

# Adverse Childhood Experiences among a Community of Resilient Centenarians and Seniors: Implications for a Chronic Disease Prevention Framework

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## ABSTRACT

**Context:** Research has linked adverse childhood experiences (ACEs) with chronic disease in adults and diminished life span. Adverse biological embedding of ACEs potentially occurs through inflammatory mechanisms; inflammatory marker alterations are identified as candidate biomarkers for mediating health consequences. Lifestyle practices of residents of California's Loma Linda Blue Zone, one of five worldwide longevity hotspots, may provide insight into inflammation remediation and chronic disease prevention. Little research has been done on centenarians' early-life experiences or on ACEs in a longevity community.

**Objective:** To interview centenarians and seniors in this region regarding their childhood experiences to inform chronic disease prevention frameworks.

**Design:** Qualitative study of Loma Linda Blue Zone community members. Childhood exposures and practices were assessed using focus groups and semistructured key informant interviews, with open-ended questions on general hardships and ACEs and supplemented with lifestyle and resiliency factor questions. Data were audiorecorded and transcribed. Integrative grounded theory methods guided coding and theming.

**Main Outcome Measures:** Exposure to ACEs and practice of resiliency factors.

**Results:** Participants (7 centenarians and 29 seniors) reported exposure to multiple ACEs (domains: Economic deprivation, family dysfunction, and community violence). Community members reported practicing resiliency factors, each with anti-inflammatory properties suggesting mitigation of ACE-related toxic stress.

**Conclusion:** This is one of the first studies of its kind to identify a community of resilient members despite their tremendous burden of ACEs. Embedding the identified resiliency factors into chronic disease prevention frameworks has potential for mitigating systemic inflammation, alleviating chronic disease burden, and promoting a culture of health.

associated with toxic chronic stress, such as those associated with ACEs, may be through inflammatory mechanisms; a growing body of research supports this theory.<sup>10-12</sup> Furthermore, the inflammatory processes may commence in early-life as studies have revealed the ACE-associated increase in systemic inflammatory markers (C-reactive protein [CRP], fibrinogen, and proinflammatory cytokines) and biological changes already evident in childhood.<sup>11,13</sup> Alterations in inflammatory markers are now identified as candidate biomarkers for mediating the health consequences associated with childhood adversities and subsequently improving healthy longevity.<sup>11</sup>

Insight to reduce the growing prevalence of chronic diseases may be found in key communities around the world where individuals have exhibited increased resilience and longevity. As researchers have identified the link between ACEs and health in adulthood, assessing hotspots with increased healthy longevity makes logical sense.<sup>3</sup> Resilient centenarian and senior members of longevity hotspot communities may have experiences in childhood but are able to mitigate ACE-related biological changes. Around the world, five communities—Sardinia, Italy; Nicoya, Costa Rica; Okinawa, Japan; Ikaria, Greece; and Loma Linda, CA, US—have been identified as “Blue Zones,” or longevity hotspots where members tend to live healthier and longer.<sup>14-20</sup>

The only Blue Zone identified in North America, and therefore having important

## INTRODUCTION

Chronic diseases are a major contributor to morbidity, mortality, and decreased quality of life and have become a national public health crisis.<sup>1,2</sup> A growing body of scientific evidence has linked environmental exposures and stressors in early life with the development of adult chronic diseases, ultimately decreasing life span.<sup>3,4</sup> Since the landmark Adverse Childhood Experiences (ACEs) Study, researchers have associated early-life adverse stress inflicted by extreme poverty, parental

mental illness or incarceration, abuse, community violence, and other adverse experiences to later manifestations of diabetes, mental illness, cancer, chronic pulmonary disease, cardiovascular disease, obesity, and premature mortality.<sup>5-8</sup> Left unabated, frequent or extreme activation of the body's stress response system can become toxic, and in the absence of protective mechanisms, lasting adverse biological changes can occur.<sup>9</sup>

Researchers postulate that the embedding of adverse biological changes

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implications for health throughout the US, is composed of Seventh-day Adventists, a religious group known for its healthy lifestyle. Adventists tend to consume a greater vegetarian diet and refrain from using tobacco, alcohol, and illegal substances. Through one of the largest lifestyle cohort studies, the Adventist Health Study, researchers at Loma Linda University found lifestyle habits linked with an overall improvement in life expectancy that is significantly greater than that for the general US population as well as a reduction in chronic health conditions, especially those associated with states of chronic inflammation such as diabetes, obesity, metabolic syndrome, high blood pressure, and cardiovascular disease.<sup>19,21-25</sup> The increased healthy longevity of this population may have major implications for health promotion, especially with disease prevention founded in early childhood.

Currently, limited research has been conducted assessing childhood experiences and exposures among centenarians, and to our knowledge, no such research has been conducted assessing ACEs or the potential for mitigating ACE-related adverse changes.<sup>26,27</sup> With a history of significant longevity, the Loma Linda Blue Zone (LLBZ) community may provide a unique perspective for chronic disease prevention. Thus, the purpose of this research study was to obtain in-depth information from LLBZ centenarians and seniors about their childhood experiences and exposures and to provide insight for chronic disease prevention framework.

## METHODS

We conducted a qualitative study using grounded theory methods from November 2015 through January 2017 and included 25 key informant interviews (KIs), 2 focus groups, and analysis of a centenarian's published memoir to gain insight into the childhood experiences of LLBZ members.<sup>28</sup> The study was approved by Loma Linda University's institutional review board.

### Participant Recruitment and Inclusion Criteria

Eligible participants were approached at various areas around the city, including

community fairs, faith-based events, a local gym, and senior living facilities. Interested participants were later contacted by telephone to arrange an interview and to provide consent for participation. Participants were included in the study if they currently reside in the City of Loma Linda and were affiliated with the Seventh-day Adventist community.

### Key Informant Interviews and Focus Groups

KIs of 7 centenarians and 18 seniors, with a high participation rate (100% centenarians and 98% seniors), were conducted using a semistructured guide with open-ended questions on adversity and hardship as well as positive experiences or resiliency factors (RFs) in their childhood. General ACE thematic areas were similar in nature to thematic areas of the ACE International Questionnaire (ACE-IQ).<sup>29</sup> *Resiliency factors* are defined as factors that support adapting well in the face of adversity, stress, trauma, and so forth, and research studies have tended to focus on the psychosocial constructs, such as caring and supportive relationships.<sup>30</sup>

In addition to the psychosocial aspects, we assessed healthy lifestyle practices (ie, diet, rest, time outdoors) as RFs. Interviews were conducted by trained bilingual (English and Spanish) facilitators and lasted between 30 and 50 minutes. Findings from KIs informed development of the validation focus group guide. Confirmatory focus groups (n = 2) were conducted among seniors (n = 11) by trained bilingual facilitators, which took place on the Loma Linda University campus and lasted between 60 and 90 minutes. Focus groups and the KI interviewees were mutually exclusive groups, and all were audiorecorded and transcribed verbatim. Excerpts from one centenarian's published memoir were collected and included in the data for coding and analysis.<sup>31</sup> Sample size was determined using thematic saturation.

### Qualitative Analysis

Once transcribed, textual data were analyzed using the constant comparative method to develop a grounded theory model for our study. To ensure

**Table 1. Demographic characteristics of Loma Linda Blue Zone study participants**

Characteristic	Total (N = 36), no. (%)	Centenarians (n = 7), no. (%)	Seniors (n = 29), no. (%)
<b>Age category, years</b>			
65-69	6 (7)	—	6 (21)
70-79	11 (31)	—	11 (38)
80-89	5 (14)	—	5 (17)
90-99	7 (19)	—	7 (24)
≥ 100	7 (19)	7 (100)	—
<b>Sex</b>			
Men	11 (31)	2 (29)	9 (31)
Women	25 (69)	5 (71)	20 (69)
<b>Race/ethnicity</b>			
African American	2 (5)	0 (0)	2 (7)
Asian	6 (17)	1 (14)	5 (17)
White	22 (61)	4 (57)	18 (62)
Hispanic-Latino	6 (17)	2 (29)	4 (14)
<b>Country of origin</b>			
US	23 (63)	2 (29)	21 (72)
Canada	3 (8)	2 (29)	1 (3)
Argentina	2 (6)	1 (14)	1 (3)
Colombia	1 (3)	1 (14)	0 (0)
China	2 (6)	1 (14)	1 (3)
Malaysia	3 (8)	0 (0)	3 (10)
Lebanon	1 (3)	0 (0)	1 (3)
Germany	1 (3)	0 (0)	1 (3)

systematic data analysis, an iterative process of individual-level review and group-level review and interpretation was implemented with a multidisciplinary team. After team consensus on the final codes, coding continued with transcriptions and the centenarian's memoir until thematic saturation was reached. Themes were further refined by multiple readings of the transcripts and memoir, and consensus was reached on the final themes through group discussion of the data. After analysis, participants were invited to a presentation on the study findings and subsequently approved our themes and model.

### Adverse Childhood Experiences and Resiliency Factors Score

Participants were defined as exposed to an ACE or an RF if they reported an adverse or resiliency experience that occurred in the first 17 years of life. A total ACE and RF score was calculated by summing the number of categories with an ACE or resiliency-promoting factor to which a participant was exposed. The number of ACEs ranged from 0 (no exposure) to 11 (all categories exposed); RFs ranged from 0 (no exposure) to 8 (all categories exposed). Descriptive statistics (eg, percentages) were used to describe study participants as well as ACEs and RFs.

### RESULTS

#### Centenarian and Senior Characteristics

In total, 36 participants (7 centenarians and 29 seniors) provided data on ACEs and RFs. Ages ranged between 65 and 102 years; most were women, US born, and white (Table 1). However, although more centenarians were white (57%), just 29% were born in the US. All the centenarians had lived in Loma Linda for 50 years or longer, except for one who had lived 5 years in the community. Centenarians lived by themselves (14%), with family members (57%), or at independent living facilities (29%). Additionally, all centenarians appeared in good

**Table 2. Adverse childhood experiences (ACEs) among Loma Linda Blue Zone study participants**

ACE domain	ACE subdomain	Participant quotes	Total (N = 36), no. (%)	Centenarians (n = 7), no. (%)	Seniors (n = 29), no. (%)
Economic hardship	Food deprivation	"We had some hard times to the point where we were barely surviving, and I know what it is to eat oatmeal 3 times a day."	16 (44)	7 (100)	9 (31)
	Low household income	"So, we were a family of 6 children, and farming was not a very good income. I grew up under very limited circumstances. My folks didn't have money to pay for me [my upkeep]."	19 (53)	7 (100)	12 (41)
Family dysfunction	Loss of parent	"My parents died, so I was with my grandmother on the streets and not knowing anything. Grandmother raised me for a few years, and then she died. After that it was horrible because nobody [would] take care of me."	7 (19)	4 (57)	3 (10)
	Loss of sibling	"Well, my brother one day he felt really, really bad, and the doctor came to our house, and [my brother] had meningitis; he died on Christmas Day. I had a sister, Helen, and she died; it was [due to] kidney failure."	2 (6)	0 (0)	2 (7)
	Family separation	"And he—father—was drafted at 51 by the German military, and that was in '44. He was placed in a camp when the war ended, a [prisoner-of-war] camp in Belgium."	16 (44)	5 (71)	11 (38)
	Parental addiction	"My mother was a smoker and she was a gambler too. So much debt and owing people money that my dad had to go to extra work to take care of the children and pay the debts off."	3 (8)	0 (0)	3 (10)
	Parental mental illness	"My mom, I am sure she had a nervous breakdown. I was in the first grade, so I was 6 years old at the time. I had just gone 2 months in, and she took me out of school to be with her because she was so lonely."	2 (6)	1 (14)	1 (3)
	Parental physical abuse	"When I grew up, I was down, you see because I came from very poor family and I was very poor in school. No achievement. I used to be beaten up and never wanted to open my mouth. If I have something [to eat], I am afraid to eat it because I should leave it alone or else ..."	2 (6)	1 (14)	1 (3)
	Parental mental abuse	"Her centenarian mother remarried when she was very young, and her stepfather was very abusive ... physically and mentally. He was just not very good to them, and that is just how it was."	5 (14)	3 (43)	2 (7)
Community violence	Witness to violence	"He—teacher—hit a girl with a stick so hard that he broke her fingers. The parents just said if they don't want to learn, beat them; it was very bad. We had to go through everything [they witnessed and experienced physical and mental abuse]."	5 (14)	3 (43)	2 (7)
	Refugee status	"We were refugees when I was 4. We had to flee and move around in China because of the invasion by Japan. During childhood we were quite poor."	1 (3)	0 (0)	1 (3)

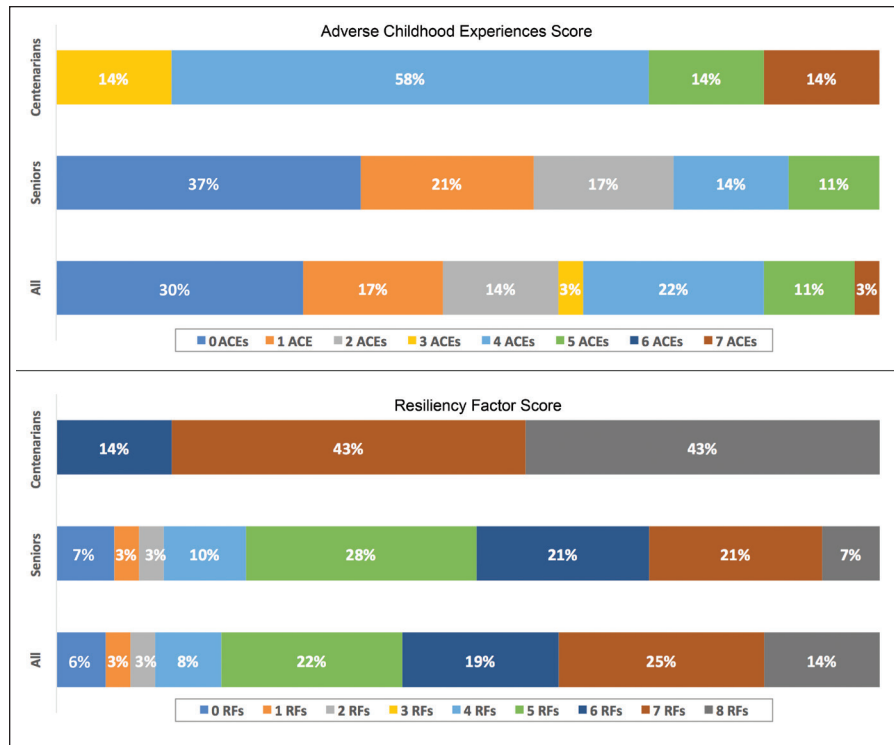


Figure 1. Percentage of Adverse Childhood Experiences (ACEs) and Resiliency Factors (RFs) for Loma Linda Blue Zone (LLBZ) study participants.

overall health without report of chronic illness and reported regular involvement in social activities. Sixty-two percent of the senior participants were white, and most (72%) were born in the US. A high percentage were well on their way to becoming centenarians themselves. Similar to centenarians, seniors were active and independent.

**Qualitative Themes**

**Adverse Childhood Exposures**

Through qualitative analysis of the transcriptions, 3 domains (economic hardships, family dysfunction, and community violence) and 11 subdomains of adversity emerged (Table 2 and Figure 1). The economic hardships subdomains included food deprivation and low household income. The family dysfunction subdomains included loss of parent, loss of sibling, family separation, parental addiction, parental mental illness, parental physical abuse, and parental mental abuse. Last, the community violence subdomains included refugee status and witnessing violence.

Among all study participants, the most reported adversities included low household income (53%), food deprivation (44%), and family separation (44%). Nearly all participants experienced profound economic disadvantage that hindered food security, access to education, and health care, and increased their odds of losing family members. Most participants (70%) had an ACE score of at least 1, and 36% had an ACE score of 4 or greater. Among centenarians, 86% reported an ACE score of 4 or more. All centenarians reported low household income and food deprivation; their families were subsistence farmers with extremely limited resources. The second most reported ACE included family separation (71%), followed by loss of a parent (57%) caused by death or abandonment. A total of 43% reported parental mental abuse and felt their parents lacked love, support, parenting, and guidance. Similarly, 43% reported witnessing violence in their communities in the form of exposure to beatings and war activities. Most seniors (63%) had at least 1 ACE, and 25%

reported 4 or more. Seniors reported having grown up in various socioeconomic backgrounds and parental education levels, and experiencing low household income (41%), family separation (38%), and food deprivation (31%) mainly during War World II, other regional wars, and the Great Depression in the US.

**Resiliency Factors**

During analysis of the RFs, 8 themes emerged of childhood practices that were sustained across centenarians' and seniors' life spans (Table 3 and Figure 1). The themes included kinetic life, spiritual practices, a helping hand, family and friends' camaraderie, nature engagement, resting reset, simple foods, and hopeful intrinsic drive. Nearly all study participants (88%) scored 4 or more RFs, and 39% had 7 or more. The most reported resiliency practice among all participants was family and friends' camaraderie (83%). Participants noted strong and long-lasting social bonds with family members (mainly siblings) and friends, and reported that these relationships offered emotional support and understanding in times of adversity. The second most commonly cited practice was kinetic lifestyle (80%); participants described an outdoor lifestyle immersed in physical activity from dawn to dusk. Centenarians and seniors from farming families raised livestock, gardened, baked, and cared for younger siblings for the most part of the day. Additionally, centenarians reported daily walks (2-3 hours) to school, a nearby town, a neighbor's house, and church. Seniors raised in urban settings also walked daily to school, experienced long hours of outdoor play, and weekly nature hikes with their family and friends. Spiritual practices (78%) were also very common; most participants described involvement in family worship activities and community participation through regular church/temple attendance and involvement in church ministries. Participants expressed diverse faith traditions during their early years of life. Consumption of simple foods was noted in 75% of participants, with home-grown foods, including abundance of vegetables and fruits, and limited meat. Their diets were modest, affordable, and mainly prepared at home. Regarding nature engagement

for study participants (75%), especially those from rural villages or farming backgrounds, “nature” was a way to earn a living: Working the soil to grow food and raising cattle to sustain their families but also as an outlet for enjoyment. For seniors from urban communities, nature was explored and enjoyed with family and friends, a time for fun, exercise, and relaxation. Participants described routine sleeping habits, with at least 8 hours of sleep each day (resting reset, 69%). They commonly held the belief that their actions would result in positive outcomes

in their life (hopeful intrinsic drive, 53%), and they regularly helped others with work (helping hand, 36%).

By study group, all centenarians were exposed to 6 or more RFs, and 58% of seniors noted exposure to 6 or more RFs. Like centenarians, seniors’ exposure to family and friends’ camaraderie (79%) was the highest, followed by kinetic life (76%), spiritual practices (76%), nature engagement (69%), and simple foods (69%). Last, participants reported overlap on RF exposure and practice as they engaged in various factors concurrently. For example,

although they indicated time in nature, they also cited participation in physical activity and friends’ camaraderie.

## DISCUSSION

Our study findings not only support the identification of resilient individuals but also, to our knowledge, are the first to identify a community of resilient members despite their tremendous burden of ACEs. The RFs practiced in childhood remained present across their life spans and addressed multiple health domains (ie, mental, physical, spiritual, social).

**Table 3. Resiliency factors practiced by Loma Linda Blue Zone study participants**

Resiliency factor	Description	Participant quotes	Total (N = 36), no. (%)	Centenarians (n = 7), no. (%)	Seniors (n = 29), no. (%)
Kinetic life	A lifestyle immersed in activities that require physical movement from early in the morning to evening	<i>“I will give you a day in my life as a boy. I had to get up in the morning and go find the cows, and our place will be half a mile or so in dimension, so the cows will be away some place in the bush. Then you have to milk the cows and separate the milk, then eat breakfast, and then go to school. Now, going to school consisted of walking 2 miles ... so, you’d be up in the morning at 5:30 or 4.”</i>	29 (80)	7 (100)	22 (76)
Spiritual practices	Familial faith-based values, traditions, and practices instilled since childhood	<i>“I will never forget, she—mother—made me kneel down by the bed before we sleep, so she taught me a prayer, and I repeated that prayer for many, many years. And up to now I still kneel beside my bed before I go to sleep. And she brought us to church and made sure that we read the Bible stories.”</i>	28 (78)	6 (86)	22 (76)
Helping hand	Charitable acts and altruism practiced in early life	<i>“Our grandfather bought a house in town, next to the church. The teachers used to live in that house as well as children; we [centenarian and siblings] cooked and cleaned so that those kids will have a good place to stay.”</i>	13 (36)	4 (57)	9 (31)
Family and friends’ camaraderie	Network of meaningful and lasting relations that provide support and value	<i>“... we still remember each other from when we went to elementary school; in fact, some of my classmates are still my friends. I saw 3 of them this morning.”</i>	30 (83)	7 (100)	23 (79)
Nature engagement	Extensive exposure to natural and outdoor environments	<i>“We spent lots of time in nature, and we would go pick huckleberries up in the mountains and swim in the lake. Even when we were working, we would pick apples from apple orchards and run and play and do things like that.”</i>	27 (75)	7 (100)	20 (69)
Resting reset	Weekly day of rest away from routine activities to rejuvenate physically and mentally with family and friends; and regular sleep patterns of at least 8 hours of rest at routine times	<i>“Sabbath afternoon we looked forward to. My brothers went horseback riding. I did too, and it was just the time to be outside if we possibly could be. We went to a mountain about a half an hour from us, and we picnicked ... there was always a place to go outside, be together, and picnic and that sort of thing.”</i>	25 (69)	7 (100)	18 (62)
Simple foods	A homegrown and home-cooked diet high in vegetables and fruits with none or limited meat intake	<i>“We lived on a farm, and my mother baked great! She baked fresh bread, and we had lots of vegetables because my mother had a garden. We had fresh stuff all the time. She canned food in jars so in the winter time we had these things ... no artificial anything; everything was good, simple food.”</i>	27 (75)	7 (100)	20 (69)
Hopeful intrinsic drive	Positive thoughts that one’s actions will improve outcomes in life/experiences	<i>“A person has to bear in mind that you can’t allow circumstances to shape what your ultimate goal is. ... [I’d] been out of school about 1 year or 2, no money, nothing, and I was just walking alone one day, and I just got to thinking about the fact that I really wanted to be a doctor. I [didn’t] have any means, but I really wanted to be a doctor, and so I made up my mind to do so.”</i>	19 (53)	7 (100)	12 (41)

Their lifestyle was simple; they tended to live a more kinetic life, heavily engaged in nature and with many RFs practiced in tandem. Although the study participants endured tremendous childhood hardships with numerous ACEs, they were remarkably resilient, especially the centenarians. Evidence shows that ACEs are a major contributor to morbidity and mortality in adults with dose-response relationships between the number of ACEs and chronic diseases.<sup>5,32</sup> With the strong relationship between ACEs, toxic stress, and adverse health outcomes, the question arises as

to how the LLBZ community members, especially the centenarians, are able to achieve such resilient longevity despite enduring tremendous childhood adversity.

**Anti-inflammatory Properties**

One important concept to consider regarding the longevity and resilience of the LLBZ is that each RF (kinetic life, spiritual practices, helping hand, family and friends' camaraderie, nature engagement, resting reset, simple foods, and hopeful intrinsic drive) practiced by LLBZ centenarians and seniors has been found in independent

studies to have anti-inflammatory properties (Table 4).<sup>33-54</sup> Overall, the LLBZ community members lived a highly physically active life, and numerous independent studies have shown that this type of activity is significantly linked to a reduction in systemic inflammatory markers.<sup>42-44</sup> In general, it is well known that increased systemic inflammation is a risk factor for increase in chronic diseases and reduction in life span.<sup>55-58</sup> The practice of these health principles since early childhood may have afforded the centenarians and seniors enhanced ability to counter the effects of

**Table 4. Loma Linda Blue Zone resiliency factors and independent study results identifying association with reduction in inflammatory markers**

Resiliency factor	Author, year	Inflammatory markers	Independent study findings
Family and friends' camaraderie	Turner-Cobb et al, <sup>33</sup> 2000	Cortisol	Quality in social relationships associated with significantly lower cortisol levels
	Costanzo et al, <sup>34</sup> 2005	IL-6	Social support significantly associated with lower levels of IL-6
	Yang et al, <sup>35</sup> 2005	IL-6, fibrinogen, CRP, ICAM-1, E-selectin	High family social strain associated with significant increase in IL-6 and fibrinogen and with overall inflammation burden (index variable created from all 5 markers)
	Kiecolt-Glaser et al, <sup>36</sup> 2005	IL-6 and TNF-α	Hostile marital interactions associated with stronger acute increase in proinflammatory markers (IL-6 and TNF-α)
Helping hand	Schreier et al, <sup>37</sup> 2013	IL-6	Volunteer time associated with significant decrease of IL-6, cholesterol, and BMI measurements
	Fuligni et al, <sup>38</sup> 2007	IL-6 and CRP	Greater sense of fulfillment in helping others associated with significantly lower IL-6 and CRP levels
Hopeful intrinsic drive	Puig-Perez et al, <sup>39,40</sup> 2017, 2015	Cortisol	Optimism related to significantly lower daily cortisol levels and faster cortisol recovery after stressful experiences
	Roy et al, <sup>41</sup> 2010	IL-6 and CRP	Optimism significantly linked with lower IL-6; pessimism significantly related to higher IL-6 and CRP levels
Kinetic life	Hopps et al, <sup>42</sup> 2011	CRP, IL-6, IL-1β, and TNF-α	Physical activity associated with significant decrease in CRP, IL-6, IL-1β, and TNF-α levels
	Autenrieth et al, <sup>43</sup> 2009	CRP and IL-6	Physical work and transportation (cycling/walking) to work associated with lower levels of CRP and IL-6
	Reuben et al, <sup>44</sup> 2003	CRP	House/yard work associated with significantly lower risk of elevated CRP levels
Nature engagement	Li, <sup>45</sup> 2010	Cortisol	Forest outing trips associated with significant decrease in salivary cortisol levels
	Roe et al, <sup>46</sup> 2013	Cortisol	Higher green space in urban city spaces associated with significant decreased stress and cortisol levels
	Guillot et al, <sup>47</sup> 2010	CRP	Vitamin D (major source is sunlight exposure) associated with significant decrease in CRP levels
Resting reset	Okun et al, <sup>48</sup> 2011	IL-6 and TNF-α	Routine sleep practices associated with significantly lower plasma levels of proinflammatory markers
	Lin et al, <sup>49</sup> 2012	IL-6	Leisure mental activities, including reading, attending lectures, and playing cards, were associated with significantly lower levels of IL-6
Simple foods	Nettleton et al, <sup>50</sup> 2006	CRP, IL-6	Whole grains, fruits, nuts, and green leafy vegetables inversely associated with significantly lower CRP, IL-6, and homocysteine levels
	Hodgson et al, <sup>51</sup> 2007	CRP	Unprocessed lean meat intake associated with significantly lower trends of CRP concentrations
	Ciardi et al, <sup>52</sup> 2012	IL-6	Food supplements, preservatives, and colorants associated with significantly increased levels of IL-6 and decreased levels of leptin
Spiritual practices	Holt-Lunstad et al, <sup>53</sup> 2011	CRP	High levels of spiritual wellness associated with significantly lower CRP levels
	Ferraro and Kim, <sup>54</sup> 2014	CRP	Religious service attendance associated with significantly lower CRP levels

BMI = body mass index; CRP = C-reactive protein; ICAM-1 = intercellular adhesion molecule-1; IL = interleukin; TNF = tumor necrosis factor.

toxic stress and inflammation. Furthermore, the possibility exists that the RFs may interact synergistically, where the full impact is greater than the sum of individual components. Our study findings identify a theory that the anti-inflammatory practices that began in early childhood potentially mitigated the negative biological impact of toxic stress and childhood adversities and potentially enable the LLBZ community members, especially the centenarians, to live a significantly longer life span with less chronic disease.

### Biological Mechanism

The mechanism behind childhood stress and health status later in life has not been fully elucidated. However, there may be an overlap between the mechanisms for longevity and that of the ACE-related biological embedding of toxic stress. With the knowledge that chronic disease in adults and shortening of life may have roots stemming from childhood exposures, an understanding of the biological mechanisms for longevity is important and has implications for early childhood health promotion. One of the longevity theories is that of “inflamm-aging” in which low-grade, chronic systemic inflammation increases over time because of the natural aging process and increases the risk of developing chronic disease.<sup>59</sup> Interleukin-6, tumor necrosis factor- $\alpha$ , and CRP have been identified as a few of the major potential inflammatory markers involved in the “inflamm-aging” process. It has been hypothesized that individuals living exceptionally long, healthy lives, such as the LLBZ centenarians, are better able to cope with stress and the inflammatory load and are subsequently able to slow or mitigate the “inflamm-aging” process. Further supporting this theory, a large body of published studies have identified a wide range of adult chronic diseases (ie, diabetes, cardiovascular disease, cancer) associated with states of chronic inflammation and life shortening.<sup>60-62</sup> On the resiliency side, a recent study of psychosocial-related RFs (ie, attending social engagements) found an association with a reduction in inflammatory markers in adults who had experienced multiple ACEs.<sup>63</sup> More research is needed to better understand how the RFs may work together to promote resilience.

### Genetic Diversity and Low-Income Implications

There are a couple of additional points for consideration in supporting the strength of lifestyle influencing resilience and longevity. There has been a large amount of research focused on genes (eg, *FOXO3*) and their identified association with enhanced longevity.<sup>64,65</sup> However, one point to consider is that differing from the other Blue Zones throughout the world, the LLBZ is a genetically diverse group, especially among centenarians because they come from countries around the globe. What they had in common was healthy lifestyle practices, which potentially gives insight into the strength of their lifestyle practices influencing resilience and longevity in this community. The second point to consider is that the LLBZ centenarians and seniors reported disadvantaged backgrounds with fewer resources. In general, household income has been found linked to poorer health outcomes and premature death, and childhood poverty predictive of age-related disease risks, such as elevated inflammation levels and the clustering of metabolic risk factors in adulthood.<sup>66-68</sup> Interestingly, the Nicoya, Costa Rica, and Okinawa, Japan, Blue Zone communities are also composed of some of the lowest income households compared with their surrounding regions yet have been recognized as experiencing some of the best survival rates in their respective countries.<sup>16,69</sup> The LLBZ findings and evidence from Nicoya and Okinawa Blue Zone communities provide additional support for the strength of lifestyle factors influencing resiliency and longevity.

### Informing Chronic Disease Prevention Framework

The findings from our research study have potential implications for informing chronic disease prevention frameworks and improving the health of our nation. One of the main goals of Healthy People 2020, an initiative striving to improve the health of all Americans, is to attain high-quality, longer lives free of preventable disease, disability, injury, and premature death.<sup>70</sup> The RFs identified in our study, which have individually been supported by independent research studies, can help to enhance current existing

chronic disease prevention frameworks to promote a culture of health.

Key stakeholders can significantly influence exposure to the RFs within the chronic disease framework. Health professionals, a critical key stakeholder, can bring awareness for factors and work to promote practicing of factors through conversation. Start the conversation on RFs with children and their families, even if only one or two sentences. Another key stakeholder critical in supporting a shift toward a culture of health is medical facilities/hospitals and their administrators because they could promote RFs in their facility, encouraging wide-ranging exposure to the RFs. Additionally, this stakeholder group could develop innovative collaborations with community organizations (ie, museums, libraries, faith-based agencies, health departments) to promote community awareness and recognition for the RFs. There is a critical need for delivering health messages not only in the health sector but also across the nonhealth sectors. A fourth key stakeholder group, which is important in promoting a culture of health, is elected government officials and politicians. Given the latest knowledge on the critical importance of early child exposures and subsequent chronic disease development, government officials and politicians in charge of spending allocation should critically rethink current funding priorities. This change will ensure significant and increased level of funding targeting programs for early childhood, especially those with health components. In supporting innovative collaborations, greater investments are needed for health promotion and disease prevention research and programs for young children. A fifth key stakeholder group, educational institutions and systems, could also facilitate promoting a culture of health via embedding of the RFs with their school systems and providing an environment that is supportive. Last, policy personnel is a potential key stakeholder group that could drive forward change by embedding RFs in their policy development initiatives.

### Limitations

Our study has some limitations that merit discussion. One potential limitation is the limited generalizability of this study

because it included only centenarians and seniors currently living in the LLBZ. However, the LLBZ centenarian and seniors included a wide age range, greatly differing ethnic background, and differing countries of origin. Similarly, there may be limited generalizability using the ACEs experienced because communities in the US may differ by the type of ACE exposures. Another potential limitation may be with the participants' ability to recall early-life experiences, with most participants likely underreporting resiliency practices and adverse exposures, especially for the oldest members. However, most of the centenarians and older seniors had family members present at the interview corroborating the information provided. Additionally, because this was a qualitative study in nature, further quantitative research studies are warranted to confirm and expand on our findings.

## CONCLUSION

The LLBZ is a community known to have enhanced longevity and fewer chronic diseases. Our findings support that the optimal health of these community members may potentially be guided by resiliency-promoting factors, each with anti-inflammatory properties, which are established in childhood and maintained across the life span. Early-life interventions targeting lifestyle behaviors are emerging as a promising area of focus for reducing the epidemic of chronic disease. The identification of the childhood RFs among this community has characterized potential foundational cornerstones on which to build a framework for promoting a culture of health for the US. Future research studies are warranted assessing health intervention approaches as informed by these RFs. In addition, research studies of childhood experiences (positive and negative) among other worldwide longevity regions and among centenarians are warranted and hold promise for addressing global pediatric toxic stress. With emphasis on early-life health promotion, we can alleviate the burden of chronic disease and enable a collaborative movement toward a more resilient country of wellness and longevity. ❖

## Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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