

Original Article

Outcome of Measles in Vaccinated versus Unvaccinated Children under 5 years of age

Amber Khalid¹, Muhammad Asim², Sana Abid³, Aden Khalid Shah⁴, Muhammad Usman Ali⁵, Hajra Afzal⁶

Abstract

Objective: To determine the frequency of measles vaccination among children under 5 years of age presenting with measles and to compare the outcomes between vaccinated and unvaccinated children. Outcomes were defined as (i) prolonged hospital admission of two days or more (primary outcome, taken as the marker of severe disease) and (ii) measles-related complications (secondary outcome).

Methodology: This descriptive cross-sectional study was conducted at the Department of Paediatrics, Benazir Bhutto Hospital, Rawalpindi, from October 2025 to December 2025, and reported in accordance with the STROBE guidelines for cross-sectional studies. A total of 150 children aged 1–5 years of either sex were enrolled using non-probability consecutive sampling. Measles was defined by the WHO clinical case definition (fever $\geq 38^{\circ}\text{C}$ with a generalised maculopapular rash lasting ≥ 3 days, together with at least one of cough, coryza, or conjunctivitis). A child was classified as vaccinated when at least one dose of a measles-containing vaccine given at or after 9 months of age was documented on the Expanded Program on Immunisation (EPI) card, and as unvaccinated when no dose was documented. Children with chickenpox, other skin infections, congenital anomalies, chronic illnesses, immunocompromised status, or incomplete vaccination records were excluded. Groups were compared using the chi-square test, and effect sizes were reported as odds ratios (OR), risk ratios (RR), and absolute risk differences with 95% confidence intervals (CI).

Results: The mean age of the children was 3.18 ± 1.21 years, and the mean weight was 12.46 ± 2.84 kg. Of the 150 children, 38 (25.3%) were vaccinated, and 112 (74.7%) were unvaccinated. Prolonged hospital admission was required by 57 of 112 (50.9%) unvaccinated children compared with 10 of 38 (26.3%) vaccinated children (OR 2.90, 95% CI 1.29–6.53; RR 1.93, 95% CI 1.10–3.39; absolute risk difference 24.6%, 95% CI 7.8–41.4; $p = 0.009$). Complications were observed in 73 (48.7%) children overall, with pneumonia being the most common complication in 34 (22.7%), followed by diarrhoea in 21 (14.0%), otitis media in 10 (6.7%), and encephalitis in 8 (5.3%). The overall frequency of complications did not differ significantly between unvaccinated (55/112, 49.1%) and vaccinated (18/38, 47.4%) children (OR 1.07, 95% CI 0.51–2.24; $p = 0.853$).

Conclusion: Unvaccinated children < 5 years of age with measles had a significantly greater need for prolonged hospital admission than vaccinated children, indicating that measles vaccination attenuates the severity of illness in children who acquire the infection. The overall frequency of complications did not differ significantly between the two groups; this null result should be interpreted cautiously, given the small number of vaccinated children and the correspondingly wide confidence interval. These findings support the need to strengthen routine measles immunisation coverage in children under 5 years of age.

Keywords: Measles; Measles Vaccine; Vaccination; Child, Preschool; Hospitalization; Treatment Outcome; Immunization Programs; Pakistan.

Introduction

Measles is an acute, highly contagious viral infection caused by the measles virus, an enveloped, single-stranded, spherical RNA virus with six structural proteins: three that form complexes with the viral RNA (nucleoprotein, polymerase, and large protein) and

Conflicts of Interest: None

Financial Support: None to report

Potential Competing Interests: None to report

Disclaimer: This study has not been published or submitted elsewhere for publication.

AI Disclosure: No generative artificial intelligence tool or large language model was used for the conception, design, conduct, analysis, or writing of this manuscript. The authors take full responsibility for the content of this work.

Data Availability Statement: The de-identified individual participant dataset and SPSS analysis files underlying the results reported in this article are available from the corresponding author upon reasonable request.

Institutional Review Board

Approval

PED-2021-126-6739

04-02-2026

Benazir Bhutto Hospital, Rawalpindi

Review began 04/02/2026

Review ended 05/09/2026

Published 30/09/2026

© Copyright 2026

Khalid et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY-SA 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



How to cite this article: Khalid A, Asim M, Abid S, Shah AK, Ali MU, Afzal H. Outcome of Measles in Vaccinated versus Unvaccinated Children under 5 years of age. JRMC. 2026 Sep. 30;30(3).

<https://doi.org/10.37939/jrmc.3302>

three located in the envelope (haemagglutinin, matrix, and fusion proteins).¹ For most children, measles is a short, self-limiting illness, but a substantial minority develop complications that lead to severe sequelae or death.^{1,2} The introduction of the measles vaccine in 1963 was followed by a dramatic and sustained fall in incidence and mortality, and measles vaccination is estimated to have averted approximately 60 million deaths between 2000 and 2023.^{3,5} However, that progress has since stalled. Global coverage with the first dose of measles-containing vaccine has remained at 83–84%, well below the 95% required to interrupt transmission, and the combination of vaccine hesitancy and pandemic-related disruption of immunisation services has been followed by large outbreaks in many countries.^{3,4,16} The consequences of infection extend beyond the acute illness: measles causes a prolonged depletion of pre-existing humoral immunity, so-called immune amnesia, which increases susceptibility to unrelated infections for months to years afterwards and is prevented by vaccination.¹

Measles remains one of the most important causes of preventable morbidity and mortality in children aged < 5 years. An estimated 10.3 million cases and 107,500 deaths occurred worldwide in 2023, with most deaths occurring in unvaccinated or incompletely vaccinated young children in low- and middle-income settings.^{2,3} The clinical spectrum ranges from a self-limited febrile rash illness to pneumonia, diarrhoea, otitis media, encephalitis, malnutrition, prolonged hospitalisation, and death; young children are particularly vulnerable because of immature immunity, nutritional deficiency, and delayed access to care.^{1,6} Pakistan continues to report recurrent measles outbreaks against a background of suboptimal EPI coverage and remains among the highest-burden countries in the Eastern Mediterranean Region.¹³ While the protective effect of measles vaccination against infection is well established, comparatively few local data describe whether vaccination also modifies the severity of disease in children who nevertheless develop measles. Therefore, this study aimed to determine the frequency of vaccination in children under 5 years of age presenting with measles and to compare the outcomes of measles between vaccinated and unvaccinated children.

Methodology

This descriptive cross-sectional study was conducted at the Department of Pediatrics, Benazir Bhutto Hospital, Rawalpindi, from October 2025 to December 2025. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies, and a completed STROBE checklist was submitted as a supplementary file.¹⁷ Approval was obtained from the ethical review board before data collection, and written informed consent was obtained from the parents or legal guardians of every participant.

Using the WHO sample size calculator, a sample size of 150 was calculated at a 95% confidence level with a 5.5% margin of error, taking the anticipated proportion of vaccinated children among measles cases as 13.5%.⁷ Participants were recruited by non-probability consecutive sampling through the Paediatric Outpatient Department.

Measles: a child fulfilling the WHO clinical case definition, that is, fever $\geq 38^{\circ}\text{C}$ with a generalised maculopapular rash of at least 3 days' duration together with at least one of cough, coryza, or conjunctivitis; Koplik spots, where present, were recorded as supportive. *Vaccinated*: documented receipt of at least one dose of a measles-containing vaccine at or after 9 months of age, verified on the child's EPI card. *Unvaccinated*: no dose of measles-containing vaccine was documented on the EPI card. *Prolonged hospital admission*: continuous inpatient stay of two days or more. *Pneumonia*: cough or difficulty in breathing with age-specific tachypnoea (≥ 40 breaths/min in children aged 1–5 years) and/or lower chest indrawing, with or without radiological consolidation. *Diarrhoea*: three or more loose or watery stools within 24 hours. *Otitis media*: ear pain or discharge with an inflamed or perforated tympanic membrane on otoscopy. *Encephalitis*: altered level of consciousness, seizures, or a focal neurological deficit arising during measles illness in the absence of another identified cause. *Socioeconomic status*: classified as low, middle, or high based on reported monthly household income.

Children aged 1–5 years of either sex who met the operational definition of measles were eligible. Children with chickenpox or another documented skin rash or skin infection; congenital anomalies or chronic medical illnesses such as congenital heart disease, immunodeficiency, chronic respiratory disease, or renal disease; immunocompromised children, including those with HIV/AIDS, malignancy, or receiving immunosuppressive therapy; and children whose medical or vaccination records were incomplete or unavailable were excluded.

A detailed history and physical examination were carried out, and information on name, age, sex, weight, duration of measles, residence, socioeconomic status, and season of presentation was recorded on a structured pro forma. Immunisation status was confirmed using the EPI card. Each child was assessed clinically, and the severity of measles was evaluated based on clinical presentation and the need for prolonged hospital admission. All patients were managed according to the standard treatment protocols for measles, including vitamin A supplementation.

Vaccination status was the exposure of interest and could be assigned only from a documented EPI card; children with an unavailable or incomplete card were therefore excluded at screening rather than being imputed. No variable had missing values in the analysed dataset; therefore, a complete-case analysis was performed, and no imputation was undertaken.

Data were entered and analyzed using IBM SPSS Statistics version 25.0. Continuous variables such as age, weight, and duration of measles are presented as mean $\pm$ standard deviation. Categorical variables such as gender, signs of measles, complications, residence, season, socioeconomic status (SES), vaccination status, and outcome are presented as frequencies and percentages. Prolonged hospital admission was compared between the groups using the chi-square test. Statistical significance was set at $p \leq 0.05$.

Results

The mean age of the participants was 3.18 ± 1.21 years, and the mean weight was 12.46 ± 2.84 kg. There were 86 (57.3%) male and 64 (42.7%) female patients. Of the children, 88 (58.7%) were from urban areas, and 62 (41.3%) were from rural areas. Regarding SES, 69 (46.0%) were from the low SES group, 51 (34.0%) from the middle group, and 30 (20.0%) from the high SES group.

Table 1: Baseline characteristics of study participants (n=150)

Variable	Category	n (%) / Mean $\pm$ SD
Age (years)	Mean $\pm$ SD	3.18 ± 1.21
Weight (kg)	Mean $\pm$ SD	12.46 ± 2.84
Gender	Male	86 (57.3%)
	Female	64 (42.7%)
Residence	Urban	88 (58.7%)
	Rural	62 (41.3%)
Socioeconomic status	Low	69 (46.0%)
	Middle	51 (34.0%)
	High	30 (20.0%)

Only 38 (25.3%) children were vaccinated against measles, whereas 112 (74.7%) were not. Fever and rash were present in all cases (150 [100.0%]), confirming the typical presentation of measles. Cough was observed in 126 (84.0%) children, coryza in 118 (78.7%), conjunctivitis in 104 (69.3%), and Koplik spots in 91 (60.7%). The mean duration of measles symptoms at presentation was 5.72 ± 1.94 . Regarding complications, 77 (51.3%) children had no complications, whereas 73 (48.7%) developed one or more complications. Pneumonia was the most frequent complication, affecting 34 (22.7%) children, followed by diarrhoea in 21 (14.0%), otitis media in 10 (6.7%), and encephalitis in 8 (5.3%).

Table 2. Vaccination status and clinical features of measles (n=150)

Variable	Category	n (%)
Vaccination status	Vaccinated	38 (25.3%)
	Unvaccinated	112 (74.7%)
Fever	Present	150 (100.0%)
Rash	Present	150 (100.0%)
Cough	Present	126 (84.0%)
Coryza	Present	118 (78.7%)
Conjunctivitis	Present	104 (69.3%)
Koplik spots	Present	91 (60.7%)
Duration of measles (days)	Mean $\pm$ SD	5.72 ± 1.94
Complications	No complication	77 (51.3%)
	Pneumonia	34 (22.7%)
	Diarrhea	21 (14.0%)
	Otitis media	10 (6.7%)
	Encephalitis	8 (5.3%)

Severe outcomes, defined as prolonged hospital admission for two days or more, were observed in 67 (44.7%) children overall, while 83 (55.3%) did not require prolonged admission. Among the vaccinated children, only 10 (26.3%) required prolonged admission, whereas 28 (73.7%) did not. In contrast, among unvaccinated children, 57 (50.9%) required prolonged admission, and 55 (49.1%) did not. Unvaccinated children were significantly more likely than vaccinated children to require prolonged admission (OR 2.90, 95% CI 1.29–6.53; RR 1.93, 95% CI 1.10–3.39; absolute risk difference 24.6%, 95% CI 7.8–41.4, $p = 0.009$).

Table 3. Outcome of measles according to vaccination status (n=150)

Vaccination status	Prolonged admission ≥ 2 days	No prolonged admission	Total	p-value
Vaccinated	10 (26.3%)	28 (73.7%)	38 (100.0%)	0.009
Unvaccinated	57 (50.9%)	55 (49.1%)	112 (100.0%)	
Total	67 (44.7%)	83 (55.3%)	150 (100.0%)	

Chi-square test. Odds ratio for prolonged admission in unvaccinated versus vaccinated children was 2.90 (95% CI 1.29–6.53), risk ratio was 1.93 (95% CI 1.10–3.39), and absolute risk difference was 24.6% (95% CI 7.8–41.4). CI: confidence interval.

Pneumonia occurred in 27 (79.4%) unvaccinated and 7 (20.6%) vaccinated children. Diarrhoea was noted in 15 (71.4%) unvaccinated children and 6 (28.6%) vaccinated children. Otitis media affected 7 (70.0%) unvaccinated children versus 3 (30.0%) vaccinated children, while encephalitis was observed in 6 (75.0%) unvaccinated children compared with only 2 (25.0%) vaccinated children. When analysed by the proportion of children affected within each vaccination group, at least one complication occurred in 55 of 112 (49.1%) unvaccinated children and in 18 of 38 (47.4%) vaccinated children, a difference that was not statistically significant (OR 1.07, 95% CI 0.51–2.24; $p = 0.853$). The distribution of individual complication categories also did not differ significantly between the two groups ($p = 0.957$).

Table 4. Type of complications according to vaccination status

		Group		Total	p-value
		Vaccinated	Unvaccinated		
Complication	No	20 (26.0%)	57(74.0%)	77(100.0%)	0.957
	Pneumonia	7(20.6%)	27(79.4%)	34(100.0%)	
	Diarrhea	6(28.6%)	15 (71.4%)	21(100.0%)	
	Otitis media	3(30.0%)	7(70.0%)	10(100.0%)	
	Encephalitis	2(25.0%)	6 (75.0%)	8(100.0%)	
Total		38(25.3%)	112(74.7%)	150(100.0%)	

The percentages in the body of the table are row percentages, that is, the proportion of children with each complication who were vaccinated or unvaccinated; they do not represent the risk of that complication within each vaccination group. Chi-square test for the distribution of complication categories, $p = 0.957$. For any complication versus none: unvaccinated 55/112 (49.1%) versus vaccinated 18/38 (47.4%); OR 1.07 (95% CI 0.51–2.24), $p = 0.853$.

Discussion

In this cross-sectional study of 150 children under 5 years of age presenting with measles, three-quarters were unvaccinated, and unvaccinated children were approximately twice as likely as vaccinated children to require prolonged hospital admission (50.9% vs. 26.3%; OR 2.90, 95% CI 1.29–6.53). The low proportion of vaccinated cases indicates a substantial immunity gap in this population, while the difference in admission rates suggests that vaccination attenuates the severity of illness in children who nevertheless acquire measles rather than acting only to prevent infection.

The proportion of vaccinated children in our cohort (25.3%) lies between the 13.5% documented by Stein-Zamir et al. during a community-wide outbreak in Jerusalem and the 37.2% reported by Ashraf et al. from a single centre in Karachi, confirming that measles continues to concentrate in under-immunised children.^{7,10} Our admission findings

concur with those of Stein-Zamir et al., who also reported significantly lower hospitalisation among vaccinated children, although their estimate was less precise than ours (OR 4.8, 95% CI 1.12–20.2).⁷ They are similarly consistent with the large United States post-elimination series of Leung et al., in which 25% of unvaccinated cases were hospitalised compared with 12% of those who had received two or more doses, and severe disease occurred in 19% versus 11%, respectively.⁸ At the population level, the pooled measles vaccine effectiveness of 68.6% (95% CI 60.0–77.2) reported by Endalamaw et al. in African children provides the wider context within which our hospital-based observations should be read.¹¹

Complications occurred in 48.7% of our cohort, with pneumonia being the most common (22.7%), followed by diarrhoea (14.0%), otitis media (6.7%), and encephalitis (5.3%). This profile closely resembles that described by Ashraf et al., who found complications in 66.9% of children with pneumonia (36%), gastroenteritis (11%), and encephalitis (9%), and by Turaiche et al., who identified pneumonia as the dominant complication among unvaccinated Romanian children with measles.^{6,10} Our findings differ, however, from those of Khalil et al., who reported significantly more bronchopneumonia (59.0% versus 46.2%, $p = 0.041$) and diarrhoea (51.3% versus 32.5%, $p = 0.003$) in non-vaccinated than in vaccinated children: in our cohort, the overall frequency of complications was almost identical in the two groups (49.1% versus 47.4%; OR 1.07, 95% CI 0.51–2.24).⁹ The most plausible explanation is statistical power. Khalil et al. studied 234 children in two equally sized groups, whereas only 38 of our participants were vaccinated, and our confidence interval remained compatible with a clinically important difference in either direction. The dose-dependent reduction in complications observed by Leung et al. suggests that a true protective effect would be expected to emerge in a larger sample.⁸ Therefore, our data are best interpreted as showing a clear reduction in the need for prolonged admission with vaccination, while remaining inconclusive with respect to individual complications.

The clinical presentation in our cohort was typical of measles, with fever and rash in every child and high frequencies of cough (84.0%), coryza (78.7%), conjunctivitis (69.3%), and Koplik spots (60.7%), supporting the validity of case ascertainment.¹ The mean duration of symptoms before presentation was 5.72 ± 1.94 days, indicating that most children sought care several days into the illness; late care-seeking is itself associated with complications and may have contributed to the high admission rate observed.²

This study had several limitations. The study was conducted in a single tertiary care hospital; therefore, the findings are not generalisable. The cross-sectional design permits the assessment of association but not causality. The vaccinated group was small ($n = 38$), which limited the statistical power for complication-specific comparisons. The number of doses received and the interval since vaccination were not recorded; therefore, primary vaccine failure could not be distinguished from waning immunity. Vaccination status depended on a documented EPI card, and the exclusion of children with incomplete records may have introduced a selection bias. Prolonged hospital admission was used as a marker of disease severity; although pragmatic and objective, it is influenced by non-clinical factors such as distance from the hospital and bed availability and does not capture every dimension of severity. Finally, no multivariable adjustment was performed, and residual confounding by nutritional and socioeconomic factors could not be excluded.

Conclusions

It was concluded that unvaccinated children under 5 years of age with measles had a significantly greater need for prolonged hospital admission than vaccinated children, indicating that measles vaccination reduces the severity of illness in children who nevertheless acquire the infection. The overall frequency of complications did not differ significantly between the two groups, and this null finding should be interpreted in light of the small vaccinated group and the resulting wide confidence interval. These findings emphasise the need to strengthen routine immunisation coverage and ensure timely vaccination to improve measles-related outcomes in young children, and they support larger, adequately powered studies on the effect of vaccination on individual measles complications.

Author Information

^{1,6}Postgraduate Trainee, Benazir Bhutto Hospital

²Senior Registrar, Pediatrics, Benazir Bhutto Hospital, Rawalpindi

³MTI Registrar, The Dudley Group NHS Foundation Trust Russells Hall Hospital, UK

⁴Registrar, Pediatrics, Portiuncula University Hospital

⁵SHO, Portiuncula Hospital Ballinasloe, Co Galway, Ireland.

Corresponding author: Dr. Amber Khalid  amberkhalid9@gmail.com

Contributions:

AK MA MUA HA - Conception, Design

AK MA SAAKS HA - Acquisition, Analysis, Interpretation

AK HA - Drafting

AK MA SAAKS MUA HA - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.

References

1. Do LAH, Mulholland K. Measles 2025. *N Engl J Med*. 2025;393(24):2447-58. <https://doi.org/10.1056/NEJMra2504516>
2. World Health Organization. Measles [Internet]. Geneva: World Health Organization; 2026 [updated 2026 Jul 15; cited 2026 Aug 9]. Available from: <https://www.who.int/news-room/fact-sheets/detail/measles>
3. Minta AA, Ferrari M, Antoni S, Portnoy A, Sbarra AN, Lambert B, et al. Progress toward measles elimination — worldwide, 2000-2023. *MMWR Morb Mortal Wkly Rep*. 2024;73(45):1036-42. <https://doi.org/10.15585/mmwr.mm7345a4>
4. Venkatesan P. Worrying global decline in measles immunization. *Lancet Microbe*. 2022;3(1): e9. [https://doi.org/10.1016/S2666-5247\(21\)00335-9](https://doi.org/10.1016/S2666-5247(21)00335-9)
5. Berche P. History of measles. *Presse Med*. 2022;51(3):104149. <https://doi.org/10.1016/j.lpm.2022.104149>
6. Turaiche M, Grigoras ML, Bratosin F, Bogdan I, Bota AV, Cerbu B, et al. Disease progression, clinical features, and risk factors for pneumonia in unvaccinated children and adolescents with measles: a re-emerging disease in Romania. *Int J Environ Res Public Health*. 2022;19(20):13165. <https://doi.org/10.3390/ijerph192013165>
7. Stein-Zamir C, Shoob H, Abramson D. Measles clinical presentation, hospitalization and vaccination status among children in a community-wide outbreak. *Vaccine*. 2023;41(17):2764-8. <https://doi.org/10.1016/j.vaccine.2023.03.043>
8. Leung J, Munir NA, Mathis AD, Filardo TD, Rota PA, Sugerman DE, et al. The effects of vaccination status and age on clinical characteristics and severity of measles cases in the United States in the postelimination era, 2001-2022. *Clin Infect Dis*. 2025;80(3):663-72. <https://doi.org/10.1093/cid/ciae470>
9. Khalil U, Masood T, Illiyas T. Comparison of frequency of measles complications among vaccinated and non-vaccinated children presenting at tertiary care hospital. *Biol Clin Sci Res J*. 2025;6(12):59-63. <https://doi.org/10.54112/bcsrj.v6i12.2194>
10. Ashraf J, Taj F, Sadia A, Shafi-u-Zaman, Afzal U, Ijaz M, et al. Frequency of measles vaccination and its complications among children: a single centred study. *J Liaquat Natl Hosp*. 2025;3(1):29-35. <https://doi.org/10.37184/jlnh.2959-1805.2.33>
11. Endalamaw D, Nibret E, Munshea A, Mekonnen F, Tadesse S, Zeru T, et al. Measles vaccine effectiveness in African children: a systematic review and meta-analysis. *BMC Infect Dis*. 2024;24(1):1330. <https://doi.org/10.1186/s12879-024-10239-w>
12. Munday JD, Atkins KE, Klinkenberg D, Meurs M, Fleur E, Hahné SJM, et al. Estimating the risk and spatial spread of measles in populations with high MMR uptake: using school-household networks to understand the 2013 to 2014 outbreak in the Netherlands. *PLoS Med*. 2024;21(10): e1004466. <https://doi.org/10.1371/journal.pmed.1004466>
13. Tariq S, Niaz F, Afzal Y, Tariq R, Nashwan AJ, Ullah I. Pakistan at the precipice: the looming threat of measles amidst the COVID-19 pandemic. *Front Public Health*. 2022; 10:1000906. <https://doi.org/10.3389/fpubh.2022.1000906>
14. Comfort H, Lafta RK, Flaxman AD, Hagopian A, Duber HC. Association between subnational vaccine coverage, migration, and incident cases of measles, mumps, and rubella in Iraq, 2001-2016. *Front Public Health*. 2021; 9:689458. <https://doi.org/10.3389/fpubh.2021.689458>
15. Alhaddad AR, Ahmadnezhad E, Fotouhi A. The vaccination coverage rate in under-5 children in Nasiriyah, Iraq before and during the COVID-19 pandemic. *Epidemiol Health*. 2022;44: e2022035. <https://doi.org/10.4178/epih.e2022035>
16. Mathis AD, Raines K, Filardo TD, Wiley N, Leung J, Rota PA, et al. Measles update — United States, January 1-April 17, 2025. *MMWR Morb Mortal Wkly Rep*. 2025;74(14):232-8. <https://doi.org/10.15585/mmwr.mm7414a1>
17. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med*. 2007;4(10): e296. <https://doi.org/10.1371/journal.pmed.0040296>