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Scientific Landscape of Cortisol-Based Biomarkers In Chronic Stress: A Bibliometric Study

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ABSTRACT

Chronic stress is a major public health issue associated with diverse adverse physical and psychological outcomes. It is strongly linked to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, a central regulator of the physiological stress response. Cortisol, a glucocorticoid hormone regulated by this axis, is among the most widely studied stress biomarkers. It can be measured non-invasively in saliva, hair, or urine, each reflecting distinct aspects of stress exposure. Despite increasing research, the global landscape of cortisol-based biomarker studies remains fragmented and insufficiently integrated across disciplines. This bibliometric study analyzed 354 peer-reviewed articles published between 2005 and 2025, retrieved from the Scopus database using a predefined keyword strategy. Eligible studies were limited to English-language journal articles. Data were processed using VOSviewer and the Biblioshiny package in R to examine publication trends, author and institutional productivity, geographical distribution, keyword co-occurrence, citation patterns, and thematic evolution. The analysis revealed a substantial increase in publications over the past decade. The United States, Canada, and Germany were leading contributors. Major themes included HPA axis regulation, allostatic load, and mental health. Hair cortisol emerged as a key indicator of chronic stress, while interest in salivary cortisol declined. Research gaps include limited longitudinal studies, insufficient cross-cultural validation, and inconsistent methodological approaches. This study provides a structured overview of global research on cortisol as a biomarker of chronic stress. Mapping research trends, themes, and collaborations, it highlights existing limitations and offers direction for future interdisciplinary studies to enhance methodological rigor and clinical applicability.

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1. Introduction

Chronic stress refers to a sustained physiological and psychological response that arises when internal or external stressors exceed an individual's adaptive capacity [1]. In contrast to acute stress, which is short-lived and may enhance performance, chronic stress is closely associated with dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in detrimental effects on various biological systems [2]. Increasing empirical evidence has demonstrated that chronic stress contributes to a broad range of negative health outcomes, including cardiovascular disease, metabolic dysfunction, immune suppression, depression, anxiety, and cognitive impairments. Furthermore, chronic stress has been implicated in the acceleration of biological aging and heightened vulnerability to morbidity and mortality, largely due to prolonged activation of inflammatory and neuroendocrine mechanisms [3].

Cortisol is recognized as one of the most thoroughly investigated and validated biomarkers among the various physiological indicators of stress. This glucocorticoid hormone is synthesized and released by the adrenal cortex under the control of the hypothalamic-pituitary-adrenal (HPA) axis in response to stressors. Due to its diverse roles in regulating glucose metabolism, immune activity, and neural processes, cortisol functions as a key mediator in the body's physiological adaptation to stress [4]. Its levels can be measured non-invasively through multiple biological matrices, including saliva, hair, and urine, each offering specific methodological strengths. Salivary cortisol provides insight into acute hormonal changes and circadian rhythm patterns. Hair cortisol reflects cumulative exposure over extended periods. Meanwhile, urinary cortisol allows assessment of both daily variation and total cortisol output [5].

Over the past few decades, cortisol has been increasingly employed as a physiological biomarker for the objective evaluation of chronic stress across a broad range of populations and contexts, including occupational environments, caregiving roles, academic settings, and circumstances involving trauma, socioeconomic hardship, or chronic disease [6].

Despite the growing volume of research in this area, the overall structure of the scientific field remains fragmented, with limited integration of global publication trends, collaborative networks, and thematic developments. To date, there has been no dedicated bibliometric study that systematically investigates the global research output on cortisol as a biomarker of chronic stress, even though the relevance of this topic continues to expand. Bibliometric analysis provides a rigorous methodological tool for mapping the organization, evolution, and intellectual dynamics of a scientific discipline [7]. This approach enables researchers to quantitatively assess patterns in publication productivity, geographic and institutional output, author collaborations, citation behavior, and keyword co-occurrence. Furthermore, bibliometric methods facilitate the identification of influential works, thematic clusters, and knowledge gaps, offering critical guidance for future research priorities [8].

Stress-related research encompasses a wide array of scientific disciplines, including physiology, psychology, neuroscience, endocrinology, and public health [9,10]. Within this multidisciplinary framework, bibliometric mapping of cortisol-focused studies in the context of chronic stress serves as a vital approach to elucidate the structural patterns and developmental trajectory of the field [11]. Such mapping not only aids in tracing research evolution but also enhances interdisciplinary collaboration and supports the application of evidence-based practices in both clinical and public health settings. Accordingly, the present study performs a comprehensive bibliometric investigation of global scientific literature concerning cortisol as a physiological biomarker of chronic stress. This analysis is designed to (1) assess the publication volume and temporal growth, (2) identify the most productive authors, institutions, countries, and journals, and (3) examine the predominant research themes and their progression over time. The resulting insights are expected to provide a data-driven foundation for researchers, healthcare professionals, and policymakers working in the field of stress- related health management.

2. Methods

Search strategy

A comprehensive literature search was conducted in the Scopus database on June 21, 2025 to retrieve publications related to cortisol as a physiological biomarker in the context of chronic stress. The following search query was applied to the title, abstract, and keywords fields: ("cortisol" OR "hair cortisol" OR "salivary cortisol" OR "urinary cortisol") AND ("chronic stress") AND ("physiological biomarker" OR "biomarker" OR "stress biomarker"). No restrictions were placed on the publication year. The search was limited to peer-reviewed journal articles written in English. A total of 354 records were identified following the removal of duplicates and based on relevance to the search criteria. The inclusion criteria focused on studies that investigated cortisol either from saliva, hair, or urine as a biomarker associated with chronic psychological stress in human populations. Exclusion criteria included articles that primarily addressed non-psychological forms of stress, cortisol-related endocrine disorders or papers in which cortisol was used without reference to its role as a stress- related biomarker. The final dataset was exported in CSV format for bibliometric analysis using VOSviewer and Bibliometrix (RStudio). Data Extraction

Relevant bibliographic information was extracted from all included publications retrieved from the Scopus database. The extracted data included the title, year of publication, language, author names, journal title, affiliated institutions, author keywords, document type, abstract, and total number of citations at the time of data collection. Data extraction was performed independently by two reviewers to ensure accuracy and consistency. Any discrepancies between reviewers were resolved through discussion, and if necessary, adjudicated by a third reviewer.

Statistical and Bibliometric Analysis

Bibliometric analysis was conducted using VOSviewer (version 1.6.20) and R software (version 4.3.0) with the Bibliometrix package. VOSviewer was used to map co-authorship, keyword co-occurrence, co-citation, and bibliographic coupling. Thematic clusters and collaborative patterns among authors, institutions, and countries were visualized. Correlation analysis was applied to explore relationships among key variables.

3. Results

Basic Characteristics of Publications

A total of 354 publications related to cortisol as a physiological biomarker of chronic stress were identified and included in this bibliometric analysis. These publications were retrieved from the Scopus database without restriction on publication year, and all were limited to peer-reviewed journal articles written in English. The included articles were published between 2005 and 2025, with a noticeable upward trend in publication volume over the last decade (**Figure 1**). The highest number of publications was recorded in 2024 (n = 39), followed by 2019 (n = 37), and 2022 (n = 35). This trend reflects the growing interest in cortisol-based biomarkers for evaluating chronic stress in recent years

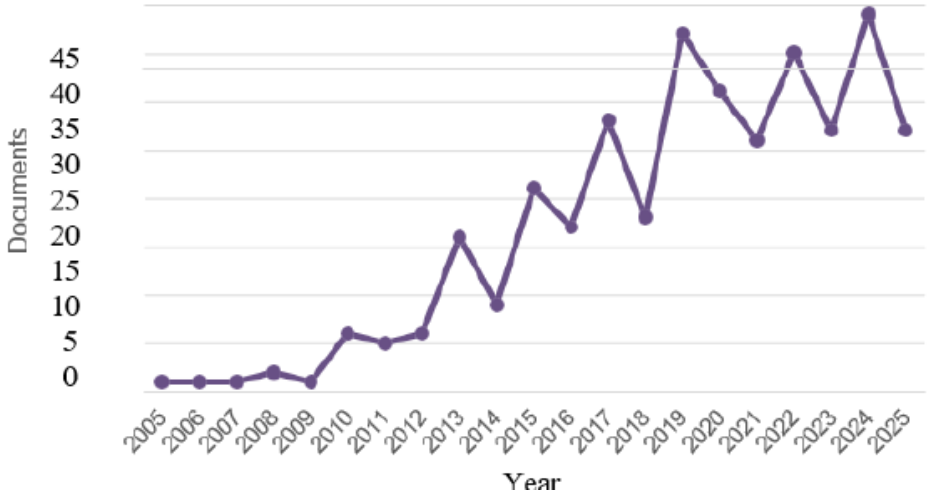


Figure 1. Annual number of publications on cortisol as a physiological biomarker of chronic stress from 2005 to 2025. The data show a consistent upward trend in publication volume, particularly over the past decade, indicating growing research interest in this field.

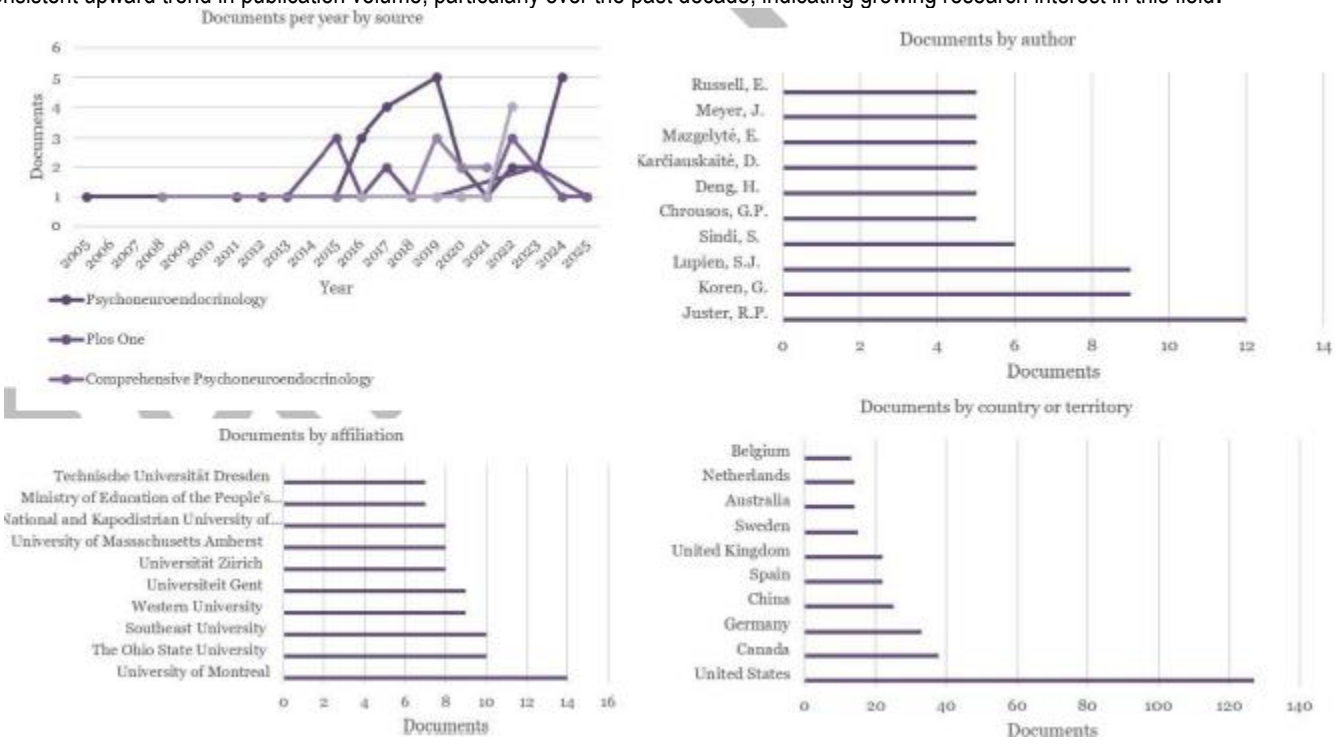


Figure 2. The top 10 most productive journals, countries, institutions, and authors contributing to the literature on cortisol as a physiological biomarker of chronic stress. The figure highlights key sources and contributors that have shaped the development and dissemination of research in this field.

The top 10 most published journals, countries, organizations, and authors are shown in **Figure 2.** The distribution by journal revealed that the most active sources were Psychoneuroendocrinology (n = 28), PLoS ONE (n = 11), Stress (n = 10), International Journal of Environmental Research and Public Health (n = 8), and Comprehensive Psychoneuroendocrinology (n = 6). These journals represent key platforms for interdisciplinary research at the intersection of stress physiology, mental health, and neuroendocrinology. The findings highlight a steady

expansion in the global research landscape on cortisol-based stress biomarkers, particularly in the last decade, aligning with increasing recognition of chronic stress as a significant contributor to public health burdens.

Most Productive Authors, Institutions, and Countries

Analysis of author productivity revealed that a small group of researchers played a central role in advancing cortisol-based biomarker research in the context of chronic stress. The most prolific authors were Juster, R.P., with 12 publications, followed by Koren, G., and Lupien, S.J., each with 9 publications. These authors are among the most frequently cited in the field, suggesting a significant intellectual influence on the development of research on physiological stress biomarkers. In terms of institutional contributions, the most active research organizations included University of Montreal, The Ohio State University, and Southeast University, reflecting strong institutional support for interdisciplinary studies involving psychoneuroendocrinology, behavioral medicine, and stress physiology. These institutions served as key hubs for scientific output and collaboration. Geographically, the United States emerged as the leading contributor, accounting for the highest number of publications in this field, followed by Canada and Germany. This indicates that high- income countries dominate the research landscape, particularly those with well-established academic and public health infrastructures. These findings are illustrated in **Figure 2**, which presents the top 10 most productive journals, countries, institutions, and authors in the field.

Keyword Co-Occurrence Analysis

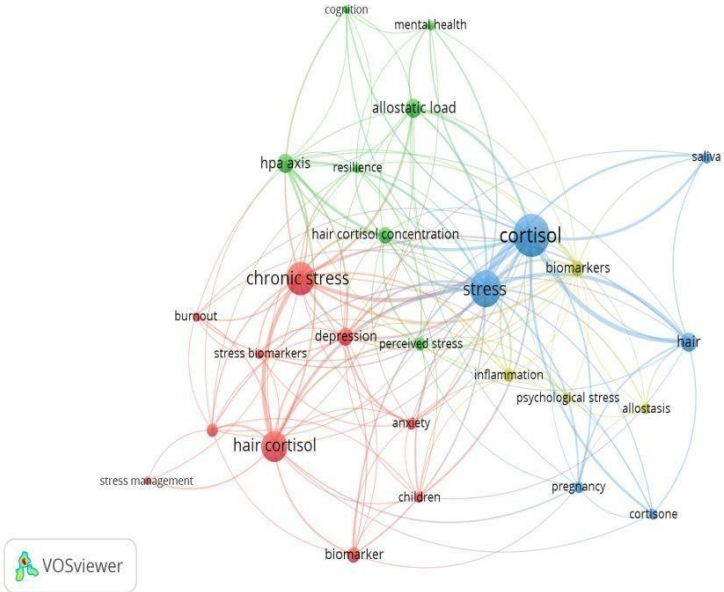


Figure 3. Keyword co-occurrence map generated using VOSviewer, showing major thematic clusters in cortisol-based chronic stress research.

Co-occurrence mapping using VOSviewer identified several main thematic clusters. One major cluster focuses on the HPA axis, allostatic load, and neuroendocrine regulation of stress, which are also linked to mental health and resilience. Another cluster highlights biomarker measurement, particularly the use of hair and saliva for detecting cortisol and cortisone. An additional cluster contains keywords related to chronic stress, depression, anxiety, and stress biomarkers, indicating a focus on both the biological and psychological consequences of prolonged stress. While inflammation appears as a related topic, it does not form a distinct primary cluster. Overall, these themes emphasize the interdisciplinary approach in cortisol-based chronic stress research, connecting biological markers with psychosocial outcomes.

Citation and Top-Cited Publications

The Supplementary Material presents the 100 top-cited papers in the field of cortisol as a physiological biomarker of chronic stress. Collectively, these papers have been cited 9,424 times, with individual citation counts ranging from 1 to 365. The average number of citations per year for these articles varied widely, from as low as 6 up to 1,267. A correlation analysis showed a negative relationship between the publication year and the total number of citations ($r = -0.55$, $p < 0.05$), suggesting that older articles have had more time to accumulate citations. Of the 100 top-cited publications, 98 were original research articles and 2 were review articles. These influential works were published between 2005 and 2025, with the most frequent publication years being 2019 (36 articles), 2022 (35 articles), and 2020 (30 articles). The journals most commonly represented among these top-cited articles included Psychoneuroendocrinology (28 articles), Stress (10 articles), and Plos One (10 articles).

Thematic Evolution and Trends

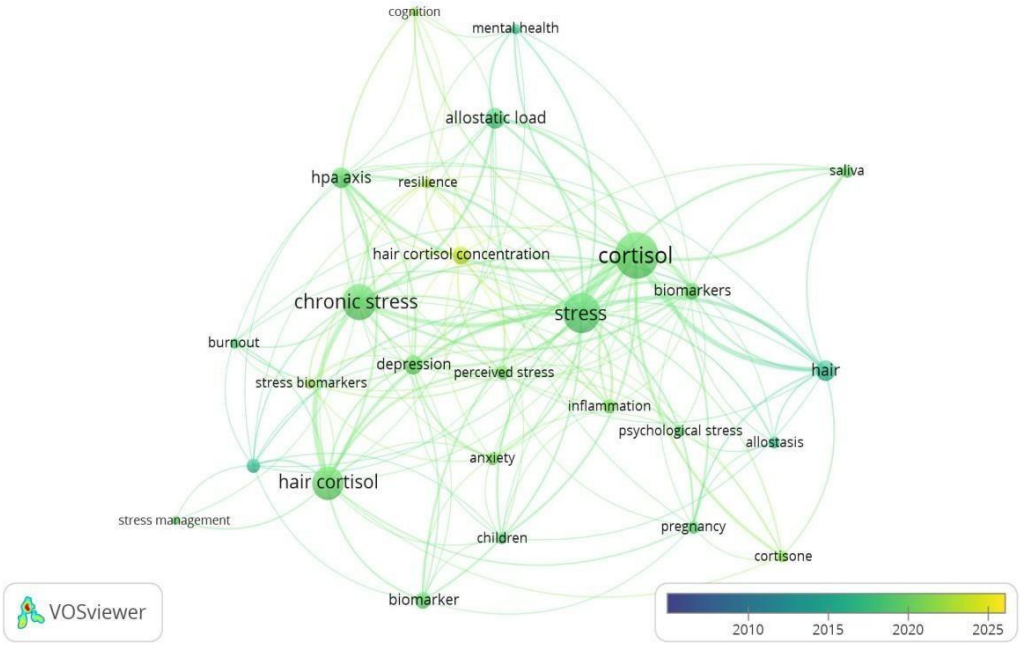


Figure 4. Thematic evolution map showing the progression of dominant research topics in cortisol- based chronic stress studies across four time periods (2005–2025).

Thematic evolution analysis revealed notable shifts in research focus over the past two decades in the field of cortisol-based biomarkers for chronic stress. During the early period of 2005– 2010, studies primarily concentrated on “salivary cortisol,” “circadian rhythm,” and “acute stress,” reflecting an emphasis on short-term physiological responses and diurnal cortisol variation.In the subsequent phase of 2011–2015, the emergence of “hair” and “mental health” as dominant keywords marked a growing interest in retrospective cortisol measurement and its psychological correlates. The trend continued and expanded in 2016–2020, with increased focus on “hair cortisol,” “resilience,” “anxiety,” and “chronic stress,” indicating a more integrative approach to studying the biological and emotional burden of prolonged stress exposure. More recently, from 2021 to 2025, the field has seen a rise in themes such as “allostatic load,” “hair cortisol concentration,” and “cognition,” reflecting a sophisticated understanding of stress adaptation mechanisms and long-term neurocognitive impacts. The keyword “hair cortisol concentration” emerged as a key topic in the latest period, suggesting a shift toward more stable, long-term biomarkers of stress. In contrast, interest in “salivary cortisol” has declined, potentially due to its limitations in capturing chronic stress profiles. These thematic transitions illustrate the field's evolution from acute biomarker assessment toward more nuanced and interdisciplinary frameworks that integrate biological, psychological, and cognitive dimensions of chronic stress.

4. Discussion

This bibliometric study presents a comprehensive synthesis of the global scientific output concerning cortisol as a physiological biomarker of chronic stress. The analysis of 354 articles published between 2005 and 2025 demonstrates a consistent upward trend in research activity, with a marked increase over the past decade. This pattern reflects growing academic and clinical interest in identifying objective and non-invasive indicators of chronic stress in response to increasing global concern regarding mental health, occupational burnout, and the long-term biological impact of psychosocial stressors [12]. The surge in publication volume also corresponds with heightened awareness of stress-related morbidity during and after global crises, including the COVID-19 pandemic, and the increasing emphasis on preventive strategies within public health systems [13,14]. The thematic analysis confirms the interdisciplinary nature of cortisol-based stress biomarker research, situated at the intersection of psychoneuroendocrinology, occupational medicine, and mental health [15]. The prominence of themes such as the hypothalamic-pituitary-adrenal axis, allostatic load, and neuroendocrine adaptation underscores the physiological dimension of chronic stress [16]. Simultaneously, the frequent co-occurrence of terms related to mental health outcomes, such as anxiety, depression, and resilience, highlights the relevance of this research to psychiatric and behavioral sciences [17]. Furthermore, the growing use of hair cortisol and salivary cortisol as non- invasive sampling matrices has expanded the methodological scope of biomarker

research, enabling more feasible applications in field studies, workplace assessments, and community health evaluations [18,19].

Despite this progress, several critical gaps remain evident within the current literature. One major limitation is the predominance of cross-sectional study designs, which restrict the ability to infer temporal relationships or causality between chronic stress exposure and health outcomes [20]. Longitudinal studies, although methodologically demanding, are essential for capturing the dynamic and cumulative nature of stress-related physiological changes. Another limitation concerns the lack of cross-cultural validation and standardization in cortisol measurement. Most studies have been conducted in high-income countries, with limited representation from low- and middle-income settings, despite the global burden of chronic stress [21]. This raises concerns regarding the generalizability of findings and the potential influence of sociocultural, ethnic, and environmental factors on cortisol expression and interpretation [22]. Furthermore, methodological heterogeneity persists in sample collection, storage, assay techniques, and reporting standards, particularly for hair and salivary cortisol, which can compromise reproducibility and limit cross-study comparability [23].

When compared to bibliometric studies in adjacent research domains, such as occupational stress or general physiological stress biomarkers, the current findings reveal a distinctive emphasis on biomarker development, neuroendocrine mechanisms, and methodological rigor [24]. In contrast, previous bibliometric reviews in occupational stress have largely focused on psychosocial models, organizational interventions, and psychological strain [13]. Similarly, broader studies on physiological stress markers often explore composite biomarker panels, including inflammatory cytokines, heart rate variability, and oxidative stress markers, with less emphasis on cortisol specifically [25,26]. This distinction highlights both the methodological maturity of cortisol-focused research and its relative underrepresentation in translational or intervention-based frameworks.

The implications of these findings are multifaceted. For research, there is an urgent need to promote longitudinal, multicenter, and interdisciplinary studies that integrate cortisol with other biological, psychological, and behavioral indicators of stress [27]. Standardization of cortisol sampling protocols, assay methods, and reference values across populations would enhance methodological reliability and enable broader clinical integration [28]. In practice, the incorporation of validated cortisol-based biomarkers into routine occupational health monitoring, mental health screening, and preventive care programs may facilitate early detection of chronic stress and inform personalized intervention strategies [29]. Moreover, the development of accessible, low-cost, and culturally adaptable tools for cortisol assessment could support global mental health initiatives, particularly in under-resourced settings where the burden of stress is often high but remains underdiagnosed and undertreated [30].

5. Conclusions

This bibliometric study provides a comprehensive overview of the global research landscape on cortisol as a physiological biomarker of chronic stress over the past two decades. The findings reveal a consistent increase in publication volume, with growing interdisciplinary interest spanning psychoneuroendocrinology, occupational health, and mental health sciences. Thematic analyses highlight a transition from acute stress measurement to more integrative approaches involving long- term biomarkers such as hair cortisol and concepts like allostatic load. Despite methodological advancements, key challenges persist, including the predominance of cross-sectional designs, limited cross-cultural validation, and heterogeneity in cortisol measurement protocols. The study underscores the need for standardized methodologies, expanded global participation, and the integration of biomarker research into practical health applications. These insights offer a data-driven roadmap to guide future investigations and promote the development of evidence-based strategies for the assessment and management of chronic stress across diverse populations and settings.

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