caregiver's level of education, maltreatment was associated with a non-significant increase in the odds of obesity, atopy, ADHD symptoms, infections, and mental health. Additionally, maltreatment did not show significant associations with other health outcomes, including global health, physical health, gastrointestinal conditions, and headaches. (See Table 4).

Household challenges were not significantly associated with most health outcomes. However, they were associated with a non-significant increase in the odds of physical health, infection, global health, gastrointestinal conditions, headaches, and ADHD symptoms. There were no significant associations with mental health, obesity, and atopy. (See Table 4).

The social context domain showed a significant association with global health, with an OR of 1.21 (95% CI 1.03; 1.51), indicating a significant increase in the odds of reporting worse global health status. Additionally, social context was associated with a non-significant increase in the odds of gastrointestinal conditions, mental health, infection, and headaches. However, no significant associations were found with physical health, ADHD symptoms, obesity, and atopy. (See Table 4).

Table 4: Multivariable analysis with logistic regression of PEARLS-BR domains associated with Child Health

Health Outcomes	Maltreatment	Household Challenges	Social Context
	Odds Ratio (95% CI)[a,b]		
PROMIS Global[c]	0.72 (0.40; 1.11)	1.14 (0.72; 1.95)	1.21 (1.03; 1.51)[d]
PROMIS Physical Health[c]	0.95 (0.16; 1.33)	1.23 (0.85; 7.46)	0.86 (0.61; 1.14)
PROMIS Mental Health[c]	1.09 (0.64; 1.52)	0.90 (0.66; 1.51)	1.05 (0.86; 1.26)
ADHD Symptoms[e]	1.11 (0.25; 1.62)	1.02 (0.71; 1.14)	0.90 (0.71; 1.14)
Infections	1.13 (0.75; 1.83)	1.17 (0.77; 1.76)	1.04 (0.85; 1.27)
Gastrointestinal Condition	0.83 (0.50; 1.34)	1.13 (0.76; 1.88)	1.13 (0.95; 1.59)
Obesity	1.42 (0.97; 2.38)	0.78 (0.49; 1.08)	0.86 (0.67; 1.00)
Headache	0.89 (0.39; 1.40)	1.07 (0.71; 2.19)	1.01 (0.84; 1.30)
Atopy	1.22 (0.82; 2.20)	0.92 (0.55; 1.37)	0.92 (0.77; 1.15)

[a]Models adjusted for child's age, sex, caregiver's educational level, and family income.
[b] 95% CI: confidence interval 95%.
[c] PROMIS: Patient-Reported Outcomes Measurement Information System.
[d] $p<0.05$
[e] ADHD: Attention Deficit Hyperactivity Disorder.

Discussion

The present study aimed to evaluate the psychometric properties of the Brazilian version of the Pediatric ACEs and Related Life Events Screener (PEARLS-BR), identify latent domains, and explore their associations with various pediatric health outcomes. The findings underscore the critical importance of culturally adapting ACEs assessment tools to accurately reflect the unique experiences of Brazilian children and adolescents.

The results from the CFA provide strong evidence based on internal structure (construct validity), confirming the robustness of the PEARLS-BR scale in capturing the multidimensional nature of childhood adversity. The CFA validated a three-factor model for PEARLS-BR, which includes "maltreatment", "household challenges", and "social context". This model aligns with previous research in diverse cultural contexts that also identified these three domains as core components of childhood adversity. (23) Other studies have similarly identified two domains – "maltreatment" and "household challenges" - within the traditional ACEs categories. For example, a Canadian study using CFA found that the domains of child "maltreatment" and "household challenges" were associated with poor mental and physical health, but did not identify a social-environmental factor. (29) Conversely, Liming et al. (24) examined three latent domains – "maltreatment", "household dysfunction", and "social stressors" - which closely relate to the domains it was examined in this current study, emphasizing the multifaceted nature of childhood adversity. However, only the original PEARLS study (23) and the present study have specifically examined these three latent domains, providing a comprehensive view of the various dimensions of childhood adversity.

The SRMR value of 0.130, although slightly higher than the conventional threshold, still

suggests an acceptable fit, indicating that the residuals between the observed and model-implied covariances are relatively low. The internal consistency and reliability of the PEARLS-BR varied across different domains. Cronbach's alpha and McDonald's omega coefficients for the "maltreatment" domain were robust, both exceeding 0.75, indicating strong reliability. For the "household challenges" and "social context" domains, the alpha coefficients were moderate, while the omega coefficients were low, following the trend observed in the original PEARLS study. (23) The original PEARLS study reported higher coefficients, potentially due to a larger sample size, which may result in more precise estimates and, consequently, higher reliability coefficients.

The results of the multigroup CFA demonstrated that the PEARLS-BR instrument maintains measurement invariance across different age groups and genders, suggesting its robustness and reliability in diverse Brazilian subpopulations. These findings align with previous studies that have explored the measurement invariance of instruments assessing ACEs. The original PEARLS study also confirmed the measurement invariance of a similar ACEs measurement tool across various demographic groups, highlighting the tool's reliability in different contexts. (23) This similarity suggests that the PEARLS-BR is a stable and reliable instrument for assessing childhood adversity in Brazil, comparable to other validated tools used internationally. (23,30) However, some differences were noted. While the original PEARLS study found strong invariance across both age and gender, (23) the current study identified that the model fit indices, although good, varied slightly between genders, with females showing a slightly better fit compared to males. This discrepancy might indicate subtle differences in how adverse experiences are reported or perceived across genders, which warrants further investigation.

The study explored the associations between the identified latent domains of the PEARLS-BR and various pediatric health outcomes, providing strong evidence based on relationships with external variables (criterion validity). In a multivariable analysis adjusting for age, sex, family income, and caregiver's level of education, the current study found that higher scores in the "maltreatment" domain were associated with non-significant increases in the odds of several health outcomes, including obesity, atopy, ADHD symptoms, infections, and mental health. Specifically, the odds ratios (OR) for these associations ranged from 1.09 (mental health) to 1.42 (obesity), but none reached statistical significance. This pattern of findings is consistent with some international studies, which also report varying levels of significance in the relationships between ACEs and mental health disorders such as anxiety, depression, and behavioral problems. (3,32)

"Household challenges" similarly showed non-significant associations with most health outcomes. For example, the odds ratios for household challenges ranged from 0.78 (obesity) to 1.23 (physical health). These results suggest that while there may be a potential impact of

household challenges on child health, the evidence is not robust enough to confirm this in our sample.

The “social context” domain showed a significant association with general and global health (OR 1.21, 95% CI 1.03; 1.51), indicating a significant increase in the odds of reporting worse global health status. This finding aligns with the broader understanding that social determinants of health, such as community violence and housing instability, can significantly impact general health.

The results of this current study are consistent with the original PEARLS study. (23) However, the original PEARLS study also identified significant associations with eczema and somatic symptoms in their underserved urban pediatric population, which contrasts with this study findings, where such associations were not statistically significant. (23)

These findings highlight the complexity of the interplay between ACEs and child health, indicating potential similarities and also differences that require further investigation. The nuanced relationships observed in this study align with existing literature, which suggests that the impact of ACEs on health outcomes can vary widely depending on a range of factors, including the type and severity of adversity, as well as individual and contextual factors. (4,33) For instance, Anda et al. (6) emphasize the importance of a multifaceted approach to understanding and addressing ACEs, incorporating both individual and community-level interventions to effectively mitigate their adverse effects. (34) Similarly, other studies have demonstrated the profound influence of social determinants of health, such as economic stability, education, and community environment, on the long-term health outcomes of children exposed to ACEs. (35)

The validation of the PEARLS-BR opens new avenues for early identification and intervention strategies tailored to the Brazilian context. Healthcare providers can utilize this tool to screen for ACEs and related life events, facilitating timely referrals to appropriate support services. Furthermore, research indicates that early intervention can improve health outcomes and reduce the risk of developing chronic conditions associated with ACEs. (5,31,36) Policymakers can leverage these findings to design and implement public health initiatives aimed at mitigating the impact of ACEs on Brazilian children’s health and development. For example, community programs focused on enhancing social support networks and reducing exposure to violence have been shown to be effective in improving resilience and overall well-being among children. (31) These strategies underscore the critical need for a comprehensive, culturally-sensitive approach to addressing childhood adversity in Brazil.

The present study has limitations that should be considered when interpreting the results. First, the reliance on caregiver reports may introduce bias, as caregivers might underestimate or overestimate both the exposure to adversities and the health outcomes of

the children. To minimize potential response biases, it is important to consider using multiple sources of information, including self-reports from adolescents. Additionally, the cultural and regional diversity within Brazil can influence the application and interpretation of the PEARLS-BR results, reflecting the sociodemographic characteristics of the sample population, predominantly from low-income backgrounds, which may limit generalizability to other regions. Another limitation is the absence of analyses for configural, metric, and scalar invariance due to the small and disproportionate sample sizes. Despite this, the robustness of the PEARLS-BR instrument across different age groups and genders within the sample provides a strong foundation for its use. Lastly, the confirmatory factor analysis was conducted only with the 17 common questions in both versions of the PEARLS-BR questionnaire, excluding the 2 additional questions in the TEEN version due to small sample size. Future research should use larger and more representative samples, include longitudinal measures.

The validation of the PEARLS-BR opens new opportunities for implementing early identification and intervention strategies in the Brazilian context. Interventions targeting both individual and community levels can help mitigate the adverse effects of negative childhood experiences. Future research should also explore specific interventions addressing the social determinants of health, such as community programs and policy changes, to reduce the impact of adversities on the health of Brazilian children.

This study illuminates the complexity of childhood adversity and its diverse impacts on pediatric health outcomes in Brazil. These results affirm the utility of the PEARLS-BR as a valuable tool for early identification and tailored intervention strategies for Brazilian children, potentially mitigating long-term health effects. Moreover, the nuanced associations observed between identified latent domains and various health outcomes underscore the necessity of targeted public health initiatives addressing social determinants of health. These efforts are crucial for enhancing child well-being and fostering resilience in the face of adversity.

Conclusions

The PEARLS-BR is a valid and reliable instrument for assessing childhood adversities in Brazilian children and adolescents. The model demonstrated a good fit with observed data, effectively representing latent variables. These findings underscore its robustness in capturing the multidimensional aspects of childhood adversity, emphasizing its clinical importance in understanding and addressing the prevalence and impact of ACEs in Brazil.

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4 **CAPÍTULO 3** – ARTIGO 3: ADVERSE CHILDHOOD EXPERIENCES AND RELATED LIFE EVENTS SCREENER (PEARLS-BR), PREVALENCE, AND HEALTH OUTCOMES IN A BRAZILIAN CONTEXT

Full title: Adverse Childhood Experiences and Related Life Events Screener (PEARLS-BR), Prevalence, and Health Outcomes in a Brazilian Context

Short title: PEARLS-BR and Health Outcomes

Abstract:

Introduction: This study explores the associations between Adverse Childhood Experiences (ACEs) and child health in Brazil using data from the PEARLS-BR study. It aims to assess the prevalence and impact of ACEs in a Brazilian cultural context and their relationship with health outcomes.

Methods: A cross-sectional study was conducted at a Multidisciplinary Health Care Clinical Center and a General Hospital - Reference Center for Child and Adolescent Care, involving 202 caregivers of children and teens aged 0 to 18 years. The PEARLS-BR instrument was used to document the frequency and distribution of ACEs and related life events and their association with health outcomes.

Results: Caregivers Participants reported a median of 2 (IQR 1-5) adversities of their child, with 78.2% reporting at least one adversity. Higher PEARLS-BR scores were significantly associated with poorer physical health (OR: 1.18, 95% CI: 1.01–1.38) and mental health (OR: 1.50, 95% CI: 1.33–1.71), ADHD symptoms (OR: 1.21, 95% CI: 1.09–1.37), infections (OR: 1.13, 95% CI: 1.02–1.26), gastrointestinal disorders (OR: 1.26, 95% CI: 1.12–1.43), and headaches/migraines (OR: 1.22, 95% CI: 1.11–1.35). Related life events were linked to higher odds of obesity (OR: 1.37, 95% CI: 1.02–1.88) and atopic conditions (OR: 1.28, 95% CI: 1.01–1.63).

Conclusions: The PEARLS-BR score identifies children at risk for various adverse health outcomes. The study highlights the need for targeted interventions and comprehensive strategies to address the impact of childhood adversities on health, providing valuable insights for public health strategies and clinical practices in Brazil.

Keywords: Adverse Childhood Experiences; Screening; Child Health; Public Health.

Introduction

Adverse childhood experiences (ACEs), such as abuse, neglect, and household challenges experienced before the age of 18, have become an increasingly important topic in public health due to their short- and long-term adverse effects on children, adolescents, and adults. (1,2) Exposure to these stressors is strongly associated with a range of problems, including behavioral issues, (3-5) neurodevelopmental challenges, (2,6-8) mental disorders, (1,9) and physical conditions that can persist throughout life. (1,2,10-12) Early recognition and intervention are crucial for implementing effective strategies to improve quality of life and prevent future negative outcomes. Addressing ACEs is essential to promoting well-being and resilience in impacted individuals and reducing the burden on healthcare systems. (13)

Despite the growing understanding of the importance of ACEs, screening for these events still faces significant challenges, particularly in Brazil's pediatric population. The absence of a comprehensive screening system and the predominant focus on tertiary prevention hinder the early detection and communication of adverse experiences. Furthermore, there is a significant gap in research focusing on diverse populations and cultural contexts, which can affect the prevalence and impact of ACEs. Most existing studies have been conducted in high-income countries, underscoring the need for research in low- and middle-income countries like Brazil to understand how different social, economic, and cultural factors may modify the effects of ACEs. (2,14,15) Addressing these gaps is crucial for developing targeted interventions and policies that can effectively mitigate the adverse effects of ACEs and promote resilience.

In the Brazilian context, research on ACEs and their health outcomes in children has been limited due to the lack of a validated screening tool. However, the recent validation of the PEARLS-BR instrument now provides a valuable means to investigate these associations within Brazil. Given the lack of comprehensive studies on the prevalence and impact of ACEs on Brazilian children's health, there is a pressing need for such research.

This article proposes to investigate the associations between ACEs and child health in Brazil, using data from the PEARLS-BR study. By focusing on a Brazilian sample, this study aims to explore the prevalence and impact of ACEs within a cultural context distinct from that observed in studies conducted in high-income countries. The objective is to document the frequency and distribution of ACEs using the PEARLS-BR instrument and to evaluate their relationship with health outcomes. Additionally, it aims to assess whether other common social determinants are comparable in their risks to child health, as measured by the Related Life Events section of the PEARLS tool. This study seeks to fill a significant gap in the existing literature by providing contextual data that can inform public health practices and clinical interventions specific to Brazil.

Materials and Methods

Participants and Study Design

This research utilized data from the PEARLS-BR Study, conducted through a cross-sectional analysis. Data collection took place from June 2023 to January 2024 at a Multidisciplinary Health Care Clinical Center and a General Hospital-Reference Center for Child and Adolescent Care. Families participating in the pilot study were recruited through convenience sampling in the waiting room, where they signed the informed consent form, and adolescents additionally signed the assent form. A total of 202 caregivers were included based on specific criteria: being over 18 years old, the primary caregiver of a child aged 18 or younger, Brazilian Portuguese speakers, and not having another child enrolled in the study. Caregivers completed surveys on sociodemographic and health data, and provided information about their children's ACEs using the PEARLS-BR instrument. Among the participants, 133 responded to the PEARLS-BR Child, while 69 responded to the PEARLS-BR Teen, and adolescents over 13 years old completed the PEARLS-BR Teen Self-Report. The entire process took approximately 25 minutes per participant. Hereafter, the acronym PEARLS refers exclusively to the "Pediatric ACEs and Related Life Event Screener," with the addition of "Br" to denote the Brazilian translated, transcultural adapted and validated version.

The study was conducted with the authorization of the original PEARLS developers under a licensing agreement between the University of California, San Francisco (UCSF) and the Universidade de Caxias do Sul (UCS). The UCS Research Ethics Committee approved the study (approval number 6.090.525).

ACEs and related life events

ACEs and related life events were assessed using the “Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados” (PEARLS-BR) questionnaire. PEARLS-BR is a self-administered questionnaire designed to screen for ACEs and related life events in individuals from birth to eighteen years old. Both the PEARLS-BR Child and PEARLS-BR Teen versions consist of 17 questions, with PEARLS-BR Teen including an additional two questions. These items assess the occurrence of sexual, physical, or emotional violence; neglect; parental mental illness, substance abuse, or incarceration; parental separation or divorce; domestic violence; as well as explore food insecurity, housing instability, community violence, and discrimination. PEARLS-BR Child and PEARLS-BR Teen are completed by a caregiver, while PEARLS-BR Teen Self-Report is completed by the adolescent. Scoring involves summing the affirmative responses on the questionnaire. (2)

Outcomes assessment

We evaluated primary pediatric clinical, mental, and behavioral health outcomes that are frequently highlighted in prior ACE studies. The general health of the children was assessed using Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health 10-item questionnaire, which evaluates various dimensions of physical, mental, and social health, along with pain, fatigue, and perceived quality of life as reported by caregivers. (16) This instrument, validated for use in Brazil, was authorized for this study under an agreement between the copyright holder and UCS. Continuous raw scores were converted into T-scores and norm-referenced. (17,18)

To identify symptoms that meet diagnostic criteria for Attention Deficit Hyperactivity Disorder (ADHD), we employed the Swanson, Nolan, and Pelham (SNAP-IV) questionnaire, a public domain tool validated for use in Brazil. (19) This questionnaire includes 18 items, with responses categorized as 'not at all' (unscored), 'just a little' (unscored), 'quite a bit' (scored as 1), and 'very much' (scored as 1). Total scores are computed across all items, and a score of 6 or higher on the attention or hyperactivity subscales indicates meeting the diagnostic criteria for ADHD.

Data regarding the presence of asthma, allergic rhinitis, and atopic dermatitis were collected using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire, which is validated and standardized for global use. (20-23) These conditions were collectively categorized as atopy. The usage of this tool in this current study was allowed through an agreement between the copyright holder of ISAAC and UCS.

Height and weight data were obtained from the most recent medical records, and sex- and age-specific body mass index (BMI) z-scores and percentiles were calculated using the World Health Organization (WHO) BMI charts. (24,27) Children were classified as eutrophic, overweight, obese, or undernourished. For analysis, comparisons were made between obese and eutrophic children, excluding those classified as overweight and undernourished.

Caregiver-reported data were used to identify the presence of acute infections (including upper and lower respiratory infections, sinusitis, bronchiolitis, pneumonia, influenza and other viral infections, scarlet fever, otitis, and conjunctivitis), gastrointestinal disorders (such as urinary tract infections, nausea, abdominal pain, epigastric pain, colic, and constipation), and headaches. The data collection covered the 12 months preceding recruitment.

Covariates assessment

Socio-demographic covariates were pre-identified based on established literature regarding childhood adversities and health outcomes. (28) These covariates included the child’s age (continuous variable), race/ethnicity (categorized as White, Black, Brown,

Indigenous, and Asian), caregiver education level (classified as never attended school, preschool, elementary school, high school, college, or higher education), and monthly family income, which was dichotomized into <R$2,589 versus ≥R$2,590. This income threshold is based on Brazil's personal income tax liability limits and the criteria defined by the Cadastro Único (Decree No. 6,135/2007) for low-income families.

Statistical analysis

The association between PEARLS-BR scores and socio-demographic covariates was examined using a negative binomial regression model. Chi-squared tests were applied to evaluate the likelihood of reporting ACEs among individuals who reported at least one Related Life Event. A logistic regression model was used to explore the relationship between reported adversities and health outcomes. Adversities were analyzed in terms of ACEs, Related Life Events, total PEARLS scores, and ACE categories (none, 1–3, ≥4). This approach enabled the estimation of the association's magnitude between PEARLS-BR scores and the likelihood of outcomes, expressed as Odds Ratios (ORs). To assess the precision of these estimates, the Bootstrap technique was employed, and 95% confidence intervals (CIs) for the ORs were calculated, indicating the most plausible range of values for the true association between ACEs, Related Life Events, and the outcomes.

All the study data were collected and managed using REDCap (Research Electronic Data Capture), hosted at UCS. REDCap is a secure web-based software platform designed to support data capture for research studies. (29,30) Statistical analysis was conducted using R software version 3.5.2. Continuous variables were expressed as median and interquartile range. Histograms and the Shapiro-Wilk test were used to test quantitative data for normality of distribution.

Results

The sample consisted mostly female children and adolescents (n = 135, 66.8%), with a median age of 10 years (IQR 6–13). Predominantly white (n = 134, 66.3%) and from low-income families (n = 117, 57.9%), with family income of 2,589 Brazilian Reais per month (approximately 504 USD) or less. Most caregivers had completed high school education (n = 113, 55.9%). Detailed characteristics of the children, adolescents, and their caregivers are presented in Table 1.

78.2% of the caregiver population reported 1 or more adversity with a median report of 2 (IQR 1-5) adversities of their child. The prevalence and type of adversities reported by caregivers are shown in Fig. 1. Regarding teen self-report, 91.3% reported 1 or more adversity

with a median report of 4 (IQR 2-7) adversities. The prevalence and type of adversities reported by teens are shown in Fig. 2.

Table 1: Sociodemographic Characteristics of Caregivers, Children, and Teens Participating in the PEARLS-BR Study

Characteristics	**Caregivers (n = 202)**	**Children and teens (n = 202)**
Age, median (IQR)	37 (31-45)	10 (5-13)
Sex, n (%)		
Male	33 (16.3)	67 (33.2)
Female	169 (83.7)	135 (66.8)
Ethnic-racial classification, n (%)		
White	123 (60.9)	134 (66.3)
Black	11 (5.4)	9 (4.5)
Brown/Mixed-race	64 (31.7)	56 (27.7)
Indigenous	4 (2)	1 (0.5)
Asian	0	2 (1)
Educational level, n (%)		
Never attended school	0	20 (9.9)
Preschool	1 (0.5)	34 (16.8)
Elementary School (1st to 9th grade)	72 (35.7)	126 (62.4)
High School (10th to 12th grade)	113 (55.9)	20 (9.9)
College or higher education	16 (7.9)	2 (1)
Caregiver-child relationship, n (%)		
Mother	146 (72.3)	
Father	28 (13.9)	
Grandmother	14 (6.9)	
Others	14 (6.9)	
Marital Status, n (%)		
Single	77 (38.1)	
Married	61 (30.2)	
Civil Union	36 (17.8)	
Divorced	20 (9.9)	
Widowed	8 (4)	
Income (in R$/per month)		
2,589.00 or less	117 (57.9)	
Greater than 2,589.00	85 (42.1)	
Housing Type, n (%)		
House	177 (87.6)	
Apartment	23 (11.4)	
Shared housing	2 (1)	
Number of rooms, median (IQR)	5 (4-6)	
Number of cohabitants, median (IQR)	4 (3-5)	

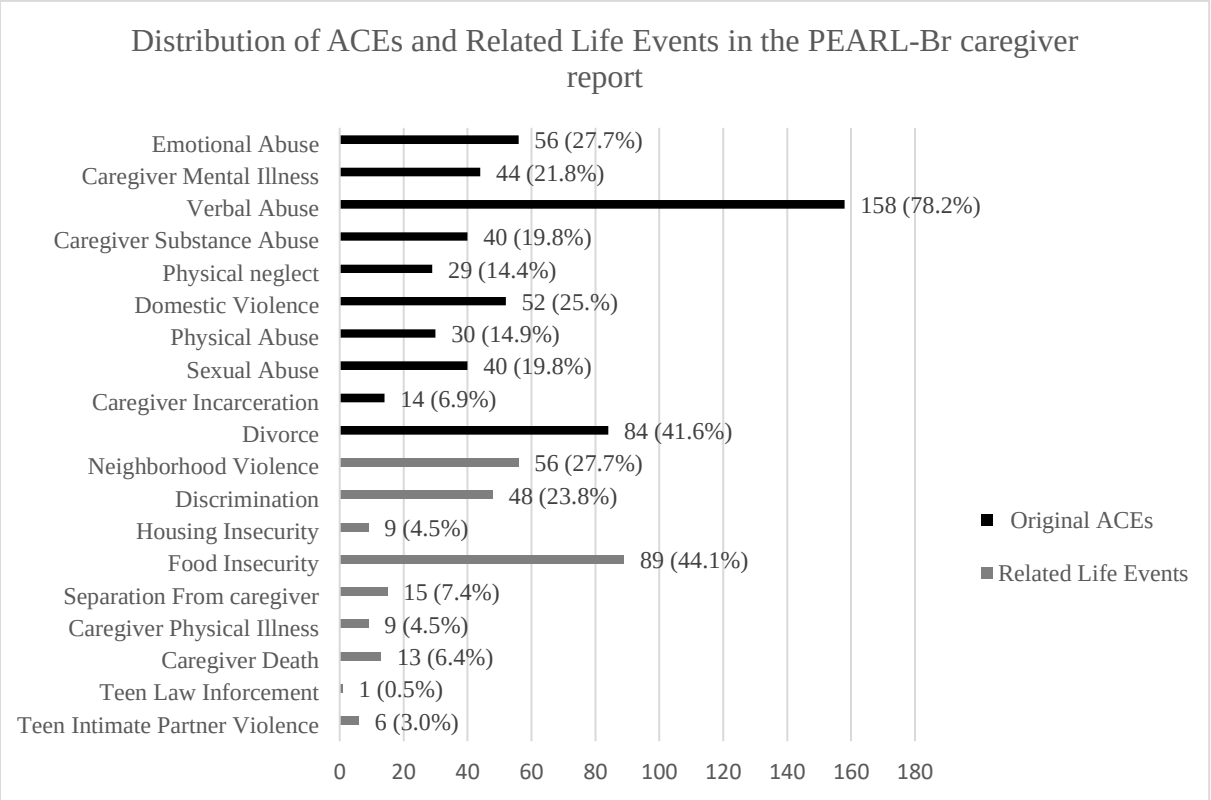

Fig. 1. Distribution of Adverse Childhood Experiences and Related Life Events in the PEARLS-BR Study. Individual responses were obtained from caregivers completing the PEARLS-BR (Child and teen versions) tool (n = 202). Responses were summarized and displayed here.

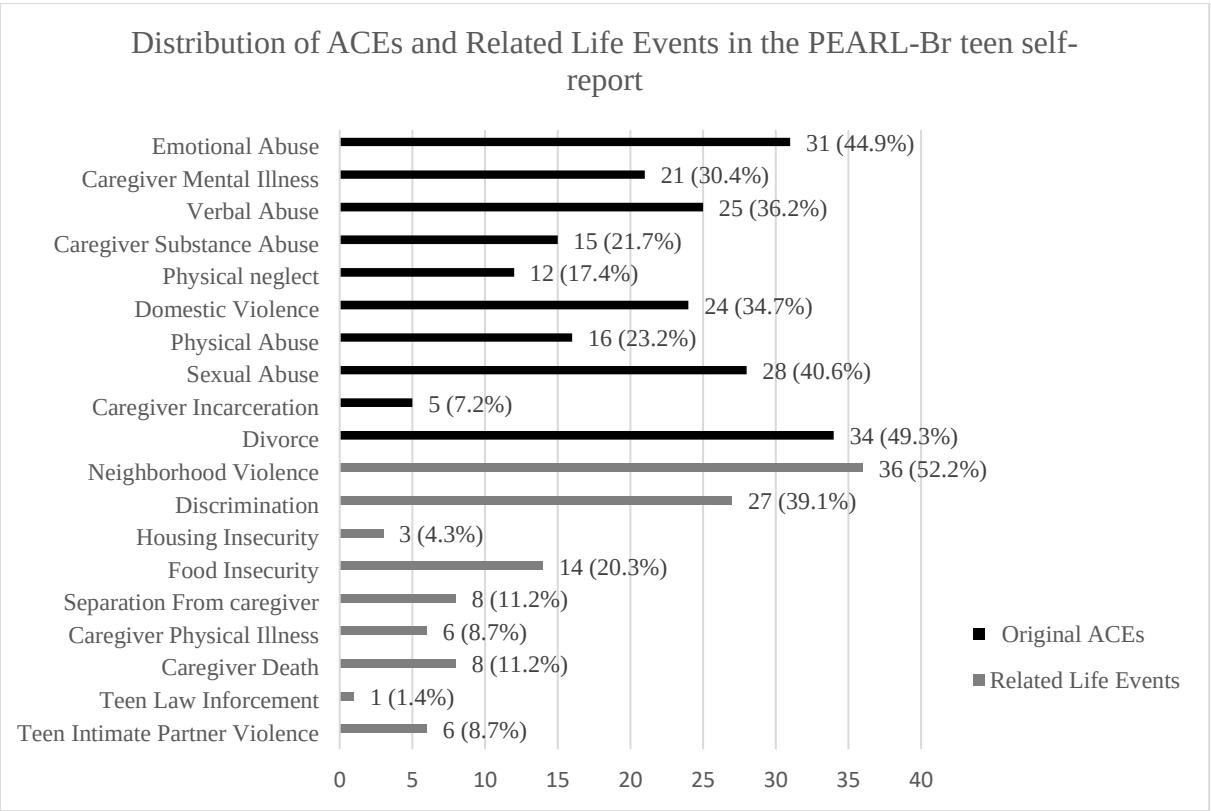

Fig. 2. Distribution of Adverse Childhood Experiences and Related Life Events in the PEARLS-BR Study. Individual responses were obtained from teens completing the PEARLS-BR (teen self-report version) tool (n = 69). Responses were summarized and displayed here.

The associations between demographic factors and the PEARLS-BR tool are presented in Table 2. Older children showed higher PEARLS scores, with an OR of 1.08 (95% CI: 1.05, 1.11) for the total PEARLS-BR score. Female children also reported higher total PEARLS-BR scores compared to male children (OR 1.46; 95% CI: 1.07, 1.99). Caregivers of Brown/Mixed-race ethnicity were associated with higher PEARLS-BR scores (OR 1.57; 95% CI: 1.17, 2.14), and a similar pattern was observed for Brown/Mixed-race children (OR 1.35; 95% CI: 0.99, 1.85), though the association was not statistically significant for the total score.

Regarding education, children attending elementary and high school exhibited higher PEARLS-BR scores compared to those who never attended school, with ORs of 2.04 (95% CI: 1.21, 3.41) and 2.94 (95% CI: 1.56, 5.59), respectively. Notably, children in high school had a significantly higher likelihood of reporting both ACEs and social determinants measured by the Related Life Events section of the PEARLS-BR tool. Grandmothers as caregivers were associated with higher PEARLS-BR scores (OR 1.92; 95% CI: 1.15, 3.35). Additionally, married caregivers reported significantly lower PEARLS-BR scores compared to single caregivers (OR 0.46; 95% CI: 0.33, 0.65). Family income, housing type, number of rooms in the house, and the number of cohabitants did not show significant associations with the total PEARLS-BR scores.

Table 2: Associations Between Demographic Factors and Adversities Identified Using the PEARLS-BR Tool in Caregivers and Children/Teens

	Adversities Identified with PEARLS-BR OR (95% CI)		
	ACEs	Related Life Events	Total PEARL-Br Score
Age			
Caregiver	1.01 (0.99, 1.03)	**1.02 (1.00, 1.03)**	**1.01 (1.00, 1.03)**
Child	**1.07 (1.03, 1.11)**	**1.08 (1.05, 1.12)**	**1.08 (1.05, 1.11)**
Caregiver Sex			
Male	Ref	Ref	Ref
Female	0.84 (0.53, 1.29)	0.90 (0.61, 1.33)	0.86 (0.58, 1.25)
Child Sex			
Male	Ref	Ref	Ref
Female	**1.72 (1.20, 2.46)**	1.13 (0.82, 1.56)	**1.46 (1.07, 1.99)**
Caregiver Ethnic-racial classification			
White	Ref	Ref	Ref
Black	0.87 (0.40, 1.92)	0.95 (0.45, 1.85)	0.90 (0.47, 1.77)
Brown/Mixed-race	**1.63 (1.15, 2.32)**	**1.47 (1.08, 2.00)**	**1.57 (1.17, 2.14)**
Indigenous	1.54 (0.53, 5.37)	1.67 (0.62, 4.09)	1.59 (0.64, 4.68)
Child Ethnic-racial classification			
White	Ref	Ref	Ref
Black	1.71 (0.83, 3,84)	1.15 (0.55, 2.24)	1.49 (0.79, 3.05)
Brown/Mixed-race	**1.51 (1.05, 2,17)**	1.10 (0.79, 1.53)	1.35 (0.99, 1.85)
Indigenous	3.31 (0.58, 54.21)	3.44 (0.77, 16.62)	3.36 (0.73, 38.03)
Asian	0.83 (0.14, 5.88)	0.86 (0.13, 3.67)	0.84 (0.20, 4.57)
Caregiver Educational level			
Elementary School (1st to 9th grade)	Ref	Ref	Ref
High School (10th to 12th grade)	0.77 (0.54, 1.10)	0.75 (0.55, 1.02)	0.77 (0.56, 1.04)
College or higher education	0.99 (0.53, 1.90)	0.73 (0.39, 1.29)	0.89 (0.52, 1.58)
Child Educational level			
Never attended school	Ref	Ref	Ref
Preschool	0.96 (0.47, 1.97)	1.34 (0.64, 2.95)	1.08 (0.58, 1.98)
Elementary School (1st to 9th grade)	**1.84 (1.01, 3.35)**	**2.50 (1.36, 5.04)**	**2.04 (1.21, 3.41)**
High School (10th to 12th grade)	**2.88 (1.39, 6.04)**	**3.09 (1.52, 6.74)**	**2.94 (1.56, 5.59)**
College or higher education	2.00 (0.41, 12.89)	2.73 (0.54, 10.87)	2.22 (0.58, 10.95)
Caregiver-child relationship			
Mother	Ref	Ref	Ref
Father	1.15 (0.72, 1.87)	0.96 (0.61, 1.48)	1.08 (0.72, 1.65)
Grandmother	**2.19 (1.24, 4.10)**	1.48 (0.86, 2.48)	**1.92 (1.15, 3.35)**
Others	1.73 (0.96, 3.28)	1.36 (0.78, 2.30)	1.59 (0.94, 2.79)
Caregiver Marital Status			
Single	Ref	Ref	Ref
Married	**0.38 (0.26, 0.57)**	**0.62 (0.43, 0.91)**	**0.46 (0.33, 0.65)**
Civil Union	0.66 (0.42, 1.03)	1.02 (0.68, 1.51)	0.78 (0.53, 1.15)
Divorced	1.32 (0.81, 2,21)	1.18 (0.73, 1.88)	1.28 (0.82, 2.03)
Widowed	1.01 (0.48, 2.25)	1.52 (0.78, 2.86)	1.78 (0.61, 2.40)
Family Income (in R$/per month)			
2,589.00 or less	Ref.	Ref	Ref
Greater than 2,589.00	0.79 (0.56, 1.11)	0.82 (0.61, 1.11)	0.80 (0.60, 1.08)
Housing Type			
House	Ref	Ref	Ref
Apartment	0.77 (0.45, 1.35)	0.73 (0.43, 1.20)	0.76 (0.48, 1.23)
Shared housing	1.37 (0.31, 9.33)	2.01 (0.58, 6.57)	1.60 (0.47, 8.23)
Number of rooms in the house			
≥5	Ref	Ref	Ref
<5	1.27 (0.86, 1,86)	1.10 (0.79, 1.56)	1.20 (0.86, 1.67)
Number of cohabitants			
2	Ref	Ref	Ref
3	0.86 (0.50, 1.48)	1.20 (0.73, 2.00)	0.97 (0.60, 1.54)
4	1.03 (0.59, 1.75)	1.26 (0.77, 2.10)	1.10 (0.68, 1.75)
5	0.84 (0.46, 1.54)	1.00 (0.57, 1.77)	0.89 (0.52, 1.50)
≥ 6	0.89 (0.47, 1.72)	1.60 (0.91, 2.83)	1.11 (0.64, 1.95)

In the PEARLS-BR study, the median number of original ACEs was 1 (IQR 0-3) for the caregiver-reported sample (n=202) and 2 (IQR 1-5) for the self-reporting teens (n=69). Among the caregiver-reported sample, 34.7% reported zero ACEs, 40.6% reported 1-3 ACEs, and 24.8% reported 4 or more ACEs. In contrast, the self-reporting teens had 18.8% reporting zero ACEs, 40.6% reporting 1-3 ACEs, and 40.6% reporting 4 or more ACEs. The median number of related life events was 1 (IQR 0-2) in the caregiver-reported sample and 1 (IQR 1-3) in the self-reporting teens. The total PEARLS-BR score had a median of 2 (IQR 1-5) for the caregiver-reported sample and 4 (IQR 2-7) for the self-reporting teens (see Table 3 for details).

Table 3: Prevalence of Adverse Childhood Experiences (ACEs) and Related Life Events Based on Caregiver Reports for Children and Teens, and Teen Self-Reports in the PEARLS-BR Study

ACE's	**PEARLS-BR Caregiver report (n=202)**	**PEARLS-BR Teen self-report (n=69)**
Original ACEs, median (IQR)	1 (0-3)	2 (1-5)
Original ACES 0 ACEs, n (%)	70 (34.7)	13 (18.8)
1-3 ACEs, n (%)	82 (40.6)	28 (40.6)
4 or more ACEs, n (%)	50 (24.7)	28 (40.6)
Related Life Events, median (IQR)	1 (0-2)	1 (1-3)
Total PEARLS-BR Score, median (IQR)	2 (1-5)	4 (2-7)

For caregiver-reported related life events, the probability of exposure to two ACEs categories ranged from 53.8% to 100% (median: 77.8%). For teen self-reports, this probability ranged from 37.5% to 100% (median: 83.3%). See Table 4 for details.

Table 4: Probability of Exposure to Original Adverse Childhood Experiences (ACEs) and Related Life Events Based on Caregiver Reports and Teen Self-Reports

Related Life Events	**Caregiver report (n = 202)**			**Teen self-report (n = 69)**		
	n (%)	Probability of 1 Original ACE	Probability of 2 Original ACEs	n (%)	Probability of 1 Original ACE	Probability of 2 Original ACEs
Neighborhood violence	56 (27.7)	87.5	73.2	36 (52.2)	88.9	77.8
Discrimination	48 (23.8)	89.6	77.1	27 (39.1)	88.9	70.4
Housing Instability	9 (4.5)	99.9	99.9	3 (4.4)	99.9	99.9
Food Insecurity	89 (44.1)	78.7	64.0	14 (20.3)	85.7	57.1
Separation from caregiver	15 (7.4)	100	93.3	8 (11.6)	87.5	87.5
Caregiver Physical Illness	9 (4.5)	88.9	77.8	6 (8.7)	100	83.3
Caregiver Death	13 (6.4)	76.9	53.8	8 (11.6)	75.0	37.5
Teen Law Enforcement[a]	1 (1.5)	99.9	99.9	1 (1.5)	99.9	99.9
Teen Intimate Partner Violence[a]	6 (8.7)	100	100	6 (8.7)	100	100
	Median	89.6	77.8		88.9	83.3
	Range	76.9-100	53.8-100		75.0-100	37.5-100

[a] These two variables are only responded to by the PEARLS-BR teen and PEARLS-BR teen self-report versions (n= 69).

Increased adversities were associated with a range of negative health outcomes as measured by the PEARLS-BR score, based on caregiver reports of children and adolescents. The analysis revealed that higher scores on the PEARLS-BR were linked to poorer physical and mental health, as well as an increased prevalence of ADHD symptoms, infections, gastrointestinal disorders, and headaches/migraines (see Table 5 for detailed results).

For physical health, higher PEARLS-BR scores were associated with poorer physical health ratings on the PROMIS Global Physical Health scale. Notably, each additional ACE increased the likelihood of poorer physical health by 1.18 times (95% CI: 1.01, 1.38). Related life events also showed a strong association with poorer physical health (OR: 1.90, 95% CI: 1.30, 2.84).

Mental health outcomes were associated with ACEs and related life events. The PROMIS Global Mental Health scale showed that children with 1-3 ACEs were over 5.70 times more likely to experience mental health deterioration (95% CI: 2.20, 17.77), and those with 4+ ACEs were over 16.55 times more likely (95% CI: 6.12, 53.59), indicating a significant deterioration in mental health. Each additional ACE increased the likelihood of poorer mental health by 1.52 times (95% CI: 1.32, 1.77). Related life events also had an impact, increasing the likelihood by 2.87 times (95% CI: 2.11, 4.04). The total PEARLS-BR score, analyzed as a continuous variable, emphasized the profound impact of adversities on mental health, with each unit increase in the score corresponding to a 1.50 times higher likelihood of mental health issues (95% CI: 1.33, 1.71).

ADHD symptoms were also associated with ACEs and related life events. Children with 4+ ACEs had an OR of 4.57 (95% CI: 1.59, 15.17), and each additional ACE increased the risk by 1.21 times (95% CI: 1.03, 1.41). Related life events demonstrated an OR of 1.81 (95% CI: 1.36, 2.46), and the total PEARLS-BR score indicated a significant relationship with ADHD symptoms (OR: 1.22, 95% CI: 1.09, 1.37).

Infections and gastrointestinal disorders also showed significant associations with PEARLS-BR scores. For infections, children with 4+ had a higher likelihood of infections (OR: 2.23, 95% CI: 1.00, 5.23), and related life events were significantly associated with infections (OR: 1.39, 95% CI: 1.07, 1.85). Gastrointestinal disorders were strongly associated with adversities, with children experiencing 1-3 ACEs having a higher likelihood (OR: 2.90, 95% CI: 1.48, 5.82) and those with 4+ ACEs having an even higher likelihood (OR: 4.00, 95% CI: 1.78, 9.61). Related life events also demonstrated an association with gastrointestinal disorders (OR: 1.86, 95% CI: 1.39, 2.58), and the total PEARLS-BR score was similarly significant (OR: 1.26, 95% CI: 1.12, 1.43).

Headaches and/or migraines were significantly associated with higher PEARLS-BR scores. Children with 4+ ACEs had a likelihood of headaches/migraines that was 4.20 times higher (95% CI: 1.96, 9.35), and each additional ACE increased the risk by 1.26 times (95%

CI: 1.11, 1.44). Related life events showed an association (OR: 1.55, 95% CI: 1.23, 1.99), and the total PEARLS-BR score also indicated a relationship (OR: 1.22, 95% CI: 1.11, 1.35).

Although obesity did not show significant associations with ACEs, either as categorical or continuous variables, nor with the total PEARLS-BR score, related life events were significantly associated with higher odds of obesity (OR: 1.37, 95% CI: 1.02, 1.88). This suggests that specific stressors may contribute to weight-related issues in children.

Atopic conditions showed a significant association with related life events (OR: 1.28, 95% CI: 1.01, 1.63). There was no statistically significant association between ACEs and atopic conditions, whether ACEs were considered as continuous variables or as part of the total PEARLS-BR score.

Table 5: Associations Between Adverse Childhood Experiences (ACEs), Related Life Events, and Health Outcomes in Children and Teens Based on Caregiver Reports in the PEARLS-BR Study

Health Outcomes	**PEARLS-BR OR (95% CI)**
PROMIS Global Physical Health	
Original ACEs - **Categorical**	
0	Ref
1-3	1.45 (0.34, 7.28)
4+	2.48 (0.58, 12.58)
Original ACEs - **Continuos**	1.12 (0.88, 1.38)
Relates Life Events - **Continuos**	**1.90 (1.30, 2.84)**
TOTAL PEARLS-BR Score - **Continuos**	**1.18 (1.01,1.38)**
PROMIS Global Mental Health	
Original ACEs - **Categorical**	
0	Ref
1-3	**5.70 (2.20, 17.77)**
4+	**16.55 (6.12, 53.59)**
Original ACEs - **Continuos**	**1.52 (1.32, 1.77)**
Relates Life Events - **Continuos**	**2.87 (2.11, 4.04)**
TOTAL PEARLS-BR Score - **Continuos**	**1.50 (1.33, 1.71)**
ADHD Symptoms	
Original ACEs - **Categorical**	
0	Ref
1-3	2.01 (0.70, 6.68)
4+	**4.57 (1.59, 15.17)**
Original ACEs - **Continuos**	**1.21 (1.03, 1.41)**
Relates Life Events - **Continuos**	**1.81 (1.36, 2.46)**
TOTAL PEARLS-BR Score - **Continuos**	**1.22 (1.09, 1.37)**
Infections	
Original ACEs - **Categorical**	
0	Ref
1-3	1.82 (0.92, 3.67)
4+	**2.23 (1.00, 5.23)**
Original ACEs - **Continuos**	1.33 (0.99, 1.32)
Relates Life Events - **Continuos**	**1.39 (1.07, 1.85)**
TOTAL PEARLS-BR Score - **Continuos**	**1.13 (1.02, 1.26)**
Gastrointestinal Tract Disorders	
Original ACEs - **Categorical**	
0	Ref
1-3	**2.90 (1.48, 5.82)**
4+	**4.00 (1.78, 9.61)**
Original ACEs - **Continuos**	**1.27 (1.10, 1.49)**
Relates Life Events - **Continuos**	**1.86 (1.39, 2.58)**
TOTAL PEARLS-BR Score - **Continuos**	**1.26 (1.12, 1.43)**
Obesity	
Original ACEs - **Categorical**	
0	Ref
1-3	1.14 (0.44, 3.01)
4+	1.52 (0.54, 4.28)
Original ACEs - **Continuos**	1.07 (0.91, 1.26)
Relates Life Events - **Continuos**	**1.37 (1.02, 1.88)**
TOTAL PEARLS-BR Score - **Continuos**	1.09 (0.97, 1.23)
Headache/Migrane	
Original ACEs - **Categorical**	
0	Ref
1-3	1.48 (0.77, 2.87)
4+	**4.20 (1.96, 9.35)**
Original ACEs - **Continuos**	**1.26 (1.11, 1.44)**
Relates Life Events - **Continuos**	**1.55 (1.23, 1.99)**
TOTAL PEARLS-BR Score - **Continuos**	**1.22 (1.11, 1.35)**
Atopic Conditions	
Original ACEs - **Categorical**	
0	Ref
1-3	1.45 (0.75, 2.80)
4+	1.04 (0.50, 2.17)
Original ACEs - **Continuos**	1.00 (0.89, 1.13)
Relates Life Events - **Continuos**	**1.28 (1.01, 1.63)**
TOTAL PEARLS-BR Score - **Continuos**	1.04 (0.95, 1.14)

Discussion

This study investigated the associations between ACEs and child health outcomes in Brazil, utilizing data from the PEARLS-BR study. By focusing on a Brazilian sample, it aimed to explore the prevalence and impact of ACEs within a cultural context distinct from that observed in studies conducted in high-income countries. Unlike other studies, this research employed a tool validated in Brazil to screen for ACEs in the pediatric population. The results highlight significant associations between several demographic variables and PEARLS-BR scores, revealing the varying impact of ACEs across different subgroups of the population. Furthermore, this investigation provides crucial insights into how ACEs and related life events influence health outcomes in a Brazilian context.

Findings reveal that older children, female, and those with Brown/Mixed-race caregivers had higher PEARLS-BR scores. Older children reported more adversities due to longer exposure. (2) The higher scores among female children might reflect gender-specific vulnerabilities or differences in reporting. (2, 31,32) The association of higher PEARLS-BR scores with Brown/Mixed-race caregivers underscores racial and ethnic disparities in childhood adversities, aligning with evidence suggesting that minority groups often face greater stress due to systemic inequalities. (2, 33, 34)

Higher PEARLS-BR scores were also observed in children attending school compared to those who never attended, suggesting increased exposure to social interactions and adversities in school settings, as well as enhanced cognitive ability to recognize and report adversities (40) The presence of grandmothers as primary caregivers was associated with higher PEARLS-BR scores, possibly reflecting the additional stressors faced by multi-generational households or the absence of parents. (32) Conversely, married caregivers had lower scores than single caregivers, highlighting the greater risk for ACEs in single-parent households due to economic and social stressors. (32) These findings emphasize the importance of supporting single-parent families to mitigate these risks.

Interestingly, no significant associations were found between family income, housing type, number of rooms, or cohabitants and PEARLS-BR scores, suggesting these factors might not directly influence reported adversities in this sample. This result is consistent with another study conducted in Brazil (32) and contrasts with findings from high-income countries, where such factors are often significant. (2,6) The lack of association may be due to the study's socio-demographic profile, which includes primarily lower-income groups and few participants from higher-income brackets. Additionally, the income cut-off of R$2500 might be too low to differentiate between different socioeconomic backgrounds.

The high prevalence of ACEs and related life events reported by both caregivers and teens underscores the pervasive nature of childhood adversities. These findings align with

previous research indicating that ACEs are common and widespread in various populations. (1,35) The most prevalent ACEs and related life events, such as verbal abuse, divorce, food insecurity, and neighborhood violence, indicate a critical need for targeted interventions addressing these specific issues. (2)

Teens reported more adversities than caregivers, suggesting differences in perception or willingness to disclose, consistent with research showing age-related variations in reporting. (3) This underscores the need for considering multiple perspectives in ACE assessments and developing age-appropriate strategies to address adversities. (6) Notably, teen-specific events such as law enforcement encounters and intimate partner violence, though less frequently reported, had a 100% probability of ACEs, highlighting their severe impact on adolescents. These findings emphasize the need for specialized, trauma-informed interventions to address these unique challenges and improve outcomes for affected teens (3,8).

The analysis of the probability of original ACEs and related life events revealed that these are often interconnected, with children frequently exposed to multiple categories of adversities. This interconnectedness underscores the complexity of adverse experiences in children's lives, suggesting that certain life events do not occur in isolation but are linked with a broader spectrum of adversities. This finding aligns with research showing that exposure to one type of adversity often leads to additional adversities, compounding their impact on health. (6,35) Recognizing this interconnectedness supports the development of comprehensive intervention strategies to address the multifaceted nature of childhood adversities. (31,34)

Neighborhood violence and discrimination were reported by a significant portion of both caregivers and teens, with high probabilities of associated ACEs highlighting the impact of community violence and discrimination on child development. This aligns with literature linking these factors to negative outcomes in children. (36,37) Despite lower reporting rates, housing instability and food insecurity had high probabilities of associated ACEs, underscoring the importance of stable housing and food security for child well-being. These results emphasize the importance of addressing basic needs as part of interventions aimed at reducing ACEs and improving child health outcomes. Studies by Cutts et al. and Coley et al. highlight the significant role that stable housing and food security play in promoting positive developmental outcomes and preventing adverse health impacts in children. (38,39) Stability in housing and access to nutritious food are fundamental to a child's development and overall health.

Separation from a caregiver, caregiver illness, and caregiver death were also associated with high probabilities of ACEs, reflecting the profound impact of family disruptions on children's health. These findings align with the study by Felitti et al., on household dysfunction and childhood abuse. (1) Similar to these results, Bethell et al. found that family-related adversities significantly impact children's school engagement and overall health, emphasizing the role of stability in a child's environment. (6) Furthermore, Thakur et al.

demonstrated that caregiver illness and family instability are critical factors in the health outcomes of children in safety-net practices. (2) The stability and health of caregivers play a pivotal role in the emotional and psychological well-being of children, making it crucial to support these family dynamics. This underscores the necessity for targeted support interventions for children experiencing such disruptions. (9) Future research should continue to explore these associations to develop comprehensive strategies for mitigating the impacts of such adversities on children's health.

The results of this study indicate that increased adversities, as measured by the PEARLS-BR, based on caregiver reports of children and adolescents, are associated with a wide range of negative physical and mental health outcomes. Higher PEARLS-BR scores were linked to poorer physical and mental health, as well as an increased prevalence of conditions such as ADHD symptoms, infections, gastrointestinal disorders and headaches/migraines. This indicates that adversities can affect children's immune and gastrointestinal health, as well as exacerbate chronic and inflammatory conditions. (40) Similar results have been observed in other studies, which also found that childhood adversities are linked to increased risks of various physical health issues. (2,40,41) These findings highlight the necessity of addressing childhood adversities as part of a comprehensive approach to managing chronic conditions and promoting overall health.

The PROMIS Global Health scale indicated that higher PEARLS-BR scores corresponded to lower physical health ratings, highlighting the impact of childhood adversities on various dimensions of health. Significant odds ratios for health impairments were observed in both the 1-3 ACEs and 4 or more ACEs categories, emphasizing the detrimental effects of ACEs on these health outcomes. These results are consistent with the findings of Felitti et al. (1), who demonstrated a strong link between ACEs and various leading causes of death in adults, underscoring the long-term impacts of childhood adversities. Additionally, Lowthian et al. noted similar associations supporting the notion that early adversities can have pervasive effects on multiple aspects of health and behavior. (42)

Regarding mental health, adversities were strongly associated with poorer outcomes, with children exhibiting significant deterioration in mental health, as measured by the PROMIS Global Health scale. Children with 1 to 3 ACEs have five times higher odds of developing mental health issues, while those with 4 or more ACEs face sixteen times higher odds. This underscores the importance of targeted interventions to mitigate the effects of childhood adversities on mental health. (9) Additionally, higher PEARLS-BR scores were associated with a higher prevalence of ADHD symptoms, with children experiencing 4 or more ACEs having four times the odds of developing ADHD. These findings align with existing literature linking ACEs to ADHD (8,43)

The interventions in order to mitigate the impacts of childhood adversities on health should include trauma-informed care, mental health support, and programs that address the specific needs of children and adolescents exposed to adversities. (44) Additionally, it is crucial to develop strategies to support caregivers and families to reduce risk factors and promote healthy environments for child development. Addressing both family-related and community-level adversities can lead to more effective and holistic intervention strategies, fostering resilience and improving long-term health outcomes. Public policies should focus on reducing community violence and discrimination by implementing intervention programs and establishing support centers. Additionally, enhancing housing stability and food security through rental subsidies and food assistance programs is crucial. These measures can significantly improve living conditions and overall health outcomes. (45,46)

Despite limitations such as the sample size, which prevented the calculation of associations for adolescent self-reports, the cross-sectional design, which restricted causal inferences, and the potential reporting bias introduced by relying on caregiver reports for younger children, this study provides valuable insights into ACEs and health outcomes in Brazil. Future research should involve larger, more diverse samples and utilize longitudinal designs to better understand these relationships and the role of protective factors.

Conclusions:

This study investigated the associations between ACEs and child health in Brazil, using data from the PEARLS-BR study. The findings confirmed the high prevalence and significant impact of ACEs on Brazilian children and adolescents, highlighting associations with poorer physical and mental health outcomes. The PEARLS-BR score effectively identified these associations, and it was found that other common social determinants measured by the Related Life Events section of the PEARLS tool also present comparable risks to child health. These findings underscore the need for targeted interventions to mitigate the effects of childhood adversities and highlight the clinical relevance of using the PEARLS-BR as a tool to identify children at risk for adverse health outcomes. This contextual data can inform public health practices and clinical interventions specific to Brazil.

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5 **CAPÍTULO 4** – CAPÍTULO DE LIVRO: EXPERIÊNCIAS ADVERSAS NA INFÂNCIA: ESTRESSE TÓXICO E O IMPACTO NA SAÚDE DA CRIANÇA

1
Experiências adversas na infância: estresse tóxico e o impacto na saúde da criança

Luciana Cristina Mancio Balico
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A reabsorção da circunstância é o destino concreto do homem.
José Ortega y Gasset, em *Meditações do Quixote*

Introdução

O impacto de experiências adversas graves na infância sobre a saúde mental já foi muito bem estudado por diversas correntes teóricas da psicologia, desde a psicanálise até as correntes cognitivistas e sistêmicas. Já é sabido que eventos graves na infância podem levar a problemas psicológicos como, por exemplo, depressão ou suicídio (SCHILLING *et al*., 2007). No entanto, evidências atuais sugerem fortemente que essas mesmas experiências adversas também levam a desfechos orgânicos, que seriam menos intuitivos à primeira análise, como, por exemplo, hepatite, isquemia cardíaca, câncer de pulmão, doença obstrutivo-crônica dos pulmões, dentre outras doenças clínicas, na vida adulta (FELITTI *et al*., 1998).

O primeiro estudo que mostrou a associação entre experiências adversas graves na infância e doença orgânica na idade adulta foi conduzido por Felitti e Anda (1998) nos Estados Unidos. Neste estudo, foram investigados mais de 13 mil adultos acerca de seu histórico de exposição àquilo que os autores chamaram de "experiências adversas na infância" (*Adverse childhood experiences* (ACE)) (FELITTI *et al*., 1998). Os autores incluíram no grupo dos ACEs eventos como violência sexual, física ou emocional; negligência física ou emocional; doenças mentais, dependência química ou prisão dos pais; separação ou divórcio dos pais, ou violência doméstica. Através de um questionário com 10 perguntas, cujas respostas eram "sim" ou "não", foi investigada a ocorrência de cada um dos ACESs. Para cada "sim", o participante da pesquisa recebia um ponto no escore. Em seguida, correlacionou-se as pontuações do escore ACE com desfechos clínicos e orgânicos de saúde. O estudo mostrou que os ACEs eram muito

prevalentes na população estudada: 67% dos participantes reportaram pelo menos uma experiência adversa na infância, e um em cada oito reportaram uma pontuação alta, com escore de quatro ou mais ACEs. Além disso, foi demonstrada uma relação dose-resposta entre a pontuação atingida no escore ACEs e o impacto na saúde; ou seja, quanto maior a pontuação do ACE, piores eram os desfechos de saúde. Inicialmente, foram analisados desfechos classicamente associados ao comportamento e com impacto psicológico, como depressão e suicídio. Foi visto que participantes que pontuavam 4 ou mais pontos na escala ACEs tinham um risco 4,5 vezes maior para desenvolverem depressão, e um risco de suicídio 12 vezes maior do que participantes com 3 ou menos pontos. As relações apontadas entre as experiências adversas e esses desfechos não diferiam muito daquilo já extensamente sabido pela ciência. No entanto, outros desfechos, com características não diretamente relacionadas à doença psíquica, como doenças orgânicas, também apresentavam associação direta com o escore ACEs. Como exemplos, pode-se citar a doença obstrutivo-crônica dos pulmões e a hepatite, que aumentam, ambas, 2,5 vezes quando o participante apresenta um escore de 4 ou mais. Também aumentam o risco de doença cardiovascular isquêmica (3,5 vezes mais) e de câncer de pulmão (3 vezes mais) quando a pontuação no escore ACE é de 7 ou mais (FELITTI *et al*., 1998).

Os estudos que avaliam mais precocemente o impacto do escore ACEs sobre desfechos de saúde, com doença manifestada ainda na infância, são mais recentes (KOITA *et al*., 2018). Resultados das pesquisas do consórcio *Bay Area Research Consortium on Toxic Stress and Health* (BARC), dos Estados Unidos, apontam que pontuações mais altas nos ACEs estão associadas a uma pior percepção da saúde geral já na infância. As crianças estudas e com alto escore apresentavam pior funcionamento executivo global, maior probabilidade de dores de estômago e aumento no risco de asma (THAKUR *et al*., 2020). Outro estudo mostrou que, em bebês, exposições aos ACEs estão associadas a atraso no crescimento, atraso cognitivo e distúrbios do sono. Escolares com alta pontuação mostraram maior prevalência de asma e pior resposta à medicação, no tratamento da doença; incidência aumentada de infecções respiratórias (virais, de ouvido e pneumonia), e maiores dificuldades de aprendizado e problemas de comportamento. Já nos adolescentes, os desfechos de saúde mais impactados por uma alta pontuação foram a incidência de obesidade, *bullying,* violência, tabagismo, gravidez e paternidade precoce (HARRIS, 2018).

Antes de as publicações sobre os ACEs surgirem para elucidar o quanto as experiências adversas na infância estão associadas à saúde orgânica, acreditava-se que os comportamentos de risco precipitados ou induzidos pelas experiências adversas seriam os fatores responsáveis pelo surgimento dessas doenças. Como exemplo desta hipótese de relação linear, pode-se citar o comportamento de tabagismo associado ao câncer de pulmão (ARAUJO *et al.*, 2018), ou ainda, ao alcoolismo predispondo à hepatite (DANTAS, 1985; LESSA, 1997). As doenças assim eram compreendidas como consequência direta de comportamentos voluntários, sendo, estes, sim, considerados os reais fatores de risco. No entanto, a partir dos estudos sobre as ACEs, evidenciou-se que os desfechos negativos de saúde apresentam-se aumentados, mesmo quando se procede ao controle estatístico das variáveis de confusão; no caso, os comportamentos de risco. Ou seja, mesmo adultos e adolescentes que não se envolviam em comportamentos arriscados ou violentos apresentavam desfechos desfavoráveis de saúde secundários ao impacto dos ACEs. A partir dessas evidências, entendeu-se que o mecanismo do surgimento das doenças não é explicado apenas por comportamentos de risco, mas também pela própria exposição aos ACEs. As experiências adversas na infância passaram então a ser entendidas como fatores de risco independentes para doença orgânica.

A partir dos resultados que demonstraram a independência dos ACEs, como fatores de risco para doença orgânica, foi necessário investigar outros mecanismos fisiopatológicos que relacionassem, causalmente, as experiências adversas graves na infância, com o desenvolvimento de patologias. Assim, postulou-se que, talvez, algum outro mecanismo bioquímico ou hormonal fosse o responsável pelos achados.

A biologia dos ACEs:

Uma vez que comportamentos de risco não explicam totalmente o impacto dos ACEs sobre a saúde, postula-se, atualmente, que o mecanismo mais provável esteja relacionado a uma resposta aumentada e frequente da ativação do eixo hipotálamo-hipófise-suprarrenal. Esse sistema de reação ao estresse comanda a reação de "luta ou fuga" do ser humano. Numa situação de perigo, imediatamente o hipotálamo envia um sinal à glândula hipófise, que, por sua vez, envia um sinal à glândula adrenal, que libera hormônios do estresse: o cortisol e a adrenalina. Essa liberação de hormônios leva a uma

série de efeitos fisiológicos como taquicardia, dilatação pupilar e expansão das vias aéreas, que preparam o corpo para a luta ou para a fuga. Essas respostas fisiológicas são normais e protetoras, em casos de ameaça real à vida, mas a ativação repetida e frequente desse sistema pode deixar de ser adaptável, tornando-se prejudicial à saúde. As crianças são especialmente sensíveis a essa ativação repetitiva por estresse, porque seu sistema nervoso ainda está em desenvolvimento (HARRIS, 2018).

O cortisol, por sua vez, leva a uma série de outras respostas fisiológicas que mantêm um estado inflamatório exacerbado ou intermitente, facilitando, por exemplo, infecções do trato respiratório superior, gastroenterites e outras infecções virais (KARLÉN *et al*., 2015). A desregulação do sistema de resposta ao estresse predispõe também a ocorrência de doenças reguladas diretamente pelo sistema imunológico, como alergias, eczemas, asma e doenças autoimunes (HARRIS, 2018). Conclusões semelhantes já haviam sido sugeridas por Felitti *et al*. (1998), ao analisarem os dados de ACEs de quinze mil participantes, verificando a frequência com que estes participantes eram hospitalizados por outras doenças autoimunes, tais como: artrite reumatoide, lúpus, diabetes tipo-1, doença celíaca e fibrose pulmonar idiopática. Participantes que apresentaram um escore ACE de dois ou mais, mostraram duas vezes mais chances de hospitalização por doença autoimune, quando comparados a controles com escore igual a zero. O impacto desses achados corroborava a impressão inicial de que comportamentos de risco não seriam a única resposta causal para os efeitos observados, pois as doenças autoimunes são muito pouco afetadas em sua indução, por comportamentos de risco. Assim, os achados relacionados às doenças infecciosas, reforçados pelos desfechos de doenças autoimunes, confirmaram a hipótese de que pessoas com alto grau de exposição ao estresse tóxico, estão mais propensas a desenvolver doenças de modo independente da adoção de comportamentos de risco (KARLÉN *et al*., 2015).

Outra estrutura envolvida no impacto das experiências adversas graves sobre desfechos orgânicos de saúde é a amigdala cerebral. Quando a amígdala é acionada repetidamente por estresse crônico, ela se torna hiperativa, e o resultado disto é uma resposta exagerada a situações que não, necessariamente, são consideradas um perigo. Um estudo com crianças severamente maltratadas em orfanatos romenos mostrou, através de

neuroimagens, um alargamento da amígdala nessas crianças (TOTTENHAM *et al*., 2010). Outro desfecho que ocorre, quando a amígdala é cronica ou repetitivamente ativada, é a desorganização do mecanismo de predição do perigo; ou seja, a amígdala começa a enviar sinais desnecessários para outras partes do cérebro, acerca de falsos estímulos, que não são verdadeiramente ameaçadores. Além disso, altas doses de adversidade não apenas afetam a estrutura e as funções cerebrais, como, também, o sistema imunológico em desenvolvimento, o sistema endócrino e até a forma como o DNA é lido e replicado (DE SOUSA *et al*., 2015).

Embora a relação entre os ACEs e os desfechos orgânicos não pareçam ocorrer em virtude da adoção direta de comportamentos de risco, os ACEs também parecem induzir alguns desses próprios comportamentos de risco, mas por um mecanismo um pouco diferente e mais complexo do que se poderia presumir, apenas por fatores socioeducacionais. O aumento do nível de cortisol, secundário à exposição precoce às adversidades, afeta também o desenvolvimento do cérebro das crianças, atingindo áreas como o núcleo *accumbens*, o centro de prazer e de recompensa, que está envolvido, por exemplo, no processo de dependência química (FELITTI *et al*., 1998). Ele inibe o córtex pré-frontal, região crucial para o aprendizado e necessário para o controle de impulso e das funções executoras. Esses achados mostram que existem mecanismos orgânicos, no neurodesenvolvimento, que explicam por que pessoas expostas a altas doses de adversidade estão mais propensas a apresentar comportamentos de alto risco (HARRIS, 2018).

As teorias que postulam que a ativação do sistema hipotálamo-hipófise-suprarrenal é o mecanismo responsável pelos efeitos negativos sobre tantos desfechos de saúde são reforçadas por recentes achados, que quantificam níveis séricos de mediadores e marcadores de inflamação, como a proteína-C-reativa (PC-R) e a interleucina-6 (IL-6) em pacientes com escores elevados no ACEs (BAUMEISTER *et al*., 2016). Mais recentemente, foi demonstrado também um aumento muito significativo em outro marcador inflamatório, o receptor do ativador de plasminogênio tipo uroquinase solúvel (suPAR). Níveis plasmáticos de suPAR refletem de modo geral o estado de ativação geral do sistema imunológico. Assim, níveis elevados de suPAR indicam atividade inflamatória aumentada, refletindo de maneira mais acurada o nível de estresse crônico, do que os marcadores de fase aguda, como a PC-R e a IL-6. Além disso, a alteração

do nível de suPAR corrobora a hipótese de maior vulnerabilidade da infância, já que os níveis de suPAR elevam-se de maneira mais intensa, quando ACEs de mesma natureza e intensidade ocorrem antes dos 12 anos de idade, em comparação aos ocorridos na adolescência (JEE *et al*., 2020). É possível que brevemente mais marcadores venham a ser adicionados nesses painéis, confirmando o impacto dos ACEs sobre a regulação neuro-hormonal.

Nos últimos anos, novas evidências têm demonstrado que esses efeitos são passíveis de transmissão intergeracional para a prole e, possivelmente, até para gerações subsequentes (JOAQUIM *et al*., 2017; ROSEBOOM *et al*., 2006). Atualmente, o mecanismo fisiopatológico mais investigado, a fim de explicar esses efeitos persistentes, envolve os telômeros, segmentos repetitivos de DNA não codificante, localizados nas extremidades dos cromossomos. Os telômeros ajudam a determinar quão rapidamente as células envelhecem e quando elas morrem, dependendo da velocidade do seu desgaste. A cada divisão celular os telômeros tendem a ficar mais curtos. Os telômeros não apenas executam os comandos emitidos por seu código genético, mas também são influenciados pelo modo de vida, ou seja, hábitos saudáveis podem aumentar os telômeros, assim como estresse pode acelerar a diminuição dos mesmos, precipitando, consequentemente, o surgimento de doenças. Os processos epigenéticos são permeáveis à influência ambiental, ajudando o organismo a se adaptar ao meio em que vive, através da metilação genética, possibilitando que as marcações epigenéticas sejam passadas de geração a geração (SOUSA, 2015). O estresse, consequência da exposição aos ACEs, impacta no comprimento e na integridade do telômero, o que por sua vez aumenta o risco do surgimento de doenças (LANG *et al*., 2020).

Os estudos sobre regulação epigenética e telômeros (LANG *et al*.; 2020) reforçam a importância da detecção precoce dos ACEs, antes que se torne crônico o estresse tóxico. A identificação precoce daqueles pacientes com altos escores e com risco aumentado, através do rastreamento ativo do ACEs, melhora também as chances de detecção precoce de doenças orgânicas a eles relacionadas, sendo plausível postular também taxas de cura mais altas, dependendo da doença. Além disso, também é possível uma abordagem de prevenção de doenças futuras, a partir do reconhecimento do mecanismo de dano que é ativado pela resposta intermitente ao estresse (KOITA *et al*., 2018).

O estresse tóxico já foi detectado e reconhecido em muitos países de contextos socioeconômicos e culturais diferentes. Os escores ACESs não são significativamente afetados em função da classe social, classe econômica, raça, credo ou escolaridade. Situações como doença mental na família, alcoolismo parental, abuso físico, maus-tratos, entre outros, são situações que são marcadores de ACEs e independem de fatores sociopolíticos ou econômicos da pessoa (HARRIS, 2018). Isso torna ainda mais desafiadora a investigação dos ACES, demandando, assim, um olhar atento de toda a sociedade.

Tratamento

A partir da compreensão não só de quais sistemas do corpo humano possam estar lesados, mas, também, sabendo de que forma ocorrem os danos, torna-se possível pensar em estratégias de prevenção e tratamento. E uma dessas estratégias advém do conceito de "alostase". Os mecanismos fisiológicos do corpo humano têm a função de manter a homeostase, que é a manutenção da estabilidade do meio interno (temperatura corporal, batimentos cardíacos, pH, dentre outros). Todavia, quando surgem desafios impostos pelo ambiente social, físico, ou ambos, de forma inesperada ou contínua, ultrapassando os limites de previsibilidade, intensidade e duração, sistemas regulatórios são ativados. Esses sistemas naturalmente buscam a homeostase, ou seja, o equilíbrio diante de situações de alta demanda metabólica ou estresse. Isso define o que ficou conhecido como alostasia (SOUSA, 2015). Em um organismo em alostasia, os sistemas orgânicos conseguem funcionar em diferentes condições de estresse e pressão, uma vez que mecanismos "moduladores" possibilitam ajustes no funcionamento do corpo, levando a uma adaptação eficiente ao contexto desafiador. A necessidade para o estabelecimento de uma nova condição de ajuste pode ser desencadeada por agentes internos (genéticos, neurais ou hormonais) ou externos (ambiente físico e social), podendo estes ser previsíveis ou não, como ocorre nos casos de aparecimento de um novo agente estressor. A intensidade e a duração da ativação dos sistemas alostáticos de um organismo são determinadas por características do próprio estímulo (natureza, previsibilidade, tempo de exposição) e pela capacidade que o organismo possui em lidar com a situação, conhecida como plasticidade fenotípica. Esta, por sua vez, está diretamente relacionada a fatores individuais (sexo, idade,

temperamento, controle sobre o agente estressor) e aos suportes sociais disponíveis. O balanço e o equilíbrio entre esses vários fatores determinam a capacidade de enfrentamento e, indiretamente, o grau de impacto que os ACEs terão sobre cada indivíduo, o que explica o porquê de algumas pessoas serem mais resilientes e outras desenvolverem patologias físicas ou mentais, quando submetidas a essas experiências (SOUSA, 2015).

Um ambiente seguro, estável e estimulante desde o início da vida prepara biologicamente as crianças para desenvolverem um sistema saudável de resposta ao estresse na idade adulta. Para evitar que uma resposta tolerável ao estresse caia na zona de estresse tóxico, é necessária a presença de um adulto protetor para mitigar, adequadamente, o impacto do fator estressor. Uma mãe afetuosa e cuidadosa, ou um pai presente e atencioso, por exemplo, podem não apenas atenuar a liberação de hormônios do estresse, como também prevenir alterações epigenéticas, que levam a uma resposta desregulada ao estresse e aos principais problemas de saúde, que podem surgir a partir dessas experiências (DANESE; MACEWEN, 2012).

Nas últimas décadas, programas sociais vêm sendo desenvolvidos em nível de saúde pública, a fim de preencher essa lacuna no Brasil. No Rio Grande do Sul, por exemplo, desde 2003 existe o programa Primeira Infância Melhor (PIM), que trabalha com a premissa de que o desenvolvimento integral da infância passa pelo fortalecimento das famílias, para que estas possam educar e cuidar, efetivamente, de seus filhos (PIM, 2021). O programa capacita os pais ou cuidadores, para qualificarem suas interações com as crianças, orientando-os para que atuem como agentes redutores dos impactos dos ACEs (assim como de outras experiências adversas menores) sobre seus filhos, minimizando os efeitos do estresse tóxico e capacitando as crianças para que desenvolvam resiliência, a partir de sua plasticidade fenotípica. O PIM, além de integrar programas estratégicos do governo gaúcho, serviu de inspiração para iniciativas previstas na "Ação Brasil Carinhoso" e no "Programa Criança Feliz" (PCF), ambos do governo federal. O "Ação Brasil Carinhoso" está vinculado ao Ministério da Educação e tem como foco crianças de zero a 48 meses, cujas famílias sejam beneficiárias do Programa Bolsa Família.

> Consiste na transferência automática de recursos financeiros aos municípios para custear despesas com manutenção e desenvolvimento da educação infantil, contribuir com as ações de cuidado integral, segurança alimentar e nutricional, além de

> garantir o acesso e a permanência da criança na educação infantil (FNDE, 2021)

O "Programa Criança Feliz" está vinculado ao Ministério da Cidadania e tem como objetivo "promover o desenvolvimento integral das crianças na primeira infância, considerando sua família e seu contexto de vida" (MINISTÉRIO DA CIDADANIA, 2021) sendo seu modo de trabalho e intervenção muito semelhante ao PIM gaúcho.

Considerações finais

A partir do reconhecimento de que o estresse tóxico é um problema grave de saúde pública, pode-se então usar as ferramentas certas para gerar soluções. O PIM e o PCF são algumas ferramentas que já vêm sendo usadas como forma de prevenção primária. No entanto, novas estratégias de enfrentamento são necessárias; envolvem outros participantes, como agentes de saúde comunitária, equipes de estratégia de saúde da família, médicos e demais profissionais da saúde. Estes profissionais têm a oportunidade de interagir nas questões das famílias e, por vezes, direcionam seu foco de modo exclusivo a desfechos orgânicos de saúde, desperdiçando, assim, oportunidades de detecção e intervenção precoce em ambientes tóxicos. Por sua posição de observadores privilegiados, esses profissionais devem investigar e manter uma escuta ativa, indo além daquilo que é manifestamente trazido pelas famílias, encontrando dessa forma aquelas experiências que têm o potencial de trazer danos em longo prazo, sejam eles de ordem física ou psicológica. O rastreamento ativo e precoce dos ACEs pode permitir aos profissionais da saúde orientar as famílias, atenuando danos e gerando assim grande impacto na saúde em longo prazo.

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6 LIMITAÇÕES DO ESTUDO

O estudo apresentou algumas limitações que devem ser consideradas ao interpretar os resultados obtidos. Primeiramente, as análises de invariância configural, métrica e escalar, que são relevantes para a análise fatorial confirmatória multigrupo, não foram realizadas devido ao tamanho pequeno e desproporcional das amostras. Embora o instrumento PEARLS-BR, nas versões para crianças e adolescentes (reportadas pelos pais), tenha demonstrado robustez entre diferentes faixas etárias e gêneros dentro da amostra, a falta de uma amostra suficientemente grande impossibilitou a realização dessas análises complexas. São necessárias pesquisas futuras com amostras maiores e mais representativas para explorar a invariância de mensuração por meio da análise fatorial confirmatória multigrupo e validar o PEARLS-BR em contextos mais variados.

Adicionalmente, a amostra reduzida de adolescentes que responderam à versão de autorrelato do PEARLS-BR não permitiu realizar a análise fatorial confirmatória desta versão, o que impacta a validade de construto do instrumento em sua forma de autorrelato. Além disso, devido ao tamanho limitado da amostra, não foi possível calcular a associação entre o escore PEARLS-BR Adolescente Autorrelato e os desfechos de saúde nesta população.

Outro ponto a considerar é que a dependência de relato dos cuidadores das crianças mais novas pode introduzir viés de relato, pois os cuidadores podem subnotificar ou interpretar erroneamente certas experiências adversas ou desfechos de saúde. A população estudada era predominantemente de famílias de baixa renda, o que deve ser levado em conta ao interpretar os resultados.

Outra limitação é a ausência de um acompanhamento longitudinal, o que estava fora do escopo deste estudo, restringindo a capacidade de fornecer informações detalhadas sobre como as experiências adversas na infância afetam a saúde ao longo do tempo. Estudos longitudinais futuros são essenciais para compreender os mecanismos causais e as trajetórias de saúde associadas às adversidades na infância.

A coleta de dados foi limitada a uma amostra da região sul do Brasil que utilizava serviços públicos de saúde. No entanto, o PEARLS-BR é aplicável em âmbito nacional. Isso se justifica pelo fato de que o Hospital Geral, local da coleta, faz parte da 5ª Coordenadoria Regional de Saúde do Rio Grande do Sul, abrangendo 49 municípios e uma população de aproximadamente 1.200.000 habitantes (Censo 2022). (16) Além disso, a Análise Fatorial Confirmatória (CFA) multigrupo confirmou a invariância das medidas em diferentes subgrupos, sustentando a validade do instrumento para utilização em diferentes contextos dentro do país. O rigor dos processos científicos seguidos, conforme a literatura, reforça ainda mais a adequação do PEARLS-BR para a aplicação nacional, similar a outros questionários e escalas validados no Brasil utilizando a mesma metodologia

7 PERSPECTIVAS FUTURAS

As perspectivas futuras para o PEARLS-BR incluem desenvolver tratamentos e intervenções eficazes para mitigar o impacto das adversidades na infância no bem-estar dos indivíduos. A triagem de rotina pode fornecer dados cruciais para avaliar o fardo econômico das adversidades na infância, evidenciado pelo custo anual de $14.1 trilhões nos Estados Unidos, e guiar investimentos em estratégias para melhorar a saúde da população. (17)

Outra área de pesquisa futura envolve a avaliação da resiliência, a partir das respostas qualitativas das famílias sobre as qualidades de seus filhos e as estratégias que ajudam a superar momentos difíceis. Ainda não existem estudos focados na resiliência avaliada pelo PEARLS. Analisar essa resiliência é crucial para compreender como fatores de proteção podem mitigar os efeitos das experiências adversas e contribuir para o desenvolvimento de intervenções mais eficazes.

A validação do PEARLS-BR abre novas oportunidades para a implementação de estratégias de identificação precoce e intervenção no contexto brasileiro. Intervenções que visem tanto o nível individual quanto comunitário podem ajudar a mitigar os efeitos adversos das experiências negativas na infância. Pesquisas futuras também devem explorar intervenções específicas que abordem os determinantes sociais da saúde, como programas comunitários e de políticas públicas, além de considerar a aplicação do rastreamento de adversidades em escolas públicas, para reduzir o impacto das adversidades na saúde das crianças brasileiras.

8 CONSIDERAÇÕES FINAIS

O presente estudo teve como objetivo traduzir, adaptar transculturalmente e validar o questionário "Pediatrics ACEs and Related Life Event Screener" (PEARLS) para uso no Brasil. Inicialmente, a tradução e adaptação transcultural do PEARLS foram realizadas seguindo rigorosos procedimentos metodológicos, assegurando que a versão brasileira do instrumento fosse culturalmente apropriada e mantivesse a validade do conteúdo original. Este processo envolveu a colaboração de especialistas em saúde infantil e a realização de pré-testes com amostras da população-alvo.

A validação do PEARLS-BR demonstrou boas propriedades psicométricas sendo capaz de identificar as ACEs de forma confiável na população pediátrica brasileira. Os resultados indicaram que o PEARLS-BR pode ser uma ferramenta valiosa para pesquisadores e profissionais de saúde, permitindo a identificação precoce de crianças e adolescentes em risco devido às adversidades vivenciadas na infância.

A pesquisa destacou a necessidade de uma abordagem multidisciplinar e integrada para abordar as ACEs, envolvendo setores como saúde, educação e assistência social. As intervenções devem ser direcionadas tanto a nível individual quanto comunitário, visando mitigar os efeitos negativos das adversidades na infância e promover a resiliência. O desenvolvimento de políticas públicas que abordem os determinantes sociais da saúde é crucial para reduzir o impacto das ACEs e melhorar os desfechos de saúde das crianças.

Em suma, este estudo contribuiu significativamente para a literatura sobre ACEs no Brasil, oferecendo uma ferramenta validada para a triagem e avaliação dessas experiências adversas em crianças e adolescentes. A validação do PEARLS-BR representa um avanço importante na identificação precoce e intervenção em ACEs, proporcionando uma base sólida para futuras pesquisas e práticas clínicas. A continuidade dos esforços de pesquisa e a implementação de políticas e intervenções eficazes são essenciais para proteger a saúde e o bem-estar das futuras gerações.

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APÊNDICE A - PEARLS-BR VERSÃO CRIANÇA

PEARLS-BR

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados

Criança

Muitas famílias experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a saúde e o bem estar do seu filho(a). Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar seu filho(a) e você mesmo.

Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a saúde do seu filho(a) e o que você pode fazer para ajudar. Suas respostas nos ajudam a apoiar você e seu filho a serem o mais saudáveis possível. A pesquisa é confidencial e opcional*.

As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar.

** Porém, é importante saber que caso você nos conte que, no momento, seu filho(a) não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.*

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados (PEARLS - BR)

CRIANÇA – deve ser preenchido pelo: **PAI/MÃE/RESPONSÁVEL**

Em algum momento desde o Nascimento de seu filho(a), ele/ela viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes.

Por favor, observe que algumas perguntas têm mais de uma parte separada por "OU". Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".

PARTE 1:	Marque "SIM" onde se aplica	X
1.	Você acha que seu filho(a) já se sentiu sem apoio, sem amor e/ou desprotegido?	☐
2.	Seu filho(a) já morou com um dos pais/responsável que apresentava problemas de saúde mental? *(Por exemplo, depressão, esquizofrenia, transtorno bipolar, transtorno de estresse pós-traumático e/ou transtorno de ansiedade.)*	☐
3.	Algum dos pais/responsável já insultou, humilhou ou rebaixou seu filho(a)?	☐
4.	Um dos pais biológicos da criança ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?	☐
5.	Seu filho(a) já teve falta de cuidados adequados por parte de algum responsável? *(Por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis.)*	☐
6.	Seu filho(a) já viu ou ouviu um dos pais/responsável: *(Assinale sim, se qualquer um for verdadeiro para você ou sua família).* **a.** Sendo tratado a gritos ou xingado(a), insultado(a) ou humilhado(a) por outro adulto? **b.** OU sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?	☐
7.	Algum adulto na casa: (Assinale sim, se qualquer um for verdadeiro para você ou sua família). **a.** Frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em seu filho(a)? **b.** OU já bateu em seu filho(a) com tanta força que deixou marcas ou o/a machucou? **c.** OU já ameaçou seu filho(a) ou agiu de maneira que o/a fez ficar com medo de se machucar?	☐
8.	Seu filho(a) já sofreu abuso sexual? *(Por exemplo, alguém tocou em seu filho(a) ou pediu a ele/ ela que tocasse essa pessoa de uma forma indesejada ou fez seu filho(a) se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com seu filho(a).)*	☐
9.	Seu filho(a) já morou com um dos pais/responsável que foi para a cadeia/prisão?	☐
10.	Já houve mudanças significativas no status de relacionamento do(s) responsável(eis) da criança? *(Por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma.)*	☐
	Quantos "Sim" você respondeu na Parte 1?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 2:	Marque "SIM" onde se aplica	X
1.	Seu filho(a) já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (Por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).	☐
2.	Seu filho(a) já experienciou discriminação? *(Por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências.)*	☐
3.	Seu filho(a) já teve problemas de moradia? (*Por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família.)*	☐
4.	Você atualmente ou alguma vez: (Assinale sim, se qualquer um for verdadeiro). **a.** Ficou preocupado que a comida para seu/sua filho(a) acabasse antes de você tivesse dinheiro para comprar mais? **b.** OU que a comida que você comprou para seu filho(a) não durou e não teve dinheiro para comprar mais?	☐
5.	Seu filho(a) já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?	☐
6.	O seu filho(a) já morou com um dos pais/responsável que sofre de uma doença física grave ou deficiência?	☐
7.	Seu filho(a) já morou com um dos pais ou responsável que tenha falecido?	☐
	Quantos "Sim" você respondeu na Parte 2?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 3:

Gostaríamos de entender mais sobre os pontos fortes do seu filho(a) e da sua família.

1. Quais são as melhores qualidades do seu filho(a)?

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2. Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?

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APÊNDICE B - PEARLS-BR VERSÃO ADOLESCENTE

PEARLS-BR

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados

Adolescente

Muitas famílias experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a saúde e o bem estar do seu filho(a). Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar seu filho(a) e você mesmo.

Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a saúde do seu filho(a) e o que você pode fazer para ajudar. Suas respostas nos ajudam a apoiar você e seu filho a serem o mais saudáveis possível. A pesquisa é confidencial e opcional*.

As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar.

** Porém, é importante saber que caso você nos conte que, no momento, seu filho(a) não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.*

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados (PEARLS-BR)

ADOLESCENTE – deve ser preenchido pelo: **PAI/MÃE/RESPONSÁVEL**

Em algum momento desde o Nascimento de seu filho(a), ele/ela viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes.

Por favor, observe que algumas perguntas têm mais de uma parte separada por "OU". Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".

PARTE 1:	Marque "SIM" onde se aplica	X
1.	Você acha que seu filho(a) já se sentiu sem apoio, sem amor e/ou desprotegido?	☐
2.	Seu filho(a) já morou com um dos pais/responsável que apresentava problemas de saúde mental? *(Por exemplo, depressão, esquizofrenia, transtorno bipolar, transtorno de estresse pós-traumático e/ou transtorno de ansiedade.)*	☐
3.	Algum dos pais/responsável já insultou, humilhou ou rebaixou seu filho(a)?	☐
4.	Um dos pais biológicos da criança ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?	☐
5.	Seu filho(a) já teve falta de cuidados adequados por parte de algum responsável? *(Por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis.)*	☐
6.	Seu filho(a) já viu ou ouviu um dos pais/responsável: *(Assinale sim, se qualquer um for verdadeiro para você ou sua família).* **a.** Sendo tratado a gritos ou xingado(a), insultado(a) ou humilhado(a) por outro adulto? **b.** OU sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?	☐
7.	Algum adulto na casa: (Assinale sim, se qualquer um for verdadeiro para você ou sua família). **a.** Frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em seu filho(a)? **b.** OU já bateu em seu filho(a) com tanta força que deixou marcas ou o/a machucou? **c.** OU já ameaçou seu filho(a) ou agiu de maneira que o/a fez ficar com medo de se machucar?	☐
8.	Seu filho(a) já sofreu abuso sexual? *(Por exemplo, alguém tocou em seu filho(a) ou pediu a ele/ ela que tocasse essa pessoa de uma forma indesejada ou fez seu filho(a) se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com seu filho(a).)*	☐
9.	Seu filho(a) já morou com um dos pais/responsável que foi para a cadeia/prisão?	☐
10.	Já houve mudanças significativas no status de relacionamento do(s) responsável(eis) da criança? *(Por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma.)*	☐
	Quantos "Sim" você respondeu na Parte 1?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 2:	Marque "SIM" onde se aplica	X
1.	Seu filho(a) já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (Por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).	☐
2.	Seu filho(a) já experienciou discriminação? *(Por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências.)*	☐
3.	Seu filho(a) já teve problemas de moradia? (*Por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família.)*	☐
4.	Você atualmente ou alguma vez: (Assinale sim, se qualquer um for verdadeiro). **a.** Ficou preocupado que a comida para seu/sua filho(a) acabasse antes de você tivesse dinheiro para comprar mais? **b.** OU que a comida que você comprou para seu filho(a) não durou e não teve dinheiro para comprar mais?	☐
5.	Seu filho(a) já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?	☐
6.	O seu filho(a) já morou com um dos pais/responsável que sofre de uma doença física grave ou deficiência?	☐
7.	Seu filho(a) já morou com um dos pais ou responsável que tenha falecido?	☐
8.	Seu filho(a) já foi detido(a), preso(a) ou encarcerado(a)?	☐
9.	Seu filho(a) já sofreu abuso verbal ou físico ou ameaças de um parceiro romântico? (Por exemplo, um namorado ou namorada.)	☐
	Quantos "Sim" você respondeu na Parte 2?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 3:

Gostaríamos de entender mais sobre os pontos fortes do seu filho(a) e da sua família.

1. Quais são as melhores qualidades do seu filho(a)?

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2. Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?

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APÊNDICE C - PEARLS-BR VERSÃO ADOLESCENTE AUTORRELATO

PEARLS-BR

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados

Adolescente (Autorrelato)

Muitas adolescentes experienciam eventos estressantes ao longo de suas vidas. Com o tempo, essas experiências podem afetar a sua saúde e o seu bem estar. Existem muitas coisas que você pode fazer ou talvez já esteja fazendo para ajudar. Como esses eventos são muito comuns, estamos oferecendo recursos a todos os cuidadores em nossa clínica sobre como apoiar você.

Estamos fazendo essas perguntas para todos(as). Para algumas pessoas, responder as questões ajuda a pensar sobre como certas experiências podem impactar a sua saúde. Suas respostas nos ajudam a apoiar você a ser o mais saudável possível. A pesquisa é confidencial e opcional*.

As experiências são suas e não importa o que você escolha compartilhar, nós estamos aqui para ajudar.

** Porém, é importante saber que caso você nos conte que, no momento, você não está seguro, ou está sendo abusado ou negligenciado física, verbal ou sexualmente, nós possivelmente teremos que compartilhar essas informações com as autoridades.*

Experiências Adversas na Infância Pediátrico e Rastreador de Eventos de Vida Relacionados (PEARLS-BR)

—ADOLESCENTE (Autorrelato) – deve ser preenchido pelo: **PAI/MÃE/RESPONSÁVEL**—

Em algum momento desde o seu nascimento, você viu ou esteve presente quando as seguintes experiências aconteceram? Inclua experiências passadas e presentes.

Por favor, observe que algumas perguntas têm mais de uma parte separada por "OU". Se alguma parte da pergunta for respondida "Sim", a resposta a toda a pergunta é "Sim".

PARTE 1:	**Marque "SIM" onde se aplica**	X
1.	Você já se sentiu sem apoio, sem amor e/ou desprotegido?	☐
2.	Você já morou com um dos pais/responsável que apresentava problemas de saúde mental? *(Por exemplo, depressão, esquizofrenia, transtorno bipolar, transtorno de estresse pós-traumático e/ou transtorno de ansiedade.)*	☐
3.	Algum dos pais/responsável já lhe insultou, humilhou ou rebaixou?	☐
4.	Um dos seus pais biológicos ou algum responsável já teve, ou atualmente tem um problema com o uso excessivo de álcool, drogas ou medicamentos prescritos?	☐
5.	Você já teve falta de cuidados adequados por parte de algum responsável? *(Por exemplo, não ser protegido de situações inseguras, ou não ser cuidado quando doente ou ferido, mesmo quando os recursos estavam disponíveis.)*	☐
6.	Você já viu ou ouviu um dos pais/responsável: *(Assinale sim, se qualquer um for verdadeiro para você ou sua família).* **a.** Sendo tratado a gritos ou xingado(a), insultado(a) ou humilhado(a) por outro adulto? **b.** OU sendo esbofeteado(a), chutado(a), socado(a), espancado(a) ou ferido(a) com uma arma?	☐
7.	Algum adulto na casa: (Assinale sim, se qualquer um for verdadeiro para você ou sua família). **a.** Frequentemente ou muito frequentemente empurrou, agarrou, deu um tapa ou jogou algo em você? **b.** OU já bateu em você com tanta força que deixou marcas ou o/a machucou? **c.** OU já ameaçou você ou agiu de maneira que o/a fez ficar com medo de se machucar?	☐
8.	Você já sofreu abuso sexual? *(Por exemplo, alguém tocou em você ou pediu a você que tocasse essa pessoa de uma forma indesejada ou o fez se sentir desconfortável, ou alguém já tentou ou realmente fez sexo oral, anal ou vaginal com você.)*	☐
9.	Você já morou com um dos pais/responsável que foi para a cadeia/prisão?	☐
10.	Já houve mudanças significativas no status de relacionamento do(s) seu(s) responsável(eis)? *(Por exemplo, um dos pais/responsável se divorciou ou se separou, ou um parceiro romântico se mudou para a mesma residência ou saiu da mesma.)*	☐
	Quantos "Sim" você respondeu na Parte 1?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 2:	Marque "SIM" onde se aplica	X
1.	Você já viu, ouviu ou foi vítima de violência em seu bairro, comunidade ou escola? (Por exemplo, bullying direcionado, agressão ou outras ações violentas, guerra ou terrorismo).	☐
2.	Você já experienciou discriminação? *(Por exemplo, foi incomodado ou se sentiu inferior ou excluído devido à sua raça, etnia, identidade de gênero, orientação sexual, religião, dificuldades de aprendizagem ou deficiências.)*	☐
3.	Você já teve problemas de moradia? (*Por exemplo, ser sem-teto, não ter um lugar estável para morar, se mudar mais de duas vezes em um período de seis meses, enfrentou despejo ou execução hipotecária ou teve que viver com várias famílias ou membros da família.)*	☐
4.	Você atualmente ou alguma vez: (Assinale sim, se qualquer um for verdadeiro). **a.** Ficou preocupado que a comida para você acabasse antes de você ou seus pais tivessem dinheiro para comprar mais? **b.** OU que a comida que você ou seus pais compraram para você não durou e não teve dinheiro para comprar mais?	☐
5.	Você já foi separado(a) de seus pais ou responsáveis devido a situações de acolhimento familiar ou imigração?	☐
6.	Você já morou com um dos pais/responsável que sofre de uma doença física grave ou deficiência?	☐
7.	Você já morou com um dos pais ou responsável que tenha falecido?	☐
8.	Você já foi detido(a), preso(a) ou encarcerado(a)?	☐
9.	Você já sofreu abuso verbal ou físico ou ameaças de um parceiro romântico? (Por exemplo, um namorado ou namorada).	☐
	Quantos "Sim" você respondeu na Parte 2?	☐

Por favor continue respondendo o restante do questionário do outro lado da página. →

PARTE 3:

Gostaríamos de entender mais sobre os seus pontos fortes e da sua família.

1. Quais são as suas melhores qualidades?

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2. Quais são as coisas que ajudam você (ou sua família) a superar os momentos difíceis (ou lidar com o estresse)?

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ANEXO 1 – ACORDO ASSINADO ENTRE UCS E A DETENTORA DOS DIREITOS AUTORAIS DA PEARLS

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
Innovation Ventures, Office of Technology Management & Advancement

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NON-EXCLUSIVE LICENSE AGREEMENT

This agreement ("Agreement") is effective December 03, 2021 ("Effective Date") by and between UNIVERSITY OF CAXIAS DO SUL, having an address of 1130 Francisco Getúlio Vargas Street, Building A, Caxias do Sul, Brazil, hereinafter referred to as "Licensee," and The Regents of the University of California ("Licensor"), a California corporation having its statewide administrative offices at 1111 Franklin Street, Oakland, California 94607-5200, and acting through its Office of Technology Management & Advancement located at 600 16th Street, Suite S-272, San Francisco, CA 94143.

WHEREAS, the Pediatric ACES and Related Life-Events Screening tool or "PEARLS" is a unique tool that assesses for both Adverse Childhood Experiences ("ACEs") such as abuse, neglect and household challenges, and related life events, like discrimination, food insecurity and community violence, thought to be risk factors for toxic stress ("Licensed IP");

WHEREAS, the California Healthcare, Research and Prevention Tobacco Tax Act of 2016 (Proposition 56) authorizes the provision of standardized ACEs screening services for adults (through 64 years of age) and children, and the ACEs questionnaire for adults (ages 18 years and older) and Pediatric ACEs and Related Life-events Screener (PEARLS) tools for children (ages 0 to 19 years) are both forms of ACEs screening;

WHEREAS, the Licensed IP was made in the course of research under the auspices of the Children's Hospital & Research Center at Oakland and the University of California, San Francisco by Dr. Dayna Long, Mindy Benson NP, Dr. Danielle Hessler and Dr. Neeta Thakur, and Licensor is a co-owner of the copyrights and other property rights recognized under United States law and international treaties in the Pediatric ACES and Related Life-Events Screening tool or "PEARLS" (as disclosed under UC Case No. SF2020-137);

WHEREAS, Dr. Dayna Long, Mindy Benson NP, Dr. Danielle Hessler and Dr. Neeta Thakur are affiliated with the Licensor and have assigned their right, title and interest in and to the Licensed IP to the Licensor;

WHEREAS, the Licensor wishes that the Licensed IP be utilized to the fullest extent so that the benefits can be experienced by the children and families of the Brazilian population.

WHEREAS, Licensee is a non-profit Institution of higher education (inst. of higher ed, non-profit entity, etc.); and

WHEREAS, Licensee desires a license to use the Licensed IP to to translate into portuguese, and to validate the "Pediatrics ACEs and Related Life Event Screener (PEARLS)" to be applied to the Brazilian population; Screening Brazilian children in order to verify the association of ACE's with

physical, psychological and social illnesses and compare with data from other countries. The project will be carried out by the PhD academic, Luciana Cristina Mancio Balico, supervised by Prof. Emerson Rodrigues da Silva, PhD (the "Licensed Use"), and Licensor is willing to grant such a license subject to the terms and conditions recited herein.

NOW, THEREFORE, for and in consideration of the mutual covenants and undertakings hereinafter set forth, and other good and valuable consideration hereby acknowledged, it is agreed as follows:

TERMS

1. **Grant of License.** Subject to the terms and conditions of this Agreement, Licensor hereby grants to Licensee a nonexclusive, nontransferable right and license to use the Licensed IP solely for the Licensed Use during the Term as defined below. No license, express or implied, is granted to Licensee to use the Licensed IP other than as specifically provided herein, and any such right is expressly withheld from this Agreement. Licensor retains all right and to the Licensed IP except as otherwise provided.

2. **Term.** The term of this Agreement shall be for a period of three (3) years from the Effective Date (the "Term"), unless otherwise terminated pursuant to the terms of this Agreement. The parties may extend the Term upon mutual written agreement.

3. **Restrictions on Use.**

    a. Licensee may not alter the Licensed IP without the prior written consent of Licensor.

    b. Licensor retains any and all intellectual property ownership rights in and to the Licensed IP. Any authorized modifications of, or derivative works based on, the Licensed IP are shall be considered part of the Licensed IP and such ownership is retained by Licensor.

    c. Licensee shall not disclose in any form the delivered Licensed IP or any modifications to third parties. Licensee further agrees and acknowledges that it will not further transfer or modify the Licensed IP and that it will use reasonable efforts to prevent use of, or access to, the Licensed IP by any third parties who are not the Licensee.

    d. Licensee is expressly prohibited from selling, licensing, or otherwise making any commercial use of the Licensed IP.

    e. No use of the Licensed IP names, logos or trademarks may be made beyond what is expressly permitted in this Agreement without Licensor's prior written approval. Licensor, or their designee, shall have the right to inspect any and all records and materials related to Licensee's activities pursuant to this Agreement and all use of the Licensed IP. All inspections shall be during regular business hours upon at least forty-eight (48) hours' notice to Licensee.

    f. For the avoidance of any doubt, except as provided herein or otherwise agreed in writing by the parties, nothing contained in this Agreement will be construed as conferring any right to use either party's name, trade name, or other designation in advertising, publicity, or other

promotional activities by the other party. Unless required by law or as set forth in Section 5, Licensee's use of the name "The Regents of the University of California" or the name of any University of California campus in advertising, publicity, or other promotional activities is expressly prohibited.

4. **Rights in the Licensed IP.**

   a. Licensee acknowledges the Licensor's ownership of and exclusive rights in and to the Licensed IP, and Licensee agrees that it will do nothing inconsistent with such ownership, and that all use of the Licensed IP by Licensee shall inure to the benefit of the Licensor. Licensee agrees that it shall not, at any time during or after the effective Term of this Agreement, dispute or contest, directly or indirectly, Licensor's exclusive right and title to the Licensed IP or the validity thereof or apply for registration or seek to obtain ownership of any Licensed IP in any nation. Licensee recognizes the goodwill associated with the Licensed IP and acknowledges that such goodwill belongs solely to the Licensor, and Licensee shall make no claim to such goodwill.

   b. Licensee agrees that it will not state or imply either directly or indirectly that Licensee or Licensee's activities, other than those permitted by this Agreement, are supported, endorsed, or sponsored by Licensor and, upon the direction of Licensor, shall issue express disclaimers to that effect.

   c. For the avoidance of any doubt, nothing in this Agreement grants to either party by implication, estoppel, or otherwise any rights to the other party's intellectual property except as explicitly set forth herein.

5. **Acknowledgement of Rights.** Any and all use of, or reference to, the Licensed IP by Licensee in any and all media whether online or otherwise must include the following:

   Copyright Notice and Disclaimer:

   Certain materials incorporated herein are Copyright © 2016 and 2018, The Regents of the University of California. All Rights Reserved.

6. **Confidentiality.**

   a. During the Term of this Agreement each party (a "Receiving Party") may receive Confidential Information of the other party (a "Disclosing Party"). "Confidential Information" means any trade secrets and other proprietary information of either party, whether in tangible or intangible form, that relate to such party's research, business operations, customers, employees, products, pricing, financial information, computer programs, designs, models, or operating procedures, other than information that (i) is or becomes public other than by breach of this Agreement, (ii) was in the Receiving Party's possession prior to the time it was received by such party under this Agreement, or (iii) was rightfully received from a third party on a non-confidential basis.

   b. During the Term of this Agreement and three years thereafter, the Receiving Party shall hold the Disclosing Party's Confidential Information in confidence, and shall not disclose it to any person, firm, corporation, or other entity without written authorization of the Disclosing Party.

c. Notwithstanding the foregoing, the Receiving Party may disclose the Confidential Information to its employees, agents and/or contractors to the extent reasonably necessary to allow the Receiving Party to perform its obligations under this Agreement and to obtain the benefits of this Agreement, provided that each such employee, agent or contractor is under an obligation of nondisclosure, which protects the Confidential Information under terms substantially similar to the terms herein.

d. Notwithstanding this section, either party may disclose Confidential Information pursuant to a subpoena or other government demand, including, specifically in response to a California Public Records Act request, provided that it gives the Disclosing Party prompt notice of such demand.

7. **DISCLAIMER OF WARRANTY. OTHER THAN AS EXPRESSLY PROVIDED HEREIN, LICENSEE AGREES THAT THE LICENSED IP IS FURNISHED "AS IS," THAT THE LICENSOR DOES NOT MAKE ANY WARRANTIES OR REPRESENTATIONS REGARDING THE LICENSED IP, AND THAT THE LICENSOR IS NOT LIABLE IN ANY WAY FOR ANY OF LICENSEE'S USES OF THE LICENSED IP.**

8. **Governing Law.** This Agreement shall be governed by and construed in accordance with the laws of the State of California, without giving effect to any conflict of law principles that require the application of laws of a different state. All disputes hereunder shall be resolved in the applicable state courts or, if jurisdiction exists, the federal court in San Francisco, California.

9. **Representations and Warranties.** Licensee represents and warrants that it has the full right, power and authority to enter into and perform this Agreement. Licensee is not a party to any agreement or understanding which would conflict with this Agreement. In connection with its use of the Licensed IP, Licensee shall, and shall cause its employees, and contractors to, comply with all applicable laws.

10. **Indemnification.** To the extent permitted by law, Licensee shall defend, indemnify, and hold harmless the Licensor, their officers, employees, and agents from and against any third party demands, causes of action, claims, suits, damages, losses and expenses (including attorneys' fees), or other liability arising out of or connected with this Agreement. In the event of any claim for indemnification, the indemnifying party shall defend the indemnified party with counsel reasonably acceptable to the indemnified party, and such counsel shall be paid promptly by the indemnifying party upon presentation of legal bills or request for retainer.

11. **Reserved.**

12. **Notices.** Any notice or payment hereunder shall be deemed to have been properly given when sent in writing in English to the respective address below and shall be deemed effective:
    a. on the date of delivery if delivered in person,
    b. on the date of mailing if mailed by first-class certified mail, postage paid, or
    c. on the date of mailing if mailed by any global express carrier service that requires the recipient to sign the documents demonstrating the delivery of such notice or payment, or

d. in the case of notices, if sent by email, on the date the recipient acknowledges having received that email by either an email sent to the sender or by a notice delivered by another method in accordance with this Section 12, provided that, automated replies and "read receipts" shall not be considered acknowledgement of receipt.

In the case of the Licensee:
For notices:
University of Caxias do Sul
Office of Research and Post-Graduation
1130 Francisco Getulio Vargas Street, Building A
Caxias do Sul, Rio Grande do Sul, Brazil
Attention: Vice-Chancellor for Research and Post-Graduation
Email: pesquisa@ucs.br

In the case of Licensor:
For notices:
University of California, San Francisco
Innovation Ventures, Office of Technology Management & Advancement
Box 2142
600 16th Street, Suite S272
San Francisco, CA 94143
(for Fed-Ex use postal code 94158)
Attention: Executive Director
Referring to: UC Case No. SF2020-137
Email: innovation@ucsf.edu

13. **Termination.**

a. This Agreement will expire, as provided in Section 2, or may be terminated by Licensor if Licensee commits a material breach of any provision of this Agreement, in which case, Licensor shall have the right to terminate this Agreement upon thirty (30) days prior written notice and such notice, which shall specify the nature of the breach, shall become effective unless Licensee, within the 30-day notice period, completely remedies the breach, or satisfies Licensor that such breach will be cured in a reasonably acceptable period. This Agreement may be terminated by either Licensor or the Licensee upon thirty (30) days advance written notice to the other party.

b. Upon termination of the Agreement, Licensee shall discontinue all use of the Licensed IP and shall return or destroy all copies of the Licensed IP and any and all Confidential Information received from Licensor. For the avoidance of any doubt, upon the expiration or termination of this Agreement, all rights granted to Licensee shall immediately revert to Licensor. Licensee shall thereafter refrain from further use of the rights or any further reference to them, either directly or indirectly, in connection with Licensee's business and/or services. Sections 5 (Acknowledgement), 14e (Amendments), 6 (Confidential Information), and 10 (Indemnification) shall survive termination of this Agreement.

14. **Miscellaneous.**

a. The parties intend that this Agreement is binding upon each of their respective heirs and assigns.

b. The license granted to Licensee hereunder may not be assigned or transferred to any other person or entity without the prior, express written consent of Licensor.

c. If any provision of this Agreement is held unenforceable, the remaining provisions shall remain in full force and effect.

d. This Agreement supersedes all other previous or contemporaneous agreements or understandings between the parties, whether verbal or written, concerning the subject matter hereof.

e. Licensee warrants that it is an non-profit Institution of higher education.

f. Amendments: Alterations of or additions to this Agreement shall be made in writing and duly executed by representatives of both parties.

g. This Agreement may be executed in one or more counterparts. Delivery of an executed counterpart of this Agreement by facsimile or a PDF data file or other scanned executed counterpart by email shall be equally as effective as delivery of a manually executed counterpart of this Agreement. Each duplicate and counterpart of this Agreement shall be equally admissible in evidence, and each shall fully bind each party who has executed it. The parties agree that a copy of the original signature (including an electronic copy) may be used for any and all purposes in respect of this Agreement for which the original signature may have been used. The parties agree that neither party will have any rights to challenge the use or authenticity of a counterpart of this Agreement based solely on that its signature, or the signature of the other party, on such counterpart is not an original signature.

The parties hereto have executed this instrument as of the dates given below:

LICENSEE:

By: JULIANO RODRIGUES GIMENEZ:71536370010 Assinado de forma digital por JULIANO RODRIGUES GIMENEZ:71536370010 Dados: 2021.12.03 14:11:27 -03'00'
(signature)

Name: Juliano Rodrigues Gimenez
(please print)

Title: Vice Chancellor for Research and Post-Graduation

Date: December 03, 2021

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA:

By: DocuSigned by: Gonzalo Barrera-Hernandez 82365B3DAA32...
(signature)

Name: Gonzalo Barrera-Hernandez
(please print)

Title: Director, Business Affairs & Strategic Partnerships, OTMA

Date: 12/7/2021

ANEXO 2 – APROVAÇÃO DA TRADUÇÃO REVERSA DOS DETENTORES DOS DIREITOS AUTORAIS DA PEARLS

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

Neeta Thakur, MD, MPH
Associate Professor in Residence
Medical Director, ZSFG Chest Clinic
ZSFG Pulmonary Director of Diversity and Social Justice
Division of Pulmonary and Critical Care Medicine
CLEAR.ucsf.edu

UCSF - ZSFG
1001 Potrero Ave, 5K1
San Francisco, CA 94143-0841
Fax: (415) 514-4365
e-mail: neeta.thakur@ucsf.edu

Dear. Ms. Balico,
After reviewing the documents presented by you, Luciana Cristina Mancio Balico, I affirm that the back-translation of the PEARLS Tool has retained the same conceptual idea as the original tool. Therefore, I permit you and your team proceeding with validation of the tool in Portuguese.

Sincerely,

Neeta Thakur, MD MPH
Co-Creator of the PEARLS Tool

ANEXO 3 – AUTORIZAÇAO DOS DETENTORES DOS DIREITOS AUTORAIS DO PROMIS PARA A UTILIZAÇAO DA FERRAMENTA NESTE ESTUDO

PHO PROMIS HEALTH ORGANIZATION
PO Box 11449 | Chicago, IL 60611
www.promishealth.org

PROMIS TRANSLATIONS LICENSE AGREEMENT

TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF PEDRIATRICS ACES AND RELATED LIFE EVENT SCREENER - PEARLS - FOR USE IN BRAZIL

This License Agreement (this "Agreement") between **Universidade de Caxias do Sul** on behalf of itself and all of its affiliates ("Licensee") and the PROMIS Health Organization ("PHO" or Licensor") is entered into as of the last date of signature (the "Effective Date"). PHO and Licensee hereby agree as follows:

1. **Materials**. Pursuant to various agreements with the investigators involved in the Patient Reported Outcomes Measurement Information System ("PROMIS") project funded by the National Institutes of Health ("NIH"), PHO represents and warrants that it has rights to license the materials identified on Exhibit A, attached hereto and made a part hereof (the "Materials"). The PHO in turn has authorized Northwestern University (NU) to distribute said materials.

2. **License**. PHO hereby grants to Licensee and the affiliates of Licensee identified on Exhibit A (the "Licensed Affiliates") a worldwide, royalty-free, fully paid, non-exclusive, non- transferable and non-assignable license to make, use, copy, store and distribute, electronically or otherwise, the Materials solely for the purpose set forth in Exhibit A (the "Licensed Purpose") in or as part of the documents or other materials identified on Exhibit A (the "Licensed Publications"). For the avoidance of doubt this License extends to the agents and the contract research organizations, sites, investigators involved in the conduct of the Licensed Purpose. Licensee shall cause the Licensed Affiliates to comply with all of the terms, conditions and limitations of the Agreement as if they were Licensee, and shall be responsible for all actions and omissions of the Licensed Affiliates as if they were conducted by Licensee itself. Licensee shall direct all of its customers that desire to use the Materials as part of the Licensed Publications in a manner that requires a license to the Material to NU to request such a license, which license NU or PHO may grant in their sole discretion.

3. **Ownership**. Licensee acknowledges and agrees that all rights, title and interest, including all worldwide copyrights, patents, trade secrets, trademarks and confidential and proprietary information rights in the Material, including all updates, modifications, enhancements and derivative works thereof, are and shall be owned exclusively by PHO and its licensors. It is expressly understood and agreed that, except as expressly set forth in Section 2, no other rights or licenses, express or implied, are granted by PHO to Licensee hereunder. Licensee may not sublicense, rent, lease, loan, lend, sell, extend, or otherwise distribute or create derivative works of the Materials except as expressly permitted in Section 2. PHO acknowledges that all right, title and interest, including all worldwide copyrights, patents, trade secrets, trademarks and confidential and proprietary information rights in the data obtained from the use of the Material shall be owned exclusively by the Licensee.

4. **Copyright Notices**. Licensee will ensure that the appropriate copyright notice in the name of PHO will appear in all published versions of the Materials, and that the Materials will not be modified without the PHO's permission. Licensee will note on the Licensed Publications with respect to the Materials:

5. **Limited Warranty; Disclaimer.** PHO represents and warrants that, as of the Effective Date, NU is authorized to coordinate and distribute its Materials, and that, to PHO's knowledge, the Materials do not infringe on the intellectual property rights of any third party. EXCEPT AS EXPRESSLY PROVIDED IN THE FOREGOING SENTENCE, THE MATERIAL IS PROVIDED "AS IS" WITHOUT ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY, TITLE, NON-INFRINGEMENT OR FITNESS FOR A PARTICULAR PURPOSE, AND PHO HEREBY DISCLAIMS ALL SUCH WARRANTIES.

6. **Limitation of Liability. EXCEPT FOR (a) A PARTY'S BREACH OF CONFIDENTIALITY OR INTELLECTUAL PROPERTY OBLIGATIONS HEREUNDER, (b) A PARTY'S, GROSS NEGLIGENCE OR WILLFUL MISCONDUCT, (c) THIRD PARTY CLAIMS, OR (d) LICENSEE's USE OF MATERIALS OUTSIDE OF THE LICENSE GRANTED HEREIN, in no event shall either Party be liable to the other party for any indirect, speculative, consequential, incidental or special damages arising out of the Agreement hereunder whether or not it has been advised of the possibility of such damage.**

7. **Fees.** All fees have been waived as indicated in Exhibit B. This waiver of fees does not guarantee future waivers.

8. **Trademark.** "PROMIS" is a registered trademark of the U.S. Department of Health and Human Services. No trademark rights or licenses are conveyed by this Agreement. Specifically, Licensee may not use the PROMIS trademark in a trademark sense or to identify itself as the source of products or services. However, Licensee may use the PROMIS name to describe the PROMIS program and resulting items as permitted by applicable law.

9. **Termination.** PHO may terminate this Agreement immediately in the event Licensee breaches this Agreement and Licensee fails to remedy such breach within thirty (30) days after PHO provides Licensee with written notice of such breach. Licensee may terminate this Agreement with or without any cause by providing thirty (30) days advance written notice to PHO. Following termination of this Agreement, Licensee shall cease all use of the Material.

10. **Assignment**. Licensee may not assign its rights or obligations hereunder without the prior written consent of PHO, and any purported assignment shall be null and void and constitute a breach of this Agreement.

11. **Notification**. Any notification required or permitted to be given by either Party to the other Party pursuant to this License Agreement will be in writing and will be delivered or mailed by first class mail (postage prepaid) or by overnight express addressed to the attention of the authorized representatives of such parties as follows (or such other address as either Party may identify in a written notice provided in accordance with this Section): (a) if to Licensee, to the address set forth on Exhibit A; and (b) if to NU, 625 N St. Michigan Avenue, 21st Floor, Chicago, IL 60611.

12. **Governing Law and Choice of Forum**. This Agreement shall be governed in accordance with the laws of the State of Illinois, United States of America, without regard to any provision that would result in the application of the laws of any other jurisdiction. The parties hereby irrevocably consent to the exclusive jurisdiction of, and venue in, any federal or state court of competent jurisdiction located in Cook County, Illinois for the purposes of adjudicating any matter arising from or in connection with this Agreement.

13. **Counterparts and Entire Agreement**. This Agreement may be executed in any number of counterparts, each of which shall be deemed to be an original instrument and all of which together shall constitute a single agreement, and each counterpart may be executed pursuant to an executed facsimile or PDF document. This Agreement constitutes the entire agreement between the parties and supersedes any understandings, agreements or representations by or between the parties, written or oral that may relate in any way to the subject matter hereof.

IN WITNESS WHEREOF, Licensee and PHO have caused this Agreement to be executed by their respective, duly authorized officers or representatives, effective as of the Effective Date.

Universidade de Caxias do Sul ("Licensee")

By: Everaldo Cescon Assinado de forma digital por Everaldo Cescon Dados: 2023.04.11 15:58:23 -03'00'

Name: Everaldo Cescon

Title: Pro-Rector of Graduate Program and Research

Date: 11/04/2023

THE PROMIS HEALTH ORGANIZATION

By: David Cella, PhD Digitally signed by David Cella, PhD Date: 2023.04.12 08:42:03 -05'00'

Name: David Cella, PhD

Title: President

Date: _____

EXHIBIT A

Materials Requested	PROMIS Scale v1.2 – Global Health in the following language: **Portuguese (Br)**
Licensed Purpose **(i.e., how and where will it be used?)**	**Universidade de Caxias do Sul** desires to use the Materials in connection with Study *TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF PEDRIATRICS ACES AND RELATED LIFE EVENT SCREENER - PEARLS - FOR USE IN BRAZIL* ("**Clinical Study**")
Licensed Publication **(i.e., what is the larger work that will include the Materials?)**	Not Applicable
Licensed Affiliates	**Universidade de Caxias do Sul**, affiliates, agents, CROs, Sites, Investigators involved in the conduct of the Clinical Study.
Distribution Fee	$850 (Waived) (i.e., $850 per language/per measure) No fee for English
Licensing Fee	Not Applicable
Royalties	Not Applicable
Licensee Notification Contact	

EXHIBIT B

Northwestern University Feinberg School of Medicine

Medical Social Sciences

NUCORE

Northwestern University Center on Outcomes Research and Education

QUOTE #1357-1742

Date: April 10, 2023
Project Title: Scale v1.2 - GH – POR(Br)
Project PI: Luciana Cristina Mancio Balico and Emerson Rodrigues da Silva
Company: Universidade de Caxias do Sul
Protocol #: TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF PEDRIATRICS ACES AND RELATED LIFE EVENT SCREENER - PEARLS - FOR USE IN BRAZIL
Address:
Email: Quote requested by: Luciana Cristina Mancio Balico, Psy, M.H.Sc lcmbalico@ucs.br
Quote prepared by: Leslie Chareunsab leslie.chareunsab@northwestern.edu

Service	Detailed Description	Total # Items	Estimated Time	Estimated Charge
Distribution fee for available translations of PROMIS Scale v1.2 – Global Health	Portuguese (Br)	1 Language Distributed	$850 per language	**$850**
	Distribution Fees waived			**($850)**
	TOTAL			**$0**