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Research Article

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Divergent estimates of subacute sclerosing panencephalitis risk after measles and the projected burden of the 2023–2026 resurgence: a Bayesian modelling study

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Abstract

Background: Published estimates of the risk of subacute sclerosing panencephalitis after measles differ more than tenfold, and the burden of the 2023–2026 measles resurgence is unknown. We examined why and projected that burden.

Methods: Nine populations with counts of subacute sclerosing panencephalitis and measles denominators were identified from the literature, and a structured search of three databases checked completeness. Counts were expressed as observed/expected ratios under the 1991 England and Wales reference model. Bayesian hierarchical Poisson models compared study design and the way measles infections were counted (a covariate specified after earlier analyses) as explanations for differences between populations, assessed by leave-one-out cross-validation, permutation tests and 30 prespecified sensitivity analyses. Risk per infection was then applied to infections implied by measles cases reported to the World Health Organization from January 2023 to mid-October 2026.

Results: The populations contributed 499 cases; observed/expected ratios ranged from 0.33 to 8.14. The three populations whose denominators estimated all infections had ratios of 1.6 or less, whereas five of six with denominators counting notifications or clinic visits had ratios of about 4 to 8 (ratio 6.7, 95% credible interval 2.1–19.3). Study design fitted about as well (ratio 5.5, 1.6–16.9); the two explanations could not be separated. Relative to older ages, risk after infection in infancy was about twice that assumed by the reference (multiplier 2.1, 1.2–3.5), although the interval included 1 when either of two strata was omitted. The reported cases correspond to about 40 million infections, which are projected to cause a median of 1,564 (95% interval 254–10,376) to 2,601 (379–18,509) cases depending on the explanation, or about half if scaled to officially reported cases. More than 90% of onsets will occur after 2026, peaking around 2030.

Conclusions: How measles infections were counted may explain much of this variation but cannot be separated from study design; published risks should not be transferred between settings without accounting for the denominator. Under either explanation, the 2023–2026 resurgence is projected to cause hundreds to thousands of cases, mostly during 2027–2035, leaving time to strengthen surveillance and protect infants.

Keywords: Subacute sclerosing panencephalitis, Measles, Measles virus, Encephalitis, Bayesian analysis, Surveillance, Vaccination, Infants, Global health

Background

Subacute sclerosing panencephalitis (SSPE) is a progressive and almost always fatal disease of the central nervous system caused by persistent measles virus infection [1, 2]. It usually begins in childhood, a median of 7 to 10 years after acute measles, and has no curative treatment. The

42 younger a child is when infected with measles, the higher the risk, and infection in infancy
43 carries the greatest risk [1, 2].

44 Measles has returned on a large scale. After routine immunization was disrupted during the
45 COVID-19 pandemic, the World Health Organization (WHO) and the US Centers for Disease
46 Control and Prevention estimated that 10.3 million measles cases occurred worldwide in 2023
47 [3], and WHO estimated about 11 million in 2024 [4]. WHO provisional monthly surveillance
48 data, which held about half of the officially reported cases in 2023, recorded 1.30 million cases
49 between January 2023 and mid-October 2026 [3, 5]. Because of the long interval between
50 measles and SSPE, most of the neurological consequences of these outbreaks have yet to appear.

51 How many children will develop SSPE depends on the risk per infection, and published
52 estimates of that risk disagree. The most widely used reference, a model fitted to the England and
53 Wales SSPE register, estimated four cases per 100,000 measles infections overall and 18 per
54 100,000 after infection in infancy [6–8]. Studies that followed up specific outbreaks have
55 reported much higher risks: about 1 in 1,700 to 1 in 3,300 among children infected before five
56 years of age in Germany [9], 1 in 1,367 among children younger than five years and 1 in 609
57 among infants in California [10], and similarly high values in Georgia and in Okinawa, Japan
58 [11, 12]. These figures, and earlier US data [13], have been taken as evidence that SSPE is more
59 common than previously thought [10].

60 These estimates cannot be compared directly. The studies counted measles infections in different
61 ways (as estimates of all infections, as notifications with or without a correction, or as medically
62 attended visits), and they differ in the age at which children were infected, in how long they
63 followed children relative to the latency of SSPE, and in how completely they found SSPE cases.
64 Observed and expected numbers of SSPE cases have been compared within single countries [6,

8], but we are not aware of any study that has placed populations on a common scale and asked why their estimates differ.

We therefore expressed SSPE counts from nine populations as ratios of observed to expected cases under one reference model, examined whether the differences between populations follow study design or the way measles infections were counted, tested whether the reference age gradient holds, and used the results to project the SSPE burden of the 2023–2026 measles resurgence by region and country.

Methods

Study design and reporting

This is a Bayesian modelling study based on published aggregate data and publicly available surveillance data (Fig. 1). It is reported following the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [14], and the literature search is reported following PRISMA 2020 [15]. An analysis plan, coding rules and quality ratings were written, and their SHA-256 hashes recorded, before any model including the last two populations was fitted (Additional file 1: Section S1). Earlier analyses had used seven of the nine populations, and rough calculations for the other two had been made before the plan was written. Deviations from the plan and post hoc analyses are listed in Additional file 1: Table S1. Ethics approval was not required because only published aggregate data were used.

Reference model

The reference is the model of Farrington [6]. It links SSPE to measles infections through a gamma-distributed latency (shape 3, mean 7.37 years) and age-specific risks per 100,000

infections of 18 at less than one year of age, 9.8 at one year, 6.8 at two years, 4.3 at three years, 1.7 at four years and 1.1 at five years or older. It assumes that 65% of measles infections were notified and that the SSPE register was 90% complete [6, 7]. We reproduced the published expected counts for England and Wales and carried the uncertainty in the reference risk into all analyses through prior distributions.

Identification of populations

Populations were first identified from the published literature, including a review of SSPE epidemiology [8]. A structured search of PubMed, Embase and Scopus from inception to 17–18 October 2026 was then used to check completeness (Additional file 1: Section S2 and Figure S1). Of 1,232 records, 658 remained after duplicates were removed. One investigator screened all records, assessed 32 full texts and extracted all data, and every extracted value was checked against the source tables. A population was eligible if a report gave a count of SSPE cases together with a measles denominator, the period of measles transmission and the period over which SSPE cases were sought. Series without a measles denominator were used only for comparison.

Populations and classifications

Nine populations were eligible (Table 1). Four outbreak follow-up studies traced SSPE back to a defined outbreak or resurgence: Georgia, 2004–2005 [11]; Germany, 1994–2001 [9]; Okinawa, 1986–2007 [12]; and California, 1988–1991 [10]. Five national registers accumulated SSPE cases during endemic transmission: Japan, 1968–1977 [16]; the Netherlands before vaccination [17]; England and Wales, 1990–2002 [18]; the United States, 1960–1968 [19]; and Israel, 1964–1969 [20].

Measles denominators were classified into two types. Type A denominators were model-based estimates of all infections: the US national estimates, which were about ten times notifications and close to annual birth cohorts; the Japanese estimate of 30 times notifications; and the Dutch estimate of annual infections. Type B denominators were counts of notifications or clinic visits, with or without a correction for incomplete reporting; all other populations had type B denominators. The classification is imperfect. Two type A estimates were derived from notifications, and the German hospital-based extrapolation could be read either way, so Germany and Japan were reclassified in a prespecified sensitivity analysis. A report from South Korea was excluded because its SSPE count exceeded the number of reported measles cases [21], and series from Papua New Guinea [22] and the Philippines [23] had no measles denominator.

Expected counts

For population j and stratum i (an age group or a year of infection), the expected number of SSPE cases under the reference is

$$E_{ij} = (D_{ij} / c_j) \times R_F \times RR_{ij} \times W_{ij} \times q_j$$

where D is the published measles denominator, c its completeness relative to all infections, R_F the reference risk per infection, RR the age-specific relative risk, W the probability that SSPE onset falls within the period in which the study looked for cases, and q the completeness with which SSPE cases were found. W integrates the reference latency over each stratum's infection period, assuming that infections were spread evenly over that period. Priors for c and q followed prespecified rules by type of denominator and type of case finding (Additional file 1: Table S2). Because c and the risk level enter the model only as a ratio, the observed/expected ratios depend

on these priors. We therefore also calculated the denominator completeness that each population would need for its count to match the reference.

Statistical analysis

Observed counts were modelled as Poisson with mean $\lambda_j \times E_{ij}$, where λ_j is the observed/expected ratio of population *j*:

$$\log \lambda_j = \mu + \beta_1 \text{ outbreak}_j + \beta_2 \text{ notification}_j + \tau z_j,\ z_j \sim \text{Normal}(0, 1)$$

We fitted the four models specified in the analysis plan: without covariates (M0), with study design (M1), with type of denominator (M2) and with both (M3). Because the denominator covariate was conceived after earlier analyses, we treat M0 as the primary description and M1 and M2 as competing explanations. Priors were Normal(0, 1.5) for μ and β and Half-Normal(0.5) for τ. Models were compared by the expected log predictive density from exact leave-one-population-out refits [24]; if two models differed by less than one standard error, both were to be reported. Models were fitted in PyMC [25] with the No-U-Turn sampler [26], using four chains of 2,000 draws after 2,500 tuning steps. For the main fits, all R-hat values were 1.002 or less, effective sample sizes were at least 3,500, and there were no divergent transitions. Prior and posterior predictive checks were run for each population (Additional file 1: Table S3). To check that results did not depend on the software, models M0 and M2 were re-implemented independently in NumPyro [27]; the ratio for type of denominator was 6.80 (2.22–19.62), against 6.74 in PyMC, and the M0 ratios for the nine populations differed by at most 0.08 (Additional file 1: Table S5).

Two further checks made fewer assumptions than the covariate models. First, we cross-classified the populations by design and type of denominator and compared the ratios between groups with

exact permutation tests on the logarithm of the ratios from M0. Second, we compared the denominator completeness needed to reconcile each population with the reference against independent published estimates of how completely measles was reported. Analysis code was developed with assistance from a large language model (Claude, Anthropic); we reviewed, ran and verified all code and results.

Age gradient

Within each age-stratified population, conditioning on the total number of SSPE cases makes the number that followed infection in infancy binomially distributed, with a probability determined by the expected numbers in infants and older children and by a multiplier φ. Risk level, case finding and denominator completeness cancel, provided that completeness does not differ by age. A value of $\varphi = 1$ means that the reference age gradient holds. We pooled φ across six strata (Georgia, Okinawa, California, the two population groups in Israel, and a Japanese national survey of infections during 1987–1998 [28]) in a random-effects model, and repeated the analysis omitting each stratum in turn because Okinawa overlaps the Japanese survey.

Sensitivity analyses

We ran 30 prespecified sensitivity analyses for each of M1 and M2 (Additional file 1: Table S4 and Figure S2). They omitted each population in turn, varied the priors, denominators and latency, reclassified Germany and Japan, added overlapping data, and excluded the populations rated as being of high concern for denominator validity or case finding. Post hoc, we refitted the models with the steeper infant gradient found below built into the expected counts, with Student t random effects, with the reference risk at five years or older halved, with England and Wales classified as a type A denominator, and omitting, two at a time, Israel and England and Wales

(the only populations the explanations classify differently) and Germany (whose coding is ambiguous). We also replaced design with era of measles transmission (before or after 1980) (Additional file 1: Table S5).

Consistency check against an independent resurgence

The 1989–1991 US resurgence, in which 12 SSPE cases were linked to at least 55,622 reported measles cases [8, 13], was not used to fit the models. Its SSPE count was known to us, and the priors for its denominator and case finding were set afterwards, so we regard this as a consistency check rather than an external validation. M1 and M2 were refitted without California, which overlaps the resurgence, and we report the probability of observing 12 or more cases and the predictive density of exactly 12 cases under each model and under the reference.

Projection

We projected SSPE onsets from measles cases reported to WHO between January 2023 and mid-October 2026 [5], using 8,000 joint posterior draws of the reference risk, the latency and the ratio for a new population. Because the ratios refer to infections, we applied them to modelled infections rather than to reported cases. For 2023 we multiplied reported cases by the ratio of the WHO and US Centers for Disease Control and Prevention estimate of 10.34 million measles cases [3] to the 2023 total in the same surveillance data (321,876). For 2024 we used the WHO estimate of 11 million cases [4] and the 2024 total (359,447). For 2025 and 2026, for which no estimates were available, we used the mean of the two factors. The relative uncertainty of the 2023 estimate was applied to all four years. Under each explanation we used the ratio of the populations that it treats as unbiased: all-infection denominators under M2 and registers under M1. Regional age distributions, survival to SSPE onset and the latency distribution completed

the calculation (Additional file 1: Section S3). M0 was not used for the main projection because its ratio for a new population averages over populations that each explanation regards as biased. In sensitivity analyses we scaled reported cases to the officially reported 2023 count (663,795) instead, and varied the age distributions and survival.

Results

Populations

The nine populations contributed 499 SSPE cases (Table 1). The search identified two populations not found initially, the United States and Israel; Embase and Scopus added none beyond PubMed.

Observed and expected SSPE

Without covariates, the ratio of observed to expected SSPE ranged from 0.33 (95% credible interval [CrI] 0.19–0.66) in Japan to 8.14 (2.82–21.05) in California (Fig. 2). The ratio was 0.41 (0.18–1.20) in the United States, 1.55 (0.96–2.63) in the Netherlands and 1.22 (0.89–1.67) in England and Wales, but between 4.36 and 8.14 in the four outbreak studies and 6.55 (2.82–13.61) in Israel. All three populations with type A denominators had ratios of 1.6 or less, whereas five of the six with type B denominators had ratios of 4 or more.

Explaining the differences

Both covariates reduced the between-population variation. The standard deviation τ fell from 1.08 without covariates to 0.82 with design and 0.75 with type of denominator, which corresponds to about 43% and 52% of the between-population variance. Type B denominators were associated with 6.74 times higher ratios than type A denominators (95% CrI 2.13–19.33),

and outbreak follow-up with 5.54 times higher ratios than registers (1.61–16.92). With both terms in the model, the association with type of denominator remained (3.99; 1.12–12.96) and that with design weakened (2.69; 0.79–9.09). M2 predicted held-out populations best, but the margins were small: it exceeded M1 by 1.6 (standard error 4.4) and M0 by 3.4 (standard error 3.2) in expected log predictive density, so neither explanation can be preferred (Fig. 3; Additional file 1: Table S6). The predictive intervals were wide, so coverage did little to separate the models. M1 failed to predict Israel (46 cases observed; 5 predicted, 95% interval 0–25), and M2 overpredicted England and Wales (47 observed; 273 predicted, 57–1,063).

The permutation tests, which do not rely on the covariate models, gave the same picture. The differences between type B and type A populations (ratio of geometric means 7.97) and between outbreak studies and registers (5.51) were each matched or exceeded by only 2.4% of possible relabellings (one-sided P = 0.024 for both; Additional file 1: Table S7). Only Israel, and England and Wales, are classified differently by the two explanations, and Germany would join them if its denominator were coded type A; with Germany so coded, the denominator contrast fell to 3.79 (P = 0.079). Replacing design with era of transmission explained less of the variation (τ 0.95; ratio for infection before 1980, 0.30, 95% CrI 0.09–1.18).

Robustness

The 95% CrI for type of denominator excluded 1 in 28 of the 30 prespecified sensitivity analyses (ratios 4.65 to 10.39). It was no longer supported when Germany and Japan were reclassified (1.63; 0.43–6.57) or when the four populations of high concern were excluded (2.71; 0.66–11.81). The CrI for design excluded 1 in 29 of 30 analyses (3.94 to 8.58) and was no longer supported when outbreak denominators were assumed to be less complete (3.20; 0.87–9.92)

(Additional file 1: Table S4). In post hoc analyses, the association with type of denominator was 7.68 (1.99–23.46) with Student t random effects, 6.76 (2.04–19.40) with the risk at five years or older halved, 6.43 (1.94–18.21) with the steeper infant gradient and 8.78 (3.37–20.61) with England and Wales classified as type A. The corresponding values for design were 6.05 (1.77–17.98), 5.30 (1.52–16.49) and 5.13 (1.49–15.42). When two of Israel, England and Wales, and Germany were omitted together, the denominator ratio ranged from 4.94 to 9.59 and its interval excluded 1 in all three analyses, and the design ratio ranged from 4.81 to 9.59 and excluded 1 in all three; with Israel and England and Wales both omitted, the two covariates coincide (Additional file 1: Table S5).

For their counts to match the reference, the outbreak studies would have had to capture only 6% to 12% of infections, against prior means of 25% to 80% (Table 2). Independent estimates of the completeness of measles reporting range from about 9% to about 50% [10, 29], so a shortfall of this size is plausible for some populations but not obviously for all. Israel's denominator already divides notifications by 0.28 [20]; to match the reference, only about 2.6% of its infections would have had to be notified. The low ratios in Japan and the United States cannot be explained through the denominator at all, because they would require more than 100% completeness; they point instead to missed SSPE cases or a genuinely lower risk. Published latency summaries were similar in outbreak studies and registers (Additional file 1: Table S8).

Age gradient

Infections in infancy accounted for more SSPE than the reference predicts in four of six strata and about as much in the other two (Okinawa and the Arab population of Israel). The pooled multiplier was $\varphi = 2.10$ (95% CrI 1.18–3.54). It was 2.16 (1.47–3.13) in a fixed-effect analysis

and between 1.65 and 2.37 when each stratum was omitted in turn. The interval included 1 when the Jewish population of Israel (1.65; 0.90–2.86) or Georgia (2.01; 0.98–3.53) was omitted (Additional file 1: Table S9).

Consistency check

For the 1989–1991 US resurgence, in which 12 SSPE cases were observed, the reference predicted a median of 2 cases; the probability of 12 or more was below 0.002 with the base priors and no more than 0.07 under any of five sets of priors. M2 and M1 predicted medians of 8 and 11 cases, with probabilities of 12 or more of 0.36 and 0.48. The predictive density of exactly 12 cases was about 97 times higher under M2, and 99 times higher under M1, than under the reference (Additional file 1: Table S10). Because the priors for this resurgence were set after its count was known, this check supports, but does not prove, the conclusion that the reference underpredicts some populations.

Projected SSPE after the 2023–2026 resurgence

The 1.30 million measles cases reported to WHO correspond to about 40 million infections (95% interval 24–67 million). Under the denominator explanation (M2) we project 1,564 SSPE cases (95% interval 254–10,376), and under the design explanation (M1) 2,601 (379–18,509) (Table 3). Applying the reference risk itself gives 2,251 (1,163–4,216), between the two. The model without covariates, whose ratio for a new population averages over all nine populations, gives 5,088 (471–55,878). Scaling to officially reported rather than surveillance cases roughly halved these figures, to 777 and 1,292. About three quarters of the projected cases follow infections in 2023–2025; the remainder follow infections in 2026, for which reporting is still incomplete. Varying the share of infants among cases younger than five years from 15% to 45%, or the

regional share of cases younger than five years by 0.15, changed the projections by about a fifth in either direction (Additional file 1: Table S11). With the steeper infant gradient built into both the models and the projection, the projections were 1,970 and 3,167.

In all scenarios, 93% of projected onsets fall after 2026, with a peak around 2030 and three quarters during 2027–2035 (Fig. 4). Ten countries reported 59% of the measles cases. The largest projected burdens under M2 were in India (196 cases), Indonesia (182), Yemen (139), Bangladesh (95) and Pakistan (85) (Additional file 1: Table S12).

Discussion

Published estimates of SSPE risk differ by much more than chance, and the 1991 reference does not transfer to all populations. The three populations whose measles denominators estimated all infections had ratios close to or below the reference, whereas five of the six whose denominators counted notified cases or clinic visits had about four to eight times more SSPE than expected. Type of denominator and study design account for this pattern about as well, and nine populations cannot separate them. One conclusion nevertheless holds under either explanation: a published risk of SSPE cannot be transferred to another setting without knowing how the measles infections behind it were counted. The projected burden of the current resurgence has medians of about 1,600 and 2,600 cases under the two explanations, close to the 2,300 implied by the reference itself, or roughly half that if official counts are used for scaling. The intervals are wide (254 to 18,509), and the model without covariates gives a higher median of about 5,100.

Two explanations

The arguments for and against each explanation, and the data that would distinguish them, are summarized in Table 4. A denominator explanation is plausible because notifications capture a

variable and often small fraction of infections: about half in US settings, as cited in [10], and about 9% in the 2013–2014 Dutch outbreak [29]. Corrections by fixed factors may still undercount infections and so inflate the apparent risk per infection. The UK register shows the effect directly. For the same three SSPE cases, 1.26 were expected from notified measles and 0.33 from laboratory-confirmed measles [30], ratios of 2.4 and 9.1. The excluded Korean report, in which SSPE cases outnumbered reported measles cases [21], is an extreme example of the same problem.

A design explanation is also plausible. Outbreak follow-up studies are often prompted by a noticed cluster of cases, and studies that find few SSPE cases are less likely to be published. Israel, a national register with a high ratio, is the main difficulty for this explanation, and England and Wales, a register with a notification-based denominator and a ratio near 1, is the main difficulty for the denominator explanation. Germany is the most ambiguous case: its denominator is an extrapolated total of infections, yet its ratio is high. Era is partly confounded with both explanations, because three of the four populations with low ratios were infected before 1980, when SSPE was diagnosed without modern imaging and with less antibody testing of cerebrospinal fluid; Israel, however, was also infected before 1980 and had a high ratio. A genuinely higher risk in some populations cannot be excluded either. In Israel, SSPE was more frequent in Arab than in Jewish children, and Arab children had measles at younger ages [20].

The steeper infant gradient is estimated within populations and so does not depend on these questions. It suggests that the reference understates the risk after infection in infancy, relative to infection at older ages, by about twofold. Because its interval included 1 when either of two strata was omitted, and the Japanese survey counted surviving and deceased cases, we regard it

as a hypothesis that needs confirmation. If true, it matters most where measles is concentrated in infants too young to be vaccinated.

What this study does not show

This study does not show that the true risk of SSPE is higher or lower than the reference; it shows that the published estimates are not comparable as they stand. It does not identify which explanation is correct. Its projections are of SSPE onsets, not of diagnosed or reported cases, and they apply to the infections behind reported measles, not to all measles worldwide.

Implications

Under any of the models, the 2023–2026 resurgence is likely to cause several hundred to several thousand SSPE cases, mostly during 2027–2035. The delay gives health systems time to prepare. Ten countries reported about 60% of the measles cases, and SSPE notification, testing of cerebrospinal fluid for measles antibody, and linkage to measles surveillance records would be most useful there. Infants carry the highest risk, which supports protecting them during outbreaks, including the supplementary measles vaccine dose from six months of age that WHO recommends in outbreak settings [31]. Deaths from SSPE occur years after the outbreaks that cause them and are generally not captured in estimates of measles mortality. Future studies of SSPE risk should report denominators that estimate all infections, for example from serological surveys or capture–recapture methods, and outbreak follow-up studies with laboratory-confirmed denominators would help to separate the two explanations.

Limitations

The most important limitation is generalizability. All nine populations are in high- or upper-middle-income settings, whereas most of the projected burden falls in countries such as India, Indonesia, Yemen, Pakistan and Bangladesh, where malnutrition, age at infection, other infections and access to diagnosis may change both the risk and its detection. Second, the analysis rests on published aggregates from nine populations, several with small counts, and risk cannot be separated from denominator completeness in such data; the ratios are conditional on the prespecified completeness priors (Table 2 shows the completeness each population would need); the permutation tests remove dependence on the covariate models but not on these priors. Third, design, type of denominator, era and region are partly confounded. The denominator covariate was specified after earlier analyses of seven of the nine populations and after rough calculations for the other two, its classification is imperfect, and the association depends on how Germany and Japan are classified. Fourth, one investigator screened the records and extracted the data, three potentially eligible reports could not be retrieved, and selective publication of outbreak studies with many SSPE cases may have inflated the ratios in outbreak studies. Fifth, the leave-one-out intervals were wide, the covariates improved prediction over the model without covariates by only about one standard error (M2) and half a standard error (M1), and the consistency check rests on one resurgence whose priors were set after the count was known. Finally, the projections rely on provisional surveillance data that are subject to reporting delay, particularly for 2026; on modelled estimates of infections for 2023 and 2024 that were extended to 2025 and 2026; and on regional age distributions and survival that were assumed rather than measured. A single scaling factor was applied to all countries, so the geographical distribution reflects reporting as well as transmission, and country estimates are illustrative.

Conclusions

Observed/expected SSPE ratios differ about 25-fold between populations, and the differences follow how measles infections were counted and study design, which nine populations cannot separate. Published risks should therefore not be transferred between settings without accounting for the denominator. Risk after infection in infancy may be about twice as steep as the reference assumes. Under either explanation, the 2023–2026 measles resurgence is projected to cause a median of about 1,600 to 2,600 SSPE cases, or about half that if official counts are used, mostly during 2027–2035. Surveillance for SSPE and protection of infants should be strengthened now, starting in the countries reporting the most measles.

List of abbreviations

CrI: credible interval; GATHER: Guidelines for Accurate and Transparent Health Estimates Reporting; PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses; SSPE: subacute sclerosing panencephalitis; WHO: World Health Organization.

Declarations

Ethics approval and consent to participate

Not applicable. This study used only published aggregate data and publicly available surveillance data.

Consent for publication

Not applicable.

Clinical trial number

Not applicable.

Availability of data and materials

All data analysed are published aggregate data or publicly available WHO surveillance data [5]. The extracted data, analysis code, analysis plan with its recorded hashes, search records and screening decisions, and model outputs are available in the Zenodo repository, https://doi.org/10.5281/zenodo.23486497.

Competing interests

The author declares that they have no competing interests.

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Authors' contributions

TO conceived and designed the study, searched the literature, screened the records, extracted the data, carried out the analyses, interpreted the results and wrote the manuscript. The author read and approved the final manuscript.

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Tables

Table 1 Populations, classifications and observed/expected ratios under the 1991 reference

Population (reference)	Design	Measles denominator (type)	Measles years	SSPE ascertainment	Size	SSPE	Concern*	Ratio, M0 (95% CrI)
Georgia [11]	Outbreak	Reported cases (B)	2004–2005	2008–2017	8,377	6	Denominator	4.36 (1.05–14.94)
Germany [9]	Outbreak	Extrapolated from hospital statistics, age <5 y (B; A in sensitivity)	1994–2001	2003–2009	43,000	13	—	7.75 (3.51–15.83)
Okinawa, Japan [12]	Outbreak	Estimated medically attended visits (B)	1986–2007	1986–2009	63,100	16	Denominator	4.98 (1.93–11.62)
California, USA [10]	Outbreak	Reported cases, age <5 y (B)	1988–1991	Diagnosed 1998–2015	9,564	7	—	8.14 (2.82–21.05)
Japan [16]	Register	30 × notifications (A; B in sensitivity)	1968–1977	1966–1985	7,650,000	122	Denominator	0.33 (0.19–0.66)
Netherlands [17]	Register	Authors' estimate of annual infections (A)	Endemic (steady state)	1976–1979	800,000	52	—	1.55 (0.96–2.63)
England and	Register	Notifications,	Preceding	1990–2002	Expected	47	—	1.22 (0.89–

Population (reference)	Design	Measles denominator (type)	Measles years	SSPE ascertainment	Size	SSPE	Concern*	Ratio, M0 (95% CrI)
Wales [18]		through the reference expected count (B)	decades		39			1.67)
United States [19]	Register	National estimated cases, about 10 × notifications (A)	1960–1968	Onset to mid-1975	27,370,000	190	Ascertainment	0.41 (0.18–1.20)
Israel [20]	Register	Notifications ÷ 0.28 (B)	1964–1969	Onset 1968–1979	164,629	46	—	6.55 (2.82–13.61)

Type A, estimate of all infections; type B, notifications or visits, with or without a correction for reporting completeness. CrI, credible interval; M0, model without covariates; SSPE, subacute sclerosing panencephalitis. *Prespecified rating of high concern for denominator validity or SSPE ascertainment; these four populations were excluded together in one sensitivity analysis. Prior distributions and all quality ratings are given in Additional file 1: Table S2.

Table 2 Completeness of the measles denominator needed for each population to match the reference

Population	Type of denominator	Prior mean completeness	Observed/expected ratio, M0	Completeness needed to match the reference
Georgia	B	25%	4.36	6%
Germany	B	80%	7.75	10%
Okinawa	B	60%	4.98	12%
California	B	50%	8.14	6%
Japan	A	80%	0.33	Not attainable (>100%)
Netherlands	A	90%	1.55	58%
United States 1960–1968	A	80%	0.41	Not attainable (>100%)
Israel 1964–1969	B	60%	6.55	9%

Completeness needed = prior mean completeness ÷ observed/expected ratio. Independent published estimates of the completeness of measles reporting: about 45%–51% in US settings, as cited in [10], and about 9% in the 2013–2014 outbreak in the Netherlands [29]. Israel's denominator already divides notifications by 0.28 [20], so a needed completeness of 9% implies that about 2.6% of infections were notified. England and Wales is not shown because its

expected count is published with completeness built in. For Japan and the United States, no denominator completeness can reconcile the count with the reference; their low ratios imply missed SSPE cases or a lower risk.

Table 3 Projected SSPE cases from measles reported to WHO, January 2023 to mid-October 2026, by WHO region and period of infection

WHO region or period	Reported measles cases	Denominator explanation (M2), median (95% interval)	Design explanation (M1), median (95% interval)
African	282,078	365 (58–2,489)	609 (89–4,388)
Americas	69,392	46 (7–327)	77 (11–596)
Eastern Mediterranean	305,321	342 (51–2,430)	573 (76–4,285)
European	239,861	235 (37–1,578)	389 (56–2,878)
South-East Asia	214,324	308 (48–2,118)	515 (75–3,811)
Western Pacific	187,072	245 (39–1,652)	408 (60–2,945)
All regions, infections in 2023–2025	963,331	1,148 (188–7,641)	1,913 (280–13,739)
All regions, infections in 2026 (January to mid-October)	334,717	409 (67–2,738)	685 (101–4,974)
Total	1,298,048	1,564 (254–10,376)	2,601 (379–18,509)

Risk per infection was applied to modelled infections: reported cases multiplied by the ratio of modelled measles cases (10.34 million in 2023 [3]; 11 million in 2024 [4]) to the total in the same provisional surveillance data (321,876 in 2023; 359,447 in 2024), with the mean of the two factors used for 2025 and 2026. M2 uses the ratio for populations with all-infection denominators and M1 the ratio for registers. Scaled to officially reported 2023 cases (663,795), the totals were 777 (126–5,155) and 1,292 (189–9,190). Regional medians do not sum to the total. WHO, World Health Organization.

Table 4 Arguments for and against the two explanations, and the data that would distinguish them

	Denominator explanation	Design explanation
What it proposes	Notifications and clinic visits undercount	Outbreak follow-up studies

	Denominator explanation	Design explanation
	infections, inflating the apparent risk per infection	overestimate risk because they are prompted by clusters and selectively published
Evidence for	All three all-infection denominators had ratios ≤1.6 and five of six count-based denominators had ratios of 4.4–8.1; for three recent UK cases, the ratio was 2.4 with notified and 9.1 with laboratory-confirmed measles as the denominator [30]; measles reporting completeness is often 9%–50% [10, 29]; the excluded Korean report had more SSPE cases than reported measles cases [21]	All four outbreak studies had ratios of 4.4–8.1; studies of clusters with few SSPE cases are less likely to be published
Evidence against	England and Wales has a notification-based denominator and a ratio near 1; Germany's denominator is an extrapolated total yet its ratio is high; the association disappears when Germany and Japan are reclassified	Israel, a national register, has a ratio of 6.55, and the design model failed to predict it
Data that would distinguish them	Outbreak follow-up with serological or laboratory-confirmed denominators; capture–recapture estimates of infections	Population-based follow-up of an outbreak chosen without regard to SSPE; registers with notification-based denominators
Implication for the projection	Use the risk from all-infection denominators: median 1,564 cases	Use the risk from registers: median 2,601 cases

Figures

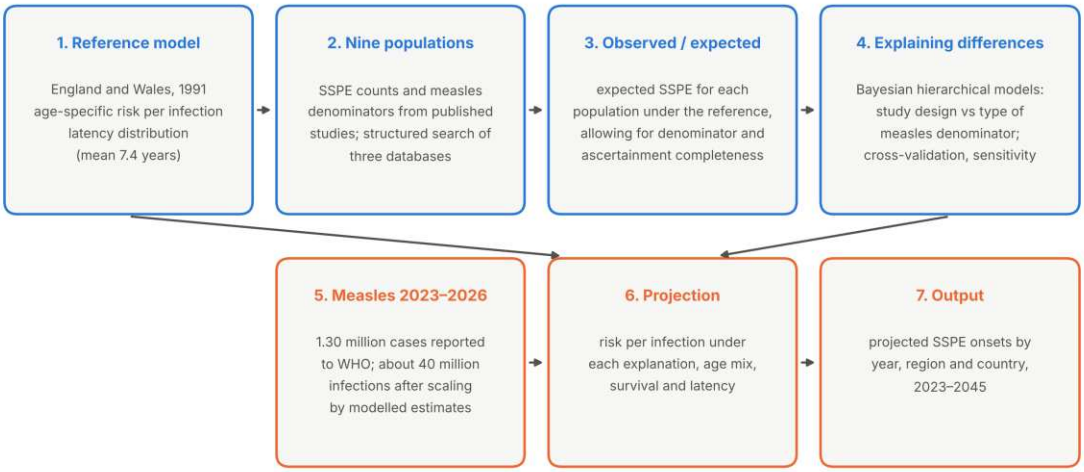
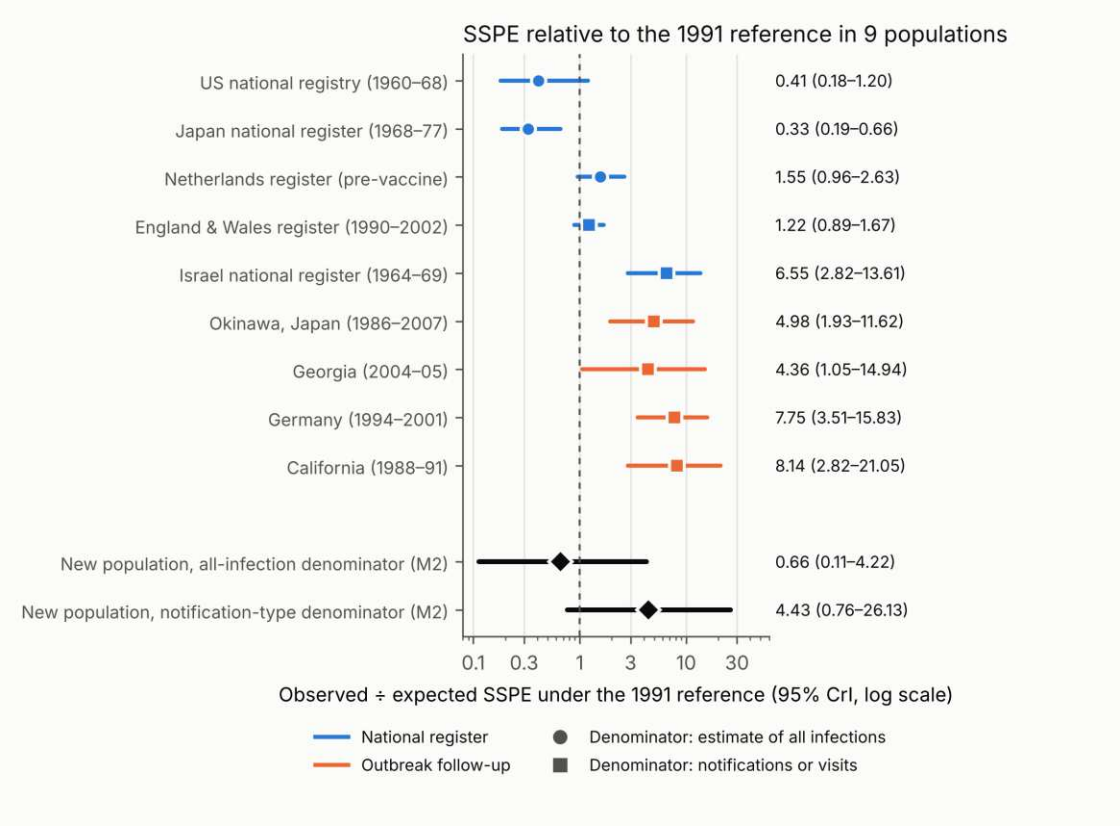


Fig. 1 Overview of the analysis. Steps 1–4 compare published SSPE counts with the reference model; steps 5–7 apply the results to measles reported during 2023–2026. SSPE, subacute sclerosing panencephalitis; WHO, World Health Organization.



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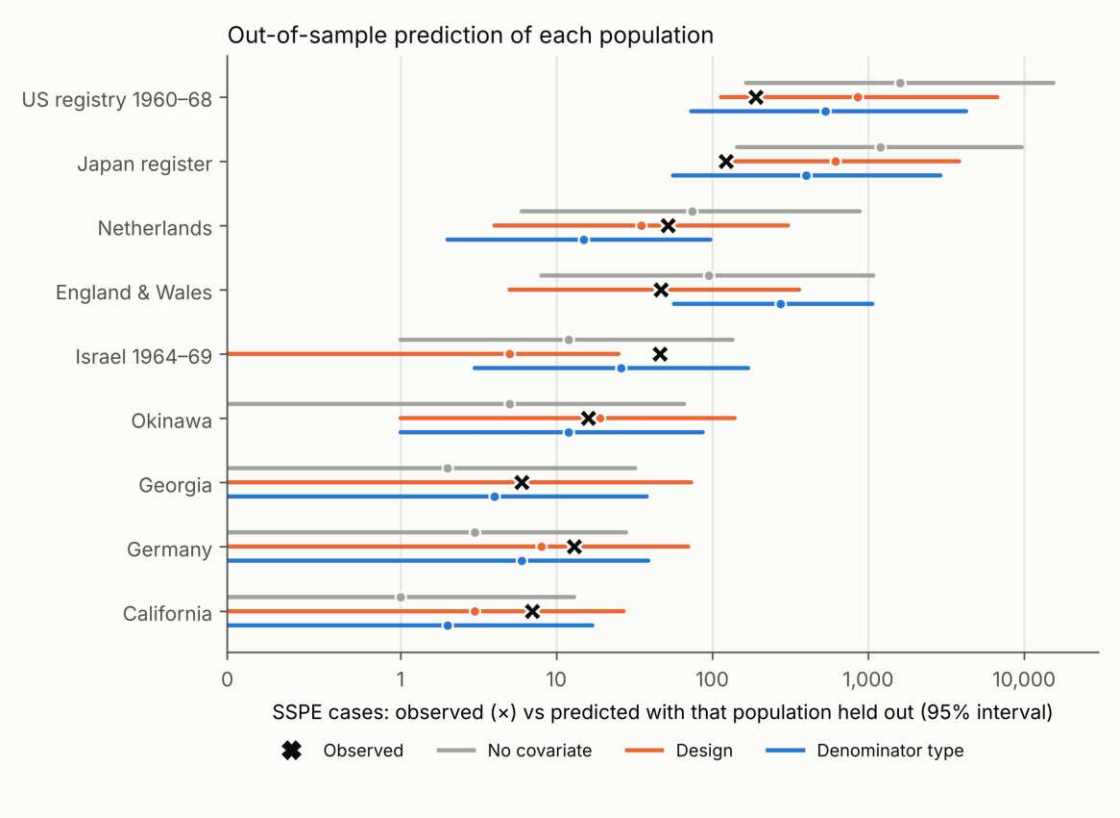
519 **Fig. 2** Observed/expected SSPE under the 1991 England and Wales reference [6] in nine

520 populations, from the model without covariates (M0). Colour shows study design and marker

521 shape the type of measles denominator. Black diamonds show the ratio predicted for a new

522 population with each type of denominator under model M2, including between-population

523 variation. Bars, 95% credible intervals (CrI); dashed line, agreement with the reference.



524

525 **Fig. 3** Observed SSPE counts (×) and counts predicted with each population held out, under the

526 models without covariates (M0, grey), with study design (M1, orange) and with type of

527 denominator (M2, blue). Bars, 95% predictive intervals. The horizontal axis is linear between 0

528 and 1 and logarithmic above 1.

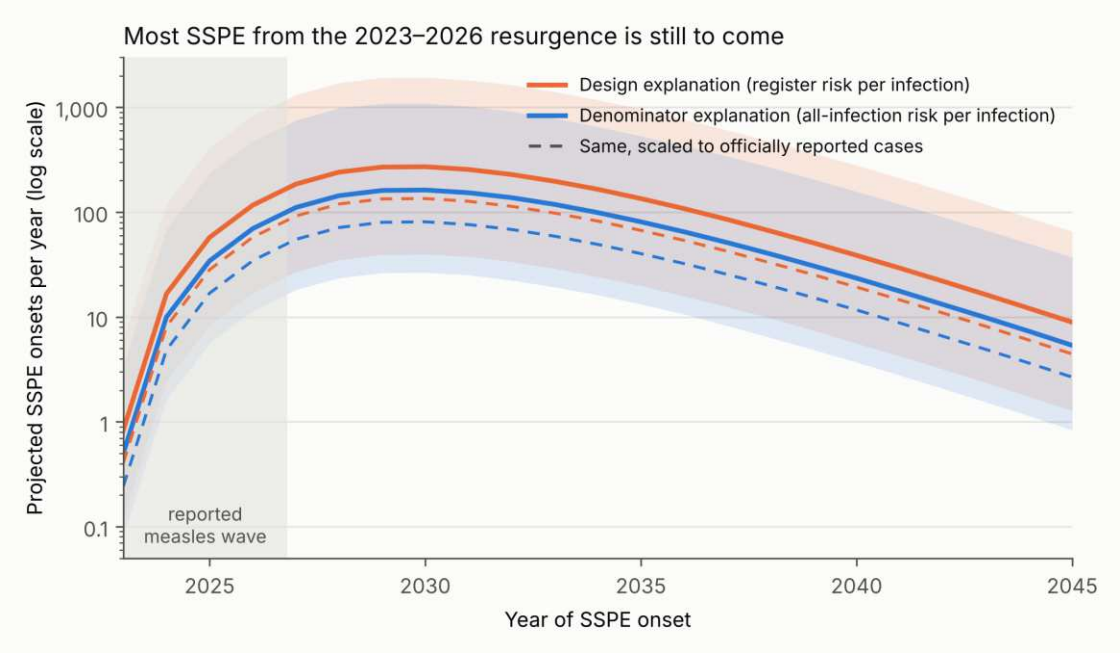


Fig. 4 Projected annual SSPE onsets from measles reported to the World Health Organization between January 2023 and mid-October 2026, applying risk per infection to modelled infections under the denominator explanation (M2, blue) and the design explanation (M1, orange). Solid lines, medians; bands, 95% intervals; dashed lines, medians when reported cases are scaled to officially reported rather than surveillance counts; shaded area, period of the reported measles cases.

Additional files

Additional file 1 (.docx). Supplementary methods, tables and figures: protocol, hashes and deviations (Section S1, Table S1); search strategy and study selection (Section S2, Figure S1); coding, priors and quality ratings (Table S2); predictive checks (Table S3); prespecified sensitivity analyses (Table S4, Figure S2); post hoc analyses (Table S5); leave-one-out validation (Table S6); two-by-two classification and permutation tests (Table S7); latency by population (Table S8); infant gradient (Table S9); consistency check (Table S10); projection inputs and

scenarios (Section S3, Table S11); projections by country (Table S12); material in the data repository (Section S4).

Additional file 2 (.docx). GATHER checklist.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SSPEBMCAdditionalfile2GATHER.docx
- SSPEBMCAdditionalfile1.docx