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Global epidemiology of atopic dermatitis: a comprehensive systematic analysis and modelling study

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Abstract

Background Atopic dermatitis (AD) is the leading cause of the global burden from skin disease; no study has provided global and country-specific epidemiological estimates of AD.

Objectives To quantify global, regional and country-specific estimates of the epidemiology of AD.

Methods A comprehensive search for epidemiological studies in AD was conducted in four electronic databases (PubMed, Embase, Web of Science and China National Knowledge Infrastructure). A Bayesian hierarchical linear mixed model was constructed to calculate epidemiological estimates of AD considering the heterogeneity of regions, countries, type of diagnoses and age strata.

Results In total, 344 studies met the inclusion criteria. Incidence varied substantially with the location and age of the surveyed participants. The global prevalence of AD and the population affected by AD were estimated to be 2.6% [95% uncertainty interval (UI) 1.9–3.5] and 204.05 million people, respectively. Around 101.27 million adults and 102.78 million children worldwide have AD, corresponding to prevalence rates of 2.0% (95% UI 1.4–2.6) and 4.0% (95% UI 2.8–5.3), respectively. Females were more likely to suffer from AD than males: the global prevalence of AD in females was 2.8% (95% UI 2.0–3.7%) and affected 108.29 million people, while in males the corresponding estimates were 2.4% (95% UI 1.7–3.3%) and 95.76 million people.

Conclusions Epidemiological AD data are lacking in 41.5% of countries worldwide. The epidemiology of AD varies substantially with age and sex and is distributed unequally across geographical regions.

What is already known about this topic?

- Most epidemiological AD data have been collected from Western European countries.
- There is a paucity of epidemiology studies of AD in developing countries.
- The absence of uniform diagnostic criteria for AD contributes to the variation in AD prevalence rates worldwide.

What does this study add?

- We focused on studies of AD epidemiology over the last 40 years to establish a model and provide an overview of the global incidence and prevalence of AD.
- More importantly, we were able to generate global, regional and country-specific estimates of AD prevalence.

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Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by intense itching and recurrent eczematous lesions.[1] As the leading cause of the global burden of skin disease, recalcitrant AD symptoms have a substantial psychosocial impact on patients and their relatives, and are associated with an increased risk of comorbidities such as attention deficit/hyperactivity disorder, other atopic diseases and mental health disorders.[1,2] AD can occur at any age; approximately 60% of patients develop the disease in the first year of their life, and the highest incidence occurs between the age of 3 and 6 months.[3]

Recent studies have indicated an increase in the incidence and prevalence of AD. However, there is a paucity of epidemiology studies of AD in developing countries. Thus far, the majority of epidemiological AD data have been collected from Western European countries.[4] The absence of uniform diagnostic criteria for AD has also contributed to the variation in prevalence rates worldwide. Although the major and minor diagnostic criteria suggested by Hanifin and Lobitz provided – to some extent – uniformity in AD diagnoses in hospital-based studies,[5] they are not suitable for population-based studies or general clinical practice.[6] Global epidemiological data for AD have mainly been generated by the Global Burden of Disease (GBD) group, as well as the International Study of Asthma and Allergies in Childhood (ISAAC). However, epidemiological data from the GBD group for individual countries contain potential bias.[7,8] Using a uniformly validated methodology to allow for a direct comparison between countries and by comparing data from phases I and III of the study, ISAAC was able to reflect a trend in AD prevalence.[9,10] However, owing to the unreliability of memory recall and misunderstanding, epidemiological questionnaires based on patient report inevitably introduced some bias. Moreover, the most recent global ISAAC survey was conducted nearly 20 years ago. Thus, an up-to-date understanding of AD epidemiology is urgently needed to better allocate resources and address health disparities.

We focused on studies of AD epidemiology published in the last 40 years, to establish a Bayesian hierarchical linear mixed model, and provide an overview on the global incidence and prevalence of AD. More importantly, we were able to generate global, regional and country-specific estimates of the prevalence of AD in the study.

Materials and methods

Search strategy and review guidelines

This systematic review followed the PRISMA guidelines.[11] PubMed, Embase, Web of Science and China National Knowledge Infrastructure were systematically searched using the main search terms 'atopic dermatitis', 'eczema', 'incidence' and 'prevalence' from 1 January 1992 to 25 December 2022. The references of all included studies and review articles were screened to identify any additional eligible studies. The detailed search strategy, study selection and screening and data extraction methods are provided in Appendixes S1–S8 (see Supporting Information). The study was registered in PROSPERO (CRD42022335562).

Data analysis

The internal validity of trials was assessed using the appraisal tool for cross-sectional studies (AXIS).[12] For duplicate studies that were eligible for inclusion, the studies with the most complete data on the variable of interest, or the most robust data in terms of the methods used, were included.

A Bayesian hierarchical linear mixed model, which is the gold standard model for sparse and heterogeneous data, was applied to estimate the global, regional and country-specific prevalence of AD.[13–16] For full details on the model construction, please refer to Appendixes S1–S8 and Tables S1–S6 (see Supporting Information) or our previously published studies.[17,18] Epidemiological data estimates on AD were informed both by study data from the same country (if available) and by study data from other countries. Countries were mapped according to the GBD classification, arranged into hierarchical groups composed of 189 countries nested in 21 regions and regions nested in 7 super-regions (Table S7; see Supporting Information). Overall, global, super-regions, regions and countries constituted the four levels of the model. Geographical clustering was used to inform and generate estimates for countries with missing information. Therefore, if a country had no data available, estimates of the higher levels were the main drivers of the country estimate, controlling for the fixed effects. The four fixed covariates in the model were age strata [infants (age <1 year), children (age <18 years), adults (age ≥ 18 years)] and the overall population (different age strata combined), type of diagnostic method (physician, dermatologist or self-reported diagnosis), sex (male, female, unclaimed) and type of prevalence measure (point, period or lifetime prevalence).

The statistical model was fitted with 4 chains of 4000 iterations each to run the model of Bayesian inference, and the Hamiltonian Markov chain Monte Carlo method was used to sample from the posterior distribution over the parameters. The target acceptance probability and maximum tree depth were set at 0.995 and 20, respectively, to avoid divergent transitions and transitions that exceeded the maximum tree depth after warm-up. We provide estimates of 1-year period AD prevalence in the context of 95% uncertainty intervals. All incidence data were normalized to per 1000 person-years (PY), and all prevalence data were normalized to percentage. As studies often hold different population structures than seen in the actual country, we weighted the local prevalence and number of people affected according to the real population structure based on the United Nations population structure for the year 2019.[19] We assessed the fit of each model by evaluating the measures relative to the effective sample size and autocorrelation, and the trace plots (Figure S1; see Supporting Information). Detailed information reported from countries with observed or missing data is provided in Appendix S9 (see Supporting Information).

All statistical analyses were conducted with r software (version 4.0.5; R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 344 studies reported on the incidence or prevalence of AD in the general population and were included in

our study (Figure S2; see Supporting Information). Five studies reported the incidence of AD, 327 reported the prevalence of AD, and 12 reported both prevalence and incidence (Tables S8, S9; see Supporting Information). The aggregated 1-year period prevalence rates in all subgroups are provided in Tables S10–S27 (see Supporting Information).

Incidence of atopic dermatitis

Most of the included studies that reported AD incidence ($n = 15/17$) were conducted in Western Europe (Table S8). Overall, incidence varied substantially with the age of the surveyed participants; the incidence of AD in infants and young children declined with age from 419.9/1000 PY (0.5 years old) to 1.3/1000 PY (0–18 years old). Data from different age groups in the UK and Norway showed a similar decreasing trend of AD incidence with age [UK: 419.9/1000 PY (0.5 years old) to 38.3/1000 PY (1.5–2.5 years old); Norway: 52–73/1000 PY (0–1 year old) to 29–34/1000 PY (0–6 years old)]. Studies conducted in the same country by different research groups also demonstrated a decline in the incidence of AD with age. In Denmark, the incidence of AD was 145.1/1000 PY for 1–3-year-old children and 6.6/1000 PY for 0–15-year-olds. In Germany, the incidence of AD in 0–6-year-old children was 38.5/1000 PY, while in 9–11-year-old children it was 1.7/1000 PY.

In the last two decades, there has been no clear time trend in AD incidence for children of the same age. There was a slight upward trend in the incidence of AD in Italy (from 4.1 to 16.5/1000 PY between 2006 and 2012) and Norway (from 29 to 34/1000 PY between 2009 and 2014). In contrast, Spain experienced a slight decline in the incidence of AD between 2002 and 2012 (from 15.9 to 13.5/1000 PY). In addition, Mohn *et al.* reported an increase in the incidence of AD in infants in Norway (from 52 to 73/1000 PY between 2009 and 2014).[20]

Regarding sex, age did not influence the incidence of AD in children aged 0–42 months.[21] However, there were conflicting results regarding the effect of sex on the incidence of AD across countries and regions. In Denmark, Sweden and the UK, the incidence rate of AD in boys and girls was comparable. A similar observation was made for participants of all ages in Finland and the UK. However, the incidence rate of AD was higher in women than in men in the Netherlands and Spain, whereas conflicting results were obtained for Greenland and Norway.

Prevalence of atopic dermatitis

The model estimates considered the heterogeneity of regions, countries, type of diagnosis (physician, dermatologist or self-report) and age groups (children, adults, all). For the overall population, current epidemiological studies covered 113 of 193 (58.5%) countries globally (Figure 1). The global 1-year period AD prevalence rate and affected population were estimated to be 2.6% [95% uncertainty interval (UI) 1.9–3.5] and 204.05 million people, respectively (Figure 2). At the regional level, the prevalence of AD in the general population varied from 1.6% (95% UI 0.8–2.5) in central Asia to 4.1% (95% UI 2.7–6.5) in central sub-Saharan Africa (Figure 3). There was a large difference in the prevalence of AD in terms of country. For the general population, the four countries with the highest prevalence estimates for AD were the United Arab Emirates [UAE; 12.0% (95% UI 11.0–13.1)], Iceland (10.0%, 95% UI 8.7–11.4), Samoa (8.4%, 95% UI 4.0–11.0) and Guinea (7.5%, 95% UI 7.1–7.9) (Table S10). Israel had the lowest AD prevalence rate worldwide (0.31%; 95% UI 0.30–0.31).

Variations in the prevalence of AD were attributed to differences in age structure and sex between regions and countries. Children were more likely to have AD than adults. For children, the global 1-year period prevalence rate and affected population were estimated to be 4.0% (95% UI 2.8–5.3) and 102.78 million people, respectively. The regional prevalence of AD in children varied from 2.4% (95% UI 1.2–3.6) in central Asia to 5.2% (95% UI 3.5–8.3) in central sub-Saharan Africa. A relatively high prevalence of AD in children was found in the UAE (19.7%, 95% UI 18.2–21.4), Iceland (15.5%, 95% UI 13.5–17.5%), Samoa (11.3%, 95%

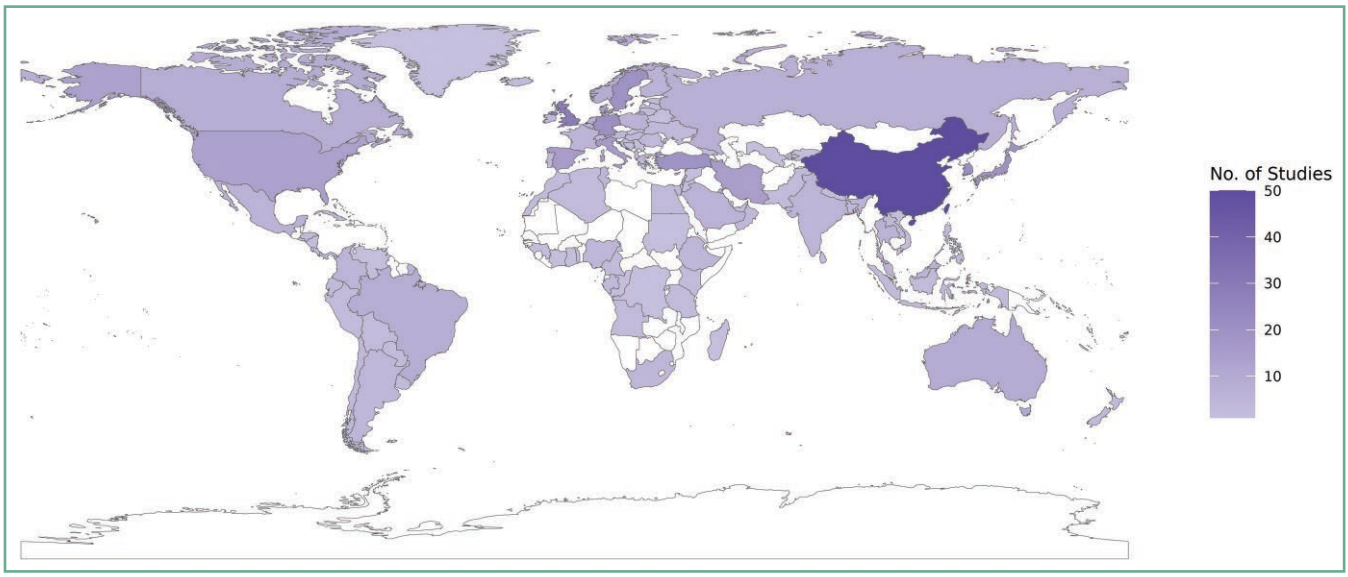

Figure 1 Distribution of the studies included in the statistical analysis by country. Countries with no observed data are white.

Figure 2 Crude 1-year period (physician or dermatologist diagnosed) prevalence of atopic dermatitis for the overall population according to world region.

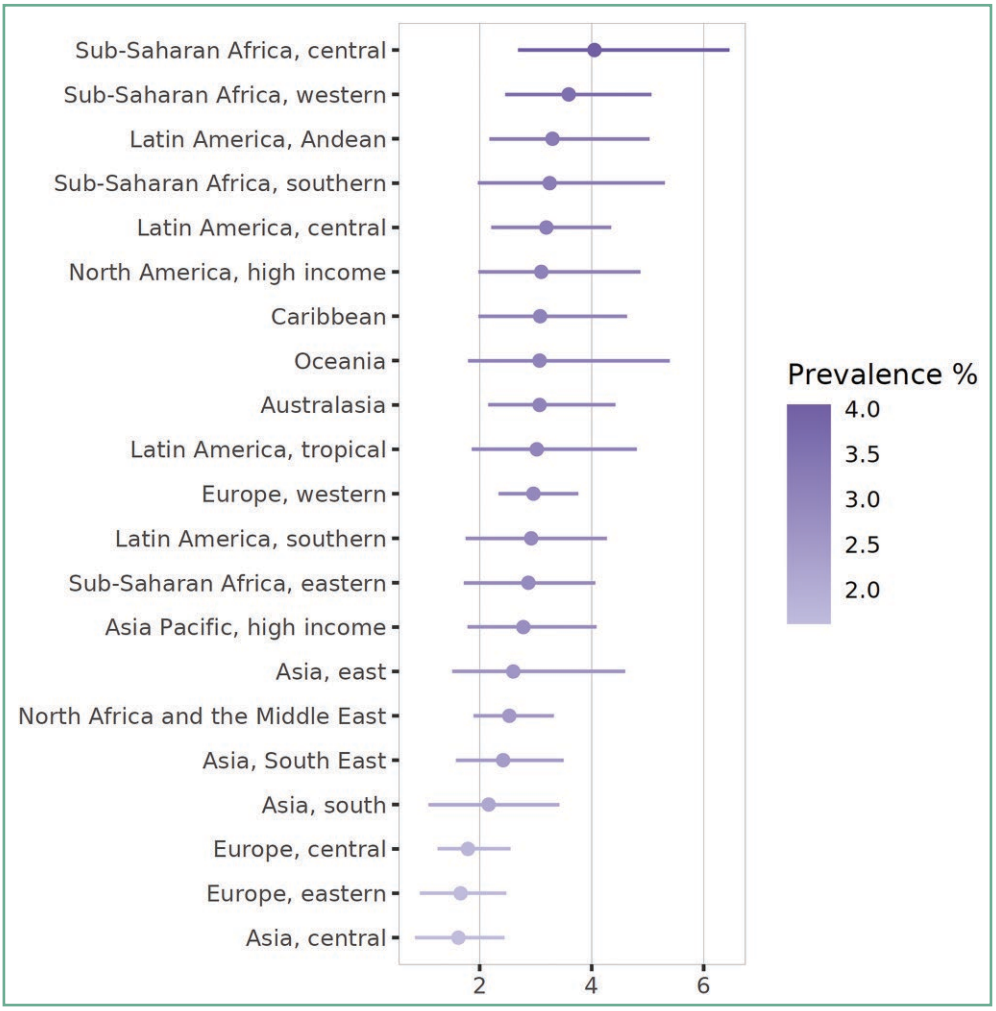

Figure 3 One-year period (physician or dermatologist diagnosed) prevalence of atopic dermatitis for the overall population by regions. Details of countries with observed or extrapolated data are given in Table S10.

UI 5.4–14.7) and Guinea (9.6%, 95% UI 9.1–10.1) (Table S11). The largest paediatric AD populations were in China (12.43 million, 12.33–12.53 million), India (8.60 million, 8.46–8.75 million), Nigeria (7.51 million, 7.26–7.74 million) and the USA (4.84 million, 4.79–4.89 million).

For adults, the global 1-year period prevalence and affected population were estimated to be 2.0% (95% UI 1.4–2.6) and 101.27 million people, respectively. The regional prevalence rate of AD in adults varied from 1.2% (95% UI 0.6–1.8) in central Asia to 2.6% (95% UI 1.7–4.2) in central sub-Saharan Africa. A relatively high prevalence of AD in adults was found in the UAE (10.2%, 95% UI 9.4–11.2), Iceland (8.1%, 95% UI 7.0–9.3), Samoa (5.8%, 95% UI 2.7–7.6) and Guinea (4.9%, 95% UI 4.6–5.2%) (Table S12). The largest adult populations with AD were in China (20.12 million, 19.90–20.33 million), India (7.66 million, 7.51–7.80 million), the USA (7.30 million, 7.22–7.38 million) and Japan (3.30 million, 3.26–3.33 million).

Women were more likely to suffer from AD than men. For women, the global prevalence rate of AD and affected population were estimated to be 2.8% (95% UI 2.0–3.7) and 108.29 million people, respectively. The regional prevalence of AD in women varied from 1.7% (95% UI 0.9–2.6) in central Asia to 4.3% (95% UI 2.9–6.9) in central sub-Saharan Africa. A relatively high prevalence of AD in women was found in the UAE (14.2%, 95% UI 13.1–15.5), Iceland (10.7%, 95% UI 9.2–12.2), Samoa (9.0%, 95% UI 4.3–11.7) and Guinea (7.9%, 95% UI 7.5–8.3) (Table S13). The largest populations of women with AD were reported in China (16.98 million, 16.83–17.14 million), India (8.41 million, 8.27–8.56 million), the USA (6.55 million, 6.48–6.62 million) and Nigeria (5.65 million, 5.47–5.82 million).

For men, the global prevalence of AD and the affected population were estimated to be 2.4% (95% UI 1.7–3.3) and 95.76 million people, respectively. The regional prevalence of AD in men varied from 1.5% (95% UI 0.8–2.3) in central Asia to 3.8% (95% UI 2.5–6.0) in central sub-Saharan Africa. A relatively high prevalence of AD in men was found in the UAE (11.1%, 95% UI 10.1–12.1), Iceland (9.4%, 95% UI 8.1–10.7), Samoa (7.8%, 95% UI 3.7–10.2) and Guinea (7.0%, 95% UI 6.6–7.4%) (Table S16). The largest male populations with AD were reported in China (15.57 million, 15.43–15.72 million), India (7.85 million, 7.71–7.98 million), the USA (5.59 million, 5.54–5.65 million) and Nigeria (5.03 million, 4.87–5.19 million).

In addition to regional difference, the type of diagnostic method (self-reported, or diagnosis made by a physician or dermatologist) and the way prevalence was estimated (period, point or lifetime prevalence) could also lead to the internal variations. Detailed results are reported in Tables S19–S27. Based on our estimate, the overall self-reported AD prevalence rate was about 1.58-fold higher than physician- or dermatologist-diagnosed AD prevalence, and the corresponding global 1-year period self-reported prevalence rate and affected population were estimated to be 4.1% (95% UI 2.9–5.5) and 321.83 million people.

Discussion

This systematic review is the first study to provide comprehensive estimates of the global epidemiology of AD, using a Bayesian hierarchical linear mixed model – the gold standard for sparse and heterogeneous data.[13,14] Our analysis complements the missing AD epidemiological data for most countries worldwide; it estimated the potential AD population in each country, excluding – as far as possible – the influence of factors such as sex, age, diagnostic method and prevalence measure used. Few studies have been done in southern and central sub-Saharan Africa, and the limited number of studies and huge variation in prevalence estimate in Oceania indicate the need for large-scale epidemiological AD studies in these regions. Age, sex and location all had an impact on the incidence and prevalence of AD. Specifically, children, women and people living in countries/regions with a high income level and younger population were more likely to have AD.

Most studies reported the lifetime prevalence of AD, but the lifetime AD prevalence in adults was dramatically lower than in children in different studies. These results were illogical as juvenile AD can clear up permanently or temporarily, and early-childhood onset may have been missed, indicating the potential heterogeneity of the current data.[22,23] When the investigated population is infants or children, parents are often able to provide detailed medical histories; however, when focusing on adults, their own childhood disease course is often overlooked. Given this, we chose to report the 1-year prevalence to achieve relatively accurate estimates and avoid the large bias introduced by lifetime prevalence. We also recommend for future studies that lifetime prevalence in the same age strata is comparable, while the lifetime prevalence in children and adults should not be compared together. The difference in diagnosis criteria might introduce potential bias, and the income and population-related patterns emphasized may have been influenced as countries were grouped and classified according to GBD classification, which is mainly based on geography and income level.[13,14]

Several studies have reviewed the current global epidemiology of AD, but only the GBD studies provide global and country-specific AD epidemiological data. According to the Institute for Health Metrics and Evaluation's most recent GBD study (2019),[24] the global prevalence of AD was 2.3% (95% UI 2.2–2.4) for both sexes [females 2.7% (95% UI 2.6–2.8); males 1.9% (95% UI 1.8–2.0)]. The higher prevalence of AD in females aligns with our results. The discrepancies in AD prevalence may stem from differences in data sources, model construction and the study period of the included studies. In comparison with the DisMod-MR 2.1 tool used by the GBD (a meta-regression tool for epidemiological modelling built on a Bayesian compartmental model framework), our Bayesian hierarchical linear mixed model encompassed broader information such as age strata, sex, type of diagnostic method and method used to measure prevalence. Furthermore, we included a larger number of data sources, more recent studies and more reliable estimates of infant AD prevalence in our model, underscoring the accuracy and representativeness of the estimations. Additionally, Bylund *et al.* found that the 1-year prevalence of AD and lifetime prevalence of doctor-diagnosed AD were higher in females (0.6–24.3% and 1.0–35.5%, respectively) than in males (0.8–17.6% and 1.4–37.3%, respectively).[25] The contradictory results were probably due to different diagnosis criteria and methods of estimation.[25] Although a high prevalence of AD in adults was indicated, global adult

AD data are still lacking.[9,26–28] Therefore, an understanding and estimate of the global prevalence of AD in adults is crucial for long-term disease management. Our study estimated that the 1-year prevalence of AD in adults is about half of that in children. These quantitative data support the notion that AD is widespread, rather than rare, in adults, challenging the view of AD as a disease that clears up with age.[29]

Finally, in terms of location, we found a higher prevalence of AD in sub-Saharan regions and Latin America. Similarly, previous studies have noted a high prevalence of AD in paediatric and adult populations in South America and Africa.[7,30] Cultural, social and diagnostic differences may potentially explain such a high regional burden of AD. For example, large prevalence studies using questionnaire tools may lead to misclassification in these regions, partly because there are many other pruritic skin conditions, such as scabies, that might be considered to be AD, or vice versa; European studies often use general practitioner or insurance datasets.[7,25] However, we did not find discrimination in AD prevalence due to latitude, humidity and temperature observed in previous studies.[27,31]

By providing estimations of global, regional and country-specific AD prevalence and affected populations, our results and interpretation provide further insight into the AD disease paradigm, support the notion of the widespread presence of AD in adults and lay a foundation for future studies in developing countries, ultimately contributing to better disease management in AD.

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Conflicts of interest

The authors declare no conflicts of interest.

Data availability

All data relevant to this study are included in the article or in the Supporting Information.

Ethics statement

Not applicable.

Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website.

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