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# Vaccination during febrile illness, what do we know? A systematic-narrative hybrid review of the literature and international recommendations

Soumaya Essalim, Chloe Tachet, Sarah Demingo, Sebastien Bruel, Amandine Gagneux-Brunon, Elisabeth Botelho-Nevers

## ► To cite this version:

Soumaya Essalim, Chloe Tachet, Sarah Demingo, Sebastien Bruel, Amandine Gagneux-Brunon, et al.. Vaccination during febrile illness, what do we know? A systematic-narrative hybrid review of the literature and international recommendations. *Vaccine*, 2024, 42 (26), pp.126473. 10.1016/j.vaccine.2024.126473 . hal-04819132

**HAL Id: hal-04819132**

**<https://hal.science/hal-04819132v1>**

Submitted on 4 Dec 2024

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1           **Vaccination during febrile illness, what do we know? A systematic-**  
2           **narrative hybrid review of the literature and international**  
3           **recommendations**

4  
5   **Soumaya Essalim<sup>1,2</sup>, Chloe Tachet\*<sup>3</sup>, Sarah Demingo\*<sup>3</sup>, Sebastien Bruel<sup>3</sup>, Amandine Gagneux-**  
6   **Brunon<sup>1,2,4</sup>, Elisabeth Botelho-Nevers<sup>1,2,4</sup>**

7   \*equally contributed to the work

8   <sup>1</sup>CIC INSERM 1408 Vaccinologie, CHU de Saint-Etienne, 42055, Saint-Etienne Cedex 2, France.

9   <sup>2</sup>Department of Infectious Diseases, CHU de Saint-Etienne, 42055, Saint-Etienne, France

10   <sup>3</sup>Department of General Medicine, Medical School of Saint-Etienne, Université Jean Monnet, 42023  
11   Saint-Etienne, France

12   <sup>4</sup>Centre International de Recherche en Infectiologie, Team GIMAP, Université Jean Monnet,  
13   Université Claude Bernard Lyon 1, Inserm, U1111, CNRS, UMR530, 42023 Saint-Etienne, France

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26 **Abstract**

27 **Introduction:** Vaccination during febrile illness (FI) is often regarded as a contraindication, leading to  
28 its postponement in most cases. Considering the doubts about the immunogenicity, efficacy and safety  
29 of the procedure among physicians and patients, we sought in this review to assess the data in the  
30 literature and international recommendations in terms of vaccination during FI.

31 **Methods:** This review was conducted according to the methodological structure for systematic-  
32 narrative hybrid reviews, using PubMed and Cochrane library databases until March 2024. Inclusion  
33 criteria were studies dealing with vaccination during FI in children or adults, and exclusion criteria  
34 were studies related to post-vaccination fever or animal experiments. A review of international  
35 recommendations was also carried out. Articles included were fully examined by the authors for  
36 eligibility.

37 **Results:** Our literature search enabled us to identify six studies about the immunogenicity and safety  
38 of vaccination during FI in children. All have shown no significant differences in seroconversion rates,  
39 protective antibody levels or adverse events between children vaccinated during FI and controls. Nine  
40 articles on physicians and patients' attitudes regarding immunization during FI were also included in  
41 this review. Vaccination was frequently postponed in cases of fever, primarily to avoid potential  
42 complications. Review of international recommendations allowed us to classify countries into three  
43 categories: those recommending vaccination regardless of the body temperature, those recommending  
44 vaccination within a temperature limit, and those with unclear recommendations.

45 **Discussion:** The immunogenicity and safety studies were only conducted in children, yet results were  
46 reassuring. Despite using the same evidence, recommendations differed from country to another. This  
47 situation may explain the reluctance of physicians and patients to embrace this practice. Postponing  
48 vaccination is however associated with low vaccine coverage and could be considered a missed  
49 opportunity to vaccinate. A higher level of evidence seems needed for a firm conclusion.

50

51 **Keywords**

52 Vaccination; immunization; fever; febrile illness; guidelines; recommendations; immunogenicity;  
53 safety

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## **Introduction**

Vaccination is considered as one of the most effective health interventions in preventing infectious diseases and reducing their associated morbidity and mortality [1]. Yet, achieving an optimal immunization coverage still represents a challenge in both children [2] and adults [3], as the current vaccination rates stand below the targets fixed by the World Health Organization [4]. Low vaccine coverages are associated with the reemergence of diseases and epidemics, which was the case for the measles outbreaks in 2019 [5]. It is therefore essential to improve vaccination coverage by overcoming vaccine hesitancy [6] and reducing missed opportunities to vaccinate [7].

Febrile illness (FI), defined as an abnormal condition of the body when the temperature exceeds 37.5 °C [8], is often associated with common infections, which represent the most frequent reasons for vaccine delay in children [9–11]. Physicians usually defer immunization to avoid potential complications or to prevent any confusion between vaccine side effects and symptoms of the existing illness [9]. This practice can result in multiple missed vaccinations [12]. The accumulation of these missed opportunities to vaccinate can cause gaps in herd immunity [13], which will undoubtedly increase the population’s vulnerability to vaccine-preventable diseases (VPDs) on the long term. Indeed, available evidence showed that postponing vaccination against a certain infectious disease could increase the risk of that disease appearing [14–16]. This was witnessed in the early 90s during the pertussis epidemic in the United States of America, where 52% of cases occurred in infants who had incomplete vaccine schedules and 20% of cases were due to failure to vaccinate on time [14]. Missed opportunities to vaccinate are associated with failures in adhering to vaccination schedules [17], and eventually catch-up immunizations which increases the risk of never being completely vaccinated against preventable infectious diseases [14].

The administration of vaccines during a FI remains a topic of concern and debate among parents and healthcare professionals [9,10,16,18,19]. Taking the decision to vaccinate during such episodes is complicated, and involves considerations for vaccine immunogenicity, reactogenicity, efficacy and safety. While some think that vaccination during FI might affect the immune response or worsen the

82 symptoms [20], others believe in the safety of the procedure and trust that fever has no effect on the  
83 immunogenicity, reactogenicity or efficacy of vaccines[21–25].

84 Unclear guidelines regarding vaccination during a FI [26–30] also affects significantly healthcare  
85 practices. The lack of clear recommendations, as is the case in France, leads to uncertainty, confusion  
86 and sometimes even reluctance to vaccinate [9,10]. Without the existence of clear guidelines that  
87 physicians could rely on to reassure themselves and their patients, missed vaccinations are inevitable  
88 [9].

89 Given that FIs are considered as a significant contributing factor to low vaccination rates [9], we  
90 investigated in this literature review, available data on vaccination during FI. By focusing on studies  
91 evaluating the immunogenicity, safety and efficacy of vaccination in the presence of fever, along with  
92 articles assessing physicians' and parents' attitudes towards immunization during FI and international  
93 vaccination recommendations, we aimed to provide an overview of the current clinical evidence, to  
94 better understand vaccination practices worldwide and to identify gaps in knowledge.

95

## 96 **Methods**

97 The approach of this review was based on the suggested methodological structure for systematic  
98 narrative hybrid reviews (HR) [31].

### 99 *Aims and research question*

100 The aim of this review was to synthesize and assess available immunogenicity, efficacy, safety data,  
101 data on the patients' and physicians' attitudes and international guidelines regarding vaccination  
102 during a febrile illness (FI) in both children and adult populations, in order to answer the following  
103 questions:

- 104 1. Has the safety, efficacy and immunogenicity of vaccination during FI been clinically proven?
- 105 2. How do physicians and patients perceive vaccination in the presence of fever?
- 106 3. What are the current recommendations in regards to vaccination during a FI in different areas  
107 of the world?

### 108 *Justification*

109 Using the systematic-narrative hybrid review approach, allowed us to combine both of the systematic  
110 and narrative review features [31]. For instance, literature search was conducted in accordance with  
111 the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [32].  
112 Since our research topic is rather unconventional, this methodology enabled us to provide a detailed  
113 and rigorous literature search through different databases with specific inclusion and exclusion  
114 criteria, and to ensure that all relevant papers would be included in this review. A narrative approach  
115 was applied to analyze our findings.

#### 116 *Literature sources*

117 An initial search was performed on MEDLINE (via PubMed) to identify relevant keywords and index  
118 terms in order to build the search strategy. A systematic search was conducted on MEDLINE (via  
119 PubMed) and Cochrane Library up until 24 March 2024 using the following search strategy  
120 (fever[Title/Abstract]) AND (vaccination[Title/Abstract]). All reference lists of the eligible articles  
121 were examined as well, and were included if relevant. Complementary data were also obtained by  
122 searching other databases including the World Health Organization and ScienceDirect.

123 (See figure 1)

#### 124 *Eligibility criteria*

125 All studies assessing vaccination during FI in human subjects in French, English or Spanish were  
126 considered. Articles related to animal experiments or post-vaccination fever were excluded. There  
127 were no limitations as to the age of the participants or the year of publication. Studies were also  
128 included if they were discussing the behavioral aspects of physicians or patients in regards to  
129 vaccination during a FI.

#### 130 *Data cleaning*

131 The screening process was performed independently by S.E, C.T. and S.D. The first step of the  
132 procedure consisted on screening only titles and abstracts. The second step of the process was to fully  
133 read the potentially eligible articles and discuss any differences of opinion if applicable between the  
134 three co-authors. A fourth author reviewer E.B.N. was consulted to settle unresolved disagreements if  
135 required.

#### 136 *Information synthesis*

137 The Data from eligible studies were divided into three categories:

- 138 1. Data on the safety, efficacy and immunogenicity of vaccination during FI;
- 139 2. Data on the practices and attitudes of physicians and patients in regards to vaccination during  
140 FI;
- 141 3. Data on international guidelines as to vaccination during a FI;

142 Information as study design, year of publication, judgement criteria, type of population, vaccine Type  
143 (VT), body temperature (BT) and country's recommendations were extracted and put into different  
144 tables using Microsoft Excel. A narrative approach was used to address all of the three research  
145 questions.

146 For the first research question, we extracted and analyzed the production of antibody titers or  
147 seroconversion rates and the occurrence of side effects in each study on vaccination in the presence of  
148 a FI and then performed a narrative synthesis. To address the second research question, we extracted  
149 data related to the acceptability of vaccination in the presence of fever, and reasons as why physicians  
150 and patients vaccinate/get vaccinated or not during a FI were outlined in a narrative approach. We then  
151 provided an overview of international guidelines regarding vaccination during FI, so we classified  
152 countries into categories that recommend vaccination and those that do not, and checked the  
153 temperature limit for each country that recommends vaccination if available. Countries were selected  
154 according to the language used (English, French or Spanish) or the availability of a translation in  
155 either of these languages.

156

## 157 **Results**

158 The flowchart (Figure 1) summarizes the process of identification, evaluation and selection of the  
159 studies as well as the reasons for excluding articles. Eight thousand, two hundred and ninety four  
160 articles issued between 1946 and 2024 were obtained after searching the PubMed and the Cochrane  
161 Library databases. One hundred and thirty three articles were completely read. Most of the excluded  
162 articles were related to post-vaccine fever. Therefore, only fifteen articles were found to be relevant  
163 according to our inclusion criteria after review of the literature [9,10,12,16,18,20–25,33–36].

164 Among the fifteen articles that were included in this review, three studies were added after analysis of  
165 the references lists [16,18,24]. Although referenced in PubMed database, they were not found with our  
166 search strategy when reviewing the literature because “fever” and “vaccination” were not in the titles  
167 or in the abstracts.

168 *The immunogenicity, efficacy and safety of vaccination during febrile illness (FI)*

169 No study provided data about the efficacy of vaccination during a FI. Studies evaluating the  
170 immunogenicity and safety of vaccination during a FI are summarized in Table 1.

171 A total of six articles matched with our eligibility criteria [20–25]. These papers were published  
172 between the years 1985 and 2000. They were all prospective studies that evaluated the  
173 immunogenicity and safety of vaccination during FI in children or infants with an age range between  
174 3.5 and 30 months. The immunogenicity of vaccination during a FI was evaluated for multiple  
175 vaccines (measles, mumps and rubella [21]; measles [22–24] ; measles, mumps, rubella and varicella  
176 [25]; and *Haemophilus influenzae* type b [20]) in ill and well children. Results showed no statistically  
177 significant differences in seroconversion rates [21–25], geometric mean antibody titers (GMTs) [22–  
178 24] or antibody levels [21,25] for five out of six studies [21–25]. In a study conducted among  
179 Gambian children by Usen *et al.* [20], to evaluate the effect of fever on the serum antibody response to  
180 *Haemophilus influenzae* type b (Hib) vaccine, some statistically significant differences were observed  
181 between the three groups investigated (malaria, febrile and healthy children). The median antibody  
182 concentrations at one month post-vaccination were lower in the malaria and febrile groups (6.3 µg/ml  
183 and 7.5 µg/ml respectively) compared to the healthy group (23 µg/ml). However, even though the  
184 proportion of children with antibody titers below 1.0 µg/ml was significantly lower in the malaria  
185 group compared to the healthy group, no significant differences in protective antibody titers were  
186 observed between the healthy and the febrile groups (Table 1).

187 The safety of vaccination during a FI was assessed for the measles [22] and the measles, mumps and  
188 rubella [21] vaccines. In these two studies [21,22], the adverse events following vaccination in ill  
189 children were comparable to those in healthy controls (Table 1).

190 In these articles [20–25], the criteria for “illness” and the threshold of temperature were not very well  
191 defined or too low. For instance, fever was defined from 37,5°C to 38°C for almost all of the



192 immunogenicity and safety studies [20–22,24,25] but one, where the threshold of temperature was  
193 unspecified [23]. The level of evidence is then low or intermediate (grade of recommendation B or C)  
194 [37]. We found no data on adult populations, although all age groups had been selected in our search  
195 strategy.

#### 196 *The practices and attitudes of physicians and patients/parents in regards to vaccination during FI*

197 Studies analyzing the practices and attitudes of physicians and patients/parents during a FI are  
198 displayed in Table 2.

199 The studies included were either cross-sectional [34,35], with hypothetical scenarios [10],  
200 retrospective [12,16,33,36], qualitative [9] or a self-administered survey [18].

201 In all of these articles, vaccination was usually postponed in the presence of an acute minor illness or  
202 fever [9,10,12,16,18,33–36]. When temperature measurement occurred in well-child visits and a fever  
203 was detected, vaccination was often delayed [10,16,33–36]. Some practitioners believed that vaccines  
204 were less immunogenic and had a reduced response when administered to a febrile patient, which  
205 motivated their decision to postpone vaccination [9]. Physicians often considered fever as a  
206 contraindication to vaccination which lead to vaccine-deferral as well [18,35,36]. Furthermore, it was  
207 a matter of safety for some physicians when they chose to postpone vaccination in case of a febrile  
208 patient [9]. Not being able to distinguish the post-vaccination fever and related symptoms from the  
209 underlying disease could make the whole situation harder to manage. Therefore, delaying vaccination  
210 was regarded as a “low risk habit” that would prevent from more vaccine hesitancy and preserve the  
211 doctor-patient relationship [9]. Some parents also shared those fears with their children’s physicians  
212 [9,16,33] which often lead to vaccine postponement as well. The few physicians that were in favor of  
213 immediate vaccination in a febrile child appeared to be somehow more comfortable giving  
214 explanations to the patients about vaccine safety [10]. (Table 2)

215 While some of these studies had a well-defined temperature [10,18,33,34,36], it was not very clear for  
216 other articles [9,12,16,35].

#### 217 *Review of international recommendations*

218 Recommendations of several countries around the world addressing the practice to adopt regarding  
219 vaccination when a patient (child/adult) presents a FI were analyzed and are summarized in Table 3.

220 This analysis included: Canada, USA, Spain, Portugal, UK, Australia, Ireland, Germany, New  
221 Zealand, France, Switzerland, Italy, India, Denmark and Czech Republic. These countries were  
222 selected according to the availability of their guidelines in English, French or Spanish. They were  
223 divided into three categories:

224 - Countries recommending vaccination regardless of the temperature.

225 - Countries recommending vaccination within a temperature limit.

226 - Countries with rather unclear recommendations.

227 Overall, in North America (Canada, USA), it is recommended to vaccinate whatever the temperature  
228 is [38,39]. Both of Spain and Portugal consider mild illness and fever as false contraindications for  
229 immunization and thus recommend vaccination regardless of the temperature [40,41]. Some countries  
230 recommend to vaccinate during FI but within a temperature limit: 38.5°C for UK, Australia, Germany  
231 and Italy [42–45] ; 38°C for Ireland and New Zealand [46,47]. For the majority of countries  
232 recommendations are unclear. India, Denmark, and Czech Republic allow vaccination during « mild  
233 fever », « mild illness » or « mild cold » but no clear definition of these terms was given [26,29,48].  
234 Some recommendations are even more ambiguous, in France for instance, fever is not a  
235 contraindication but vaccination may be deferred [27]. Denmark’s recommendations explain the  
236 importance of vaccination at the recommended time but they do not clearly allow vaccination during a  
237 FI [48] as seen in Table 3.

238

## 239 **Discussion**

240 Faced with the dogma “do not vaccinate during a febrile illness” and its obvious impact on  
241 vaccine coverages worldwide, we sought to review the evidence behind this statement, as to our best  
242 knowledge no another review has addressed this issue. In the process, we were slightly disappointed  
243 by the findings. Indeed, the few studies available were exclusively based on children populations, they  
244 were conducted several years ago and the level of evidence was intermediate to low. Moreover, they  
245 focused on humoral immunogenicity and safety, while none assessed the efficacy or explored the  
246 immune response in depth.

247 Results on the immunogenicity and safety were however in favor of vaccination during a febrile  
248 illness (FI). No statistically significant differences were found in achieving protective antibody titers  
249 [20–25] or seroconversion rates [21–25] between ill children and controls. As for the safety, there was  
250 no increase in the number or severity of adverse events in ill children for measles [22] and MMR [21]  
251 vaccines. Which makes us wonder why is there such heterogeneity among the guidelines [26–30,38–  
252 48] of many different countries around the world. Since on the basis of the same data [20–25], some  
253 countries recommend vaccination during FI, others tend to postpone it, and for still others, the  
254 guidelines are unclear as seen in Table 3.

255 Vaccination was delayed in cases of a mild fever, even in healthy children [33] and in countries that  
256 strongly recommend it [12,16,18,33,34,36]. This phenomenon is perhaps attributable to more recent  
257 data on the immunogenicity of vaccination in other inflammatory contexts than fever, which may have  
258 indirectly called into question doubts about the potentially impaired vaccine immune response in FIs.  
259 Beyond the literature reviewed here in febrile conditions, some works showed that vaccine  
260 immunogenicity among people vaccinated during chronic inflammatory contexts such as uncontrolled  
261 HIV replication is lower indeed [49,50]. Other chronic viral or parasitic infections have also been  
262 associated with an impaired vaccine immune response as reviewed by Zimmermann *et al* [51].  
263 Furthermore, studies have shown an altered vaccine immune response when antibiotics are used, due  
264 to their impact on the human gut microbiota, as it has been established that some bacterial  
265 communities of the gut microbiota do indeed play a role in enhancing antibody response to  
266 vaccination [52,53]. These data possibly contribute to the confusion of healthcare providers since  
267 acute fever is associated with inflammation, and is a condition in which antibiotics are frequently  
268 administered. However, these data do not answer at all the questions regarding vaccine’s safety and  
269 efficacy (beyond immunogenicity) when administered during an acute FI. Therefore, as far as we  
270 know, there are no strong available data to contraindicate vaccination during FI. At least for benign  
271 infections, this does not seem legitimate. Moreover, in countries where vaccination is performed  
272 whatever the grade of fever is (Table 3), safety and effectiveness issues have not been reported to our  
273 best knowledge.

274 Differences in recommendations may be in part responsible for the observed variations in  
275 vaccine coverages worldwide [54]. For instance, Portugal, Spain, the USA and Canada are countries  
276 with quite high vaccine coverages [55,56], in children, teenagers and adults, based on the  
277 recommended vaccines for each age category [57–60]. Specifically, these countries have achieved  
278 over 80% HPV vaccine coverage among teenagers [58,59] and more than 65% influenza vaccine  
279 coverage among adults [60]. In countries where fever is not considered a contraindication to  
280 vaccination [61,62], the idea is also to ensure that all vaccination opportunities are seized. Many  
281 physicians however, do not seem to consider all consultations as a chance to vaccinate their patients  
282 [9,10,12,16,18,33–36]. In the presence of fever, vaccination was almost always differed as it would be  
283 considered a contraindication for immunization [12,35,36]. It seems to be a rooted habit passed along  
284 from older generations of much more experienced physicians [9,10]. This being an “established  
285 practice” do not direct healthcare professionals into immediate vaccination when they have the  
286 opportunity to do so [9]. By postponing vaccination, they are not only trying to “play it safe” and  
287 avoid any further complications when not necessary, but to reassure anxious parents as well in order to  
288 preserve the doctor-patient relationship [9]. Furthermore, it is a way to avoid vaccine hesitancy issues  
289 when physicians aren’t very comfortable dealing with the matter [9,10]. After all, immediate  
290 vaccination regardless of the patient’s clinical state was never the focus of medical attention, as  
291 vaccination is not considered as an urgent act by most of healthcare providers. The fact that “acute  
292 illness” and the body temperature threshold were not very well defined or too low (37, 5°C) in the  
293 studies supporting the recommendations, along with a level of evidence being low or intermediate,  
294 may also have contributed to vaccine reluctance. However, the consequences of delaying vaccination  
295 could be more serious than they seem. Not getting vaccinated on time contributes to low vaccine  
296 coverage when the catch-up strategies cannot not be applied [12,18,36]. Surely, at an individual scale,  
297 the unvaccinated people may have encountered the VPDs before to be *in fine* vaccinated as described  
298 in children [14,15] and adults [63–65]. For potentially severe VPDs such as pneumococcal invasive  
299 diseases, it can have serious consequences including in adults [63]. Delayed administration of a  
300 vaccine can also reinforce parents' reluctance, fears and beliefs about vaccination [9]. A child who has  
301 missed a vaccination due to an acute illness (respiratory tract illnesses, acute otitis media, non-specific

302 viral illnesses, skin infections...), is 3.1 times less likely to be fully vaccinated than a child who has  
303 never missed an opportunity for vaccination [66]. Moreover, at a collective scale, to postpone  
304 vaccination contributes to a low immunization coverage, regardless of the reason for postponement  
305 being vaccine hesitancy, or a missed vaccination opportunity due to a FI or other reasons [11]. All  
306 causes of low vaccine coverage could compromise herd immunity [13] or even contribute to the re-  
307 emergence of VPDs as pertussis [67,68] and recent measles outbreaks [34].

308 Some experts believe that systematic temperature measurement, although a clinical practice, favors  
309 bias [17] and may do more harm than good to the child, with increased rates of antibiotic prescriptions  
310 and vaccine delay if a fever was detected [33]. In adults, addressing missed opportunities for  
311 vaccination is also crucial, especially in an era where more and more vaccines are being recommended  
312 for them [69]. Adult hospitalizations, including for a FI, account for a significant number of  
313 admissions to emergency departments' [70], which can be an opportunity to vaccinate. However many  
314 adult patients at-risk for VPDs often miss necessary vaccinations before discharge [64,71,72].  
315 Moreover, vaccines may in the future reduce the burden of healthcare-associated infections in ICU at-  
316 risk patients [73]. However, a considerable number of these patients present with a FI. Therefore, a  
317 better understanding of the immune responses and safety associated with vaccination during a FI  
318 would help address our research question more accurately.

319 Our review has some limitations. Since data retrieved were only found in pediatric populations  
320 with no available data in adults to our best knowledge, generalization of these reassuring data to adults  
321 is not possible. However, we anticipate similar outcomes in adult populations, offering valuable  
322 insights for future research on adult vaccination. Additionally, while some studies used vague terms  
323 like "illness" or "fever," the global consistency in fever definitions suggests the findings remain  
324 robust. Finally, among the studies included, vaccination was performed in people with no severe  
325 febrile illnesses, the reassuring data are then limited to vaccination in patients without severity criteria.

326 In conclusion, this review do not find concerns about vaccination during a benign FI. Fighting  
327 missed opportunities for vaccination is a major issue at all times, but particularly after the COVID-19  
328 crisis with globally a need for catch-up programs. This review also demonstrated that the level of  
329 evidence is still low, and even non-existent in adults. There is a need for additional clinical trials on

330 vaccination during FI with a good level of evidence. Such research should enable the evaluation of  
331 short and long-term immune humoral and cellular responses, efficacy, and safety of vaccine  
332 administration by randomizing people to be vaccinated during or after an acute febrile illness. A  
333 higher level of evidence will help reassure doctors and patients, homogenize guidelines internationally  
334 and encourage healthcare providers to reconsider their current practices.

335

336 **Author contributions:** Study design; SE, SB, EBN. Resources, conception, data extraction, analysis  
337 and interpretation; SE, CT, SD, EBN. Data validation; AGB, SB, EBN. Editing and writing: SE, CT,  
338 SD, EBN. Critical review of the manuscript; EBN, AGB, SB. Supervision; EBN. All authors have  
339 read and agreed to the published version of the manuscript and attest they meet the ICMJE criteria for  
340 authorship.

341 **Funding:** This work received no financial support.

342 **Conflict of interests:** No conflict of interests are associated with this publication. EBN is the  
343 coordinator and principal investigator of a clinical trial about the immunogenicity and safety of the  
344 PCV-20 vaccine during a febrile illness (PHRC-N 2019 PREVHOSPIT). The study is not yet  
345 recruiting.

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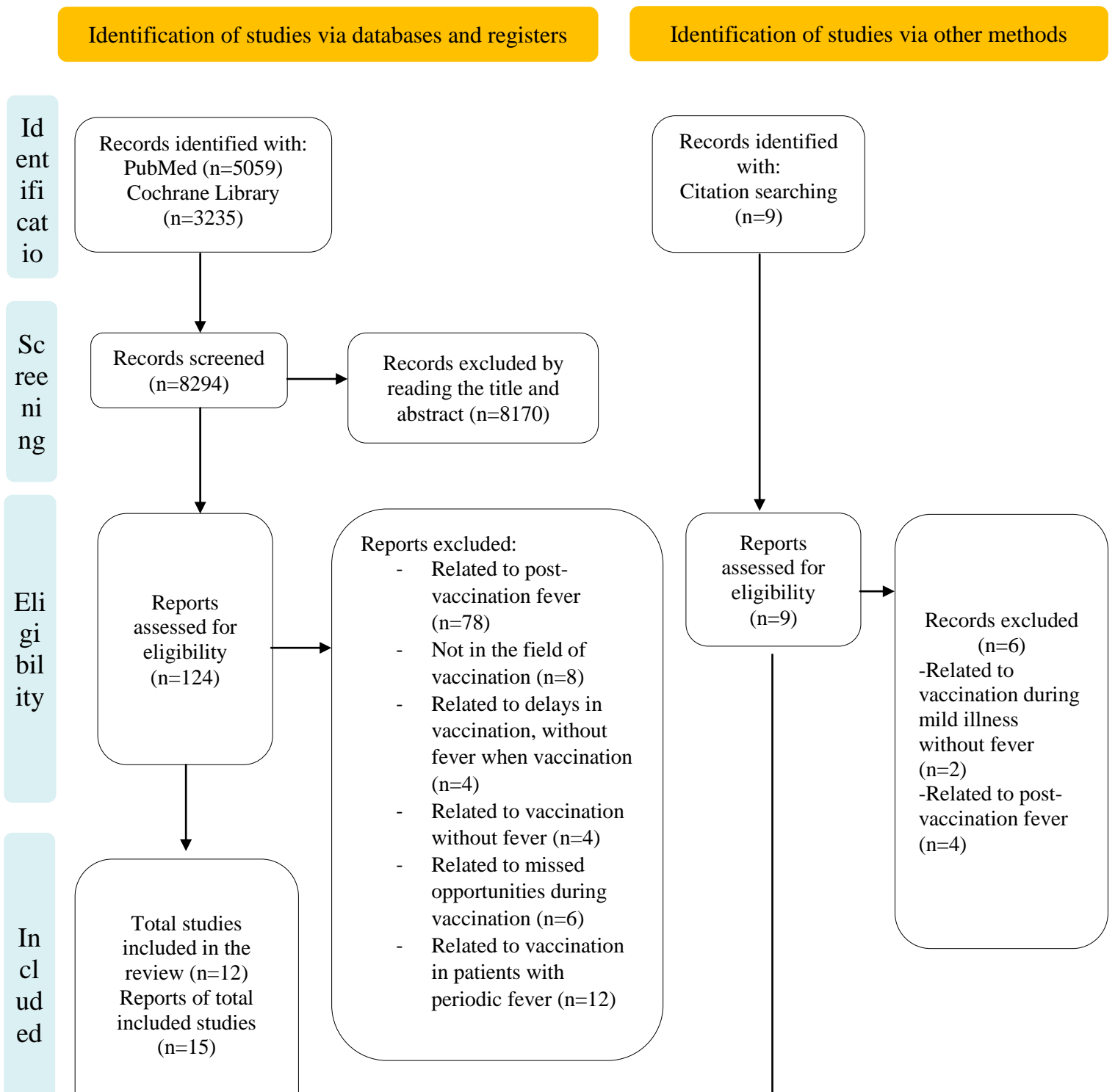
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Figure 1: PRISMA 2020 flowchart for the identification, screening and inclusion procedure of eligible articles found in the literature from 1946 until 2024.







366 Table 1: Characteristics of the studies on safety, efficacy, and immunogenicity:

Title	Authors	Date of publication	Study design	Population	Vaccine	Judgement criteria	Results	Febrile or no febrile illness
<b>Antibody Response to Measles-Mumps-Rubella Vaccine of Children with Mild Illness at the Time of Vaccination.</b> [21]	King GE <i>et al</i>	1996	Prospective cohort Study	Children aged 15 to 23 months (n=386). 157 children had a mild illness (acute upper respiratory tract infection, otitis media, or diarrhea) and 229 were well.	MMR	Seroconversion rates to measles, mumps, and rubella in ill and well children 6 to 8 weeks after vaccination.	There were no significant risk differences for seroconversion between ill and well children for measles, mumps and rubella except for measles seroconversion in children with diarrhea (risk difference -2, CI 95% [-4; -1].  Differences between groups were not statistically significant for increased rates and severity of adverse events reported in the 2 weeks after vaccination (p>0.05).	Children with axillary temperature greater than 37.8°C were excluded.
<b>Immunogenicity and Safety of Measles Vaccine in Ill African Children.</b> [22]	Ndikuyeze A <i>et al</i> .	1988	Concurrent prospective study	Children aged 8 to 19 months (n=518) attending the curative care and immunization services of the clinics.	Measles	Seroconversion rates to measles 40 days after vaccination.	Among the 208 ill children and 216 well children [...] seroconversion rates were 81% and 80% respectively. Side effects were modest and were equally frequent in the two study groups (15.4% among ill children versus 15.1% among well children).	“Ill child” had at least one of the following symptoms: fever (axillary temperature greater than 37.5°C), diarrhea [...] or vomiting.

<b>Response to Measles Vaccine in Haitian Infants 6 to 12 Months Old: Influence of Maternal Antibodies, Malnutrition, and Concurrent Illnesses.</b>	Halsey NA <i>et al.</i>	1985	Prospective cohort study	Haitian infants from 6 through 12 months of age.	Measles	Seroconversion rates to measles 5 to 6 weeks after vaccination.	No difference in the overall seroconversion rate between ill infants and healthy infants.	12% of ill infants affected by fever.
[24]								
<b>Seroconversion Rates to Combined Measles-Mumps-Rubella-Varicella Vaccine of Children with Upper Respiratory Tract Infection.</b>	Denney PH <i>et al.</i>	1994	Prospective cohort study	Children 15 to 18 months of age with URI or recent history of URI symptoms within the 4 weeks before vaccination and well infants. Children with fever $\geq 38^{\circ}\text{C}$ were excluded.	MMRV	Seroconversion rates or magnitude of antibody response to all components of the combined measles-mumps-rubella-varicella vaccine 4 to 6 weeks after immunization.	Seroconversion to measles, mumps, and rubella occurred in 100% of children in both groups. Mean antibody levels did not differ between the healthy and URI groups for measles (111 vs 122), mumps (97 vs 108) or rubella (96 vs 102). The mean varicella antibody level was 11.3 +/- 1.4 in healthy children, which was not significantly different from the level of 9.5 +/- 0.9 in the URI group.	Children with fever $\geq 38^{\circ}\text{C}$ rectally [...] were excluded.
[25]								

<p><b>Effect of fever on the serum antibody response of Gambian children to <i>Haemophilus influenzae</i> type b conjugate vaccine.[20]</b></p>	<p>Usen et al.</p>	<p>2000</p>	<p>Prospective cohort study</p>	<p>Children aged 12 to 30 months with fever associated with malaria (n=57), fever associated with other causes (n=57) or no fever (n=60).</p>	<p>HIB</p>	<p>Seroconversion rates to anti-polyribosylribitol phosphate antibodies of the children in the malaria, febrile and healthy group one month post-vaccination.</p>	<p>The median antibody titers at baseline were low and similar in the three groups; 0.07, 0.08 and 0.10 µg/ml in the malaria, febrile and healthy groups, respectively. After vaccination, they were 6.3, 7.5 and 23 µg/ml in the malaria, febrile and healthy groups, respectively (significantly different). 5 children in the malaria group (11%), and 2 children in the febrile group (4.4%) (p=0.047) still had antibody titers below 0.15 µg/ml. 10 children in the malaria group (23%), 6 children in the febrile group (13%) and 3 children in the healthy group (6.3%) (p=0.077) had antibody titers below 1.0 µg/ml. The proportion in the malaria group with concentrations &lt;1.0 µg/ml was significantly higher than in the healthy group (P=0.036, Fisher's exact test), <b>the other pairwise differences were not statistically significant (malaria/febrile and febrile/healthy).</b></p>	<p>Children were enrolled into the malaria group if they had fever (rectal temperature ≥ 37.5°C) or a history of fever and parasitemia.</p>
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<p><b>Mild illness at or after measles vaccination does not reduce seroresponse in young children.</b></p>	<p>S Scott et al.</p>	<p>1999</p>	<p>Randomized trial</p>	<p>1045 infants aged between 3.5 and 6 month old either well or presenting with a mild illness (rhinorrhea, cough, diarrhea, fever, conjunctivitis or rash).</p>	<p>AIK-C EZ-H and EZ-M measles vaccines</p>	<p>Seroresponse at 6 weeks and 6 months post-vaccination among children with and without mild illness at or after vaccination.</p>	<p>Seroconversion rates were similar in ill and well infants. In fact, seroresponse rates were slightly higher in those with an illness. In the EZ-H group, 3.5 months infants with diarrhea had significantly higher seroresponse than well children (adjusted O.R, 2.29; 95% C.I: 0.98-5.33, p= 0.055). Fever on the day of vaccination, or at home visits on 7, 10 or 14 days post vaccination, did not affect seroconversion or GMTs.</p>	<p>Unspecified</p>
<p>[23]</p>							<p>In the AIK-C vaccine group, the proportion reaching the median titer was significantly lower among those with symptoms (OR adjusted for maternal antibodies: 0.52, 95% CI: 0.28-0.95, p= 0.03).</p>	
							<p>In the EZ-M group, the proportion reaching the median was higher among those with symptoms (adjusted OR: 5.18, 95% CI: 2.26-11.85, p&lt; 0.001).</p>	

367 MMR: measles, mumps and rubella; URI: upper respiratory infection; MMRV: measles, mumps, rubella and varicella; HIB: *Haemophilus influenzae* type b; GMT:  
368 Geometric mean titers  
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374 Table 2: Characteristics of the studies on the practices and attitudes of physicians and patients/parents regarding vaccination during febrile illness:

Title	Authors	Date of publication	Study design	Population	Vaccine	Judgement criteria	Results	Febrile or no febrile illness
<b>Measles Vaccination in Pediatric Emergency Departments During a Measles Outbreak.</b> [34]	Lindegr en ML <i>et al.</i>	1993	Cross-sectional study	Children 6 months to 5 years of age seen in the emergency departments (EDs).	Measles	The proportion of eligible children attending the EDs for measles vaccination and the proportion of eligible children who were vaccinated.	Among vaccine-eligible children, 59% at both hospitals did not receive measles vaccine during the ED visit. [...] Although it was not associated with a vaccination failure, a larger proportion of patients with a low-grade fever in the ED (temperature, at least 38.2°C but less than 38.9°C) were not vaccinated during the ED visit compared to patients without a fever.	Patients with a at least a temperature of 38.2°C but less than 38.9°C were less likely to get vaccinated compared to patients without fever.
<b>Influence of Parental Knowledge and Opinions on 12-Month Diphtheria, Tetanus, and Pertussis Vaccination Rates.</b> [16]	Lewis T <i>et al.</i>	1988	Retrospective cohort study	1-year-old children in Utah.	DTP	The pertussis immunization rate for 1-year-old Utah residents, the reasons for noncompliance with immunization, and whether parental opinions and knowledge of the DTP vaccine influence immunization rates.	Data from 601 of the 619 parents of the inadequately immunized children indicated that the most common reason for failure to get the vaccine (396 cases or 65.9%) was that the children were ill at the time they were to receive their shots. [...] More parents of partially immunized children cited illness as the reason for inadequate immunization than those who had received none (69% [n=361] vs 44% [n=35]).	Unclear.

<b>Vaccination Levels and Missed Opportunities for Measles Vaccination: A Record Audit in a Public Pediatric Clinic.</b> [12]	Farizo KM <i>et al.</i>	1992	Retrospective record audit	Children 15 months to 4 years of age who attended the clinic for any reason during April 1988.	MMR	Vaccination levels and factors associated with delayed receipt of MMR vaccine, especially missed opportunities by health care providers to vaccinate children.	77 (32%) children had a total of 137 visits that represented missed opportunities for MMR vaccination. Out of the visits considered to be missed opportunities for vaccination, the most frequently diagnosed illness was otitis media, [...] URI alone accounted for 12 (9%) visits and mucocutaneous conditions (e.g., impetigo, atopic dermatitis, otitis externa, and conjunctivitis) accounted for 13 (9%) visits. Bronchitis, pneumonia, and gastroenteritis each accounted for 3 visits (7%) and asthma for 1 visit.	A rectal or unspecified temperature $\geq 38^{\circ}\text{C}$ or an oral temperature $\geq 37,5^{\circ}\text{C}$ was considered to be a possible indicator of moderate or severe illness, and thus, a valid reason to postpone MMR vaccine administration in this study.
<b>GPs and vaccination of Children presenting with benign infection</b> [10]	M. Le Marechal <i>et al.</i>	2016	A cross-sectional survey. Hypothetical scenario	Hypothetical child (4 or 11 months) presenting with an uncomplicated febrile ( $38^{\circ}$ or $39^{\circ}\text{C}$ ) common cold.	DTP-HIB Poliomyelitis hepatitis B	Immediate vaccination of the child with hexavalent vaccine or postpone it.	Almost all GPs postponed the hexavalent vaccination of the febrile child (Only 6% recommended immediate vaccination of the febrile child). Feeling comfortable giving explanations to the patients about the vaccine's safety and the intensity of the fever were the 2 major factors that significantly influenced the GP's attitude towards vaccination (10% recommended vaccination when the temperature was $38^{\circ}\text{C}$ vs. Three percent when the temperature was $39^{\circ}\text{C}$ [ $P < 0.001$ ]).	$38^{\circ}\text{C}$ or $39^{\circ}\text{C}$ .

<b>Postponing vaccination in children with an infection: a qualitative study among GPs and pediatricians [9]</b>	D. Gonthier <i>et al.</i>	2020	A qualitative study with interviews	Child with an infection (febrile or not febrile).	unspecified	Factors motivating the practice of vaccination postponement in a child with an infection by GPs	Vaccination postponement during children infections is rooted in doctors' practices. Most of the doctors interviewed chose to postpone vaccination in case of a febrile or non-febrile infection. Vaccine hesitancy and uncertainty about the vaccine's safety and effectiveness justified postponing vaccination. Parent's fear was also a factor motivating the vaccine delay as a way to reassure parents and improve the doctor-patient relationship.	Viral infection, whether febrile or not, is the most frequent cause of vaccine postponement.
<b>Frequency and Consequences of Routine Temperature Measurement at Well-Child Visits [33]</b>	R. Dang <i>et al.</i>	2022	Retrospective cohort study	Children with or without incidental fever during their well-child visit	unspecified	Reasons and occurrence of vaccine deferral in well-child visits when incidental fever was detected	274 351 well-child visits in 50 571 children were analyzed. Temperature measurement occurred at 58.9% of well-child visits. When incidental fever was detected, vaccines were deferred at 50% of these visits (12 of 24) mainly due to "parental preference" (50%) or "physician choice" (25%) or "unable to be determined" (16.7%).	"Incidental fever" was defined as temperature $\geq 38^{\circ}\text{C}$ .
<b>Physician Knowledge of Catch-up Regimens and Contraindications for Childhood Immunizations [18]</b>	Nicole J. Cohen <i>et al.</i>	2003	Self-administered survey	Hypothetical children delayed in immunization	MMR Hib	The number of correct vignettes describing hypothetical children for whom physicians were asked to design catch-up regimens	550 physicians completed the survey. The mean score of correct responses was 1.83 of 6.0. About 32% of respondents answered all 6 vignettes incorrectly. The proportion of incorrect responses was high for all 6 vignettes (39%–86%). Fever was considered as a contraindication for vaccination in more than 85% of physicians	103.8°F or 39.9°C

							81% of respondents agreed that the catch-up regimens were difficult or very difficult to design. The results of the contraindication scenarios suggest that physicians have important knowledge gaps regarding immunization contraindications.	
<b>Survey of contraindications in children's routine vaccination in Hangzhou, China [35]</b>	S Liu <i>et al.</i>	2017	A cross-sectional survey	Children aged (0-12 year old) coming to Community health centers for routine vaccination	Hep series OPV, Jen series MR, MMR, DT, DTaP DTaP-IPV/Hib Men series	The epidemiological characteristics about vaccine contraindications and the ability of physicians to determine contraindications.	There were 2801 children with 2969 contraindications. The most common contraindications in children routine vaccination were Cough (24.78%), fever (21.86%) and medication (19.54%) and occurred mostly in children aged 1 year old or less. The proportion of false contraindications were higher for DTaP (16.13%) and Men series (15.8%). The prevalence of contraindications were the highest for MR (6.78%) and MMR (5.87) vaccines. The vaccinating physicians misdiagnosed 13.53% of contraindications. Females, educational background and older age were associated with making better decisions.	Unspecified
<b>Vaccination Levels in Los Angeles Public Health Centers: The Contribution of Missed</b>	D. Wood <i>et al.</i>	1995	Retrospective record study	Children aged between 6 weeks and 36 months attending five public health	DTP MMR Oral poliovirus	The proportion of children up-to-date with all their vaccinations and the rate and factors associated with	Of the 752 participating children, only 202 (27%) were up-to-date at 24 months. Missed opportunities to vaccinate occurred twice as often when the nurses' assessment of the children's immunization status was	Temperature over 101°F (38.3°C) was considered as a contraindication to vaccination.



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**Opportunities to  
Vaccinate and  
Other Factors [36]**

centers

missed  
opportunities to  
vaccinate.

inaccurate which occurred in 73% of all well-child visits. The presence of minor illnesses that were not contraindications to vaccination was also associated with Missed opportunities to vaccination. Missed opportunities to vaccinate reduced the children's chances to be fully immunized at 24 months by nearly half.

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375 MMR: measles, mumps and rubella; EDs: emergency departments; DTP: diphtheria, tetanus and pertussis; URI: upper respiratory infection; DTP-HIB: diphtheria, tetanus,  
376 pertussis, *Haemophilus influenzae* type b; GPs: general practioners; Hib: *Haemophilus influenzae* type b; Hep: hepatitis; OPV: oral poliomyelitis vaccine; Jen: Japanese  
377 encephalitis vaccine; IPV: inactivated poliomyelitis vaccine; Men: meningococcal vaccine.  
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389 Table 3: Vaccine recommendations in case of acute fever or illness in different countries for both  
 390 children and adults:  
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Recommendations	Countries	Citations	Date
<b>To vaccinate regardless of the temperature</b>	Canada	<b>Canada:</b> “In general, people with minor or moderate acute illness may receive vaccines. There is no increase in risk of adverse events following immunization and no interference with response to vaccine”. [39]	October 2023
	Portugal		September 2020
	Spain		March 2022
	USA		October 2022
<b>To vaccinate within a temperature limit</b>	Australia	<b>Australia:</b> “False contraindications to vaccination: People with these conditions can receive all recommended vaccines: mild illness without fever (temperature < 38.5°C)”. [45]	December 2023
	Germany		August 2017
	Ireland		August 2022
	Italy		
	New Zealand		
	UK		

the concurrent illness”.[47]

**Italy:** “Mild fever is not a contraindication to vaccination. Fever defined as a temperature above 38.5°C is a valid reason for postponing vaccination, which should be carried out immediately after recovery. Vaccination of people with fever and moderate-to-severe infections does not lead to an increase in adverse reactions or a reduced response to vaccination. The precaution is intended to avoid interference of any adverse reactions with the underlying disease and to complicate its management, but also to prevent the manifestations of the present disease from being considered as complications to vaccination. In situations of particular risk (e.g. post-exposure prophylaxis), vaccinations may also be carried out in the presence of moderate or severe fever or infection. Fever measurement is not included in the vaccination eligibility assessment procedures”.[42]

2018

**New Zealand:** «Conditions that are not contraindications to immunisation - Individuals with these conditions should be vaccinated with all the recommended vaccines: Mildly unwell, with a temperature ≤ 38°C ». [46]

March 2024

**UK:** “Minor illnesses without fever or systemic upset are not valid reasons to postpone immunization. If an individual is acutely unwell (for example with a fever above 38.5°C), immunization may be postponed until they have fully recovered”.[43]

August 2017

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**Unclear recommendations**

Czech Republic  
Denmark  
France  
India  
Switzerland

**Czech Republic:** “When should one not vaccinate? [...] The child is seriously ill or has a fever (a slightly elevated temperature and a mild cold may not always be a barrier), more attention should be paid to the child's current state of health when vaccinated with 'live' vaccines (e.g. measles)”.[26]

Date not specified

**Denmark:** “It may be necessary to postpone vaccination, for example, if your child is ill and has a fever. However, it is possible to for your child to get vaccinated if they have a cold. Talk to your doctor, who can help assess whether your child's vaccination is to be postponed”.[48]

2022

**France:** “The existence of febrile illness (> 38°C) or a moderate or severe acute illness does not contraindicate vaccination but may lead to a delay of a few days. The presence of a minor infection or low-grade fever should not delay catch-up vaccination.” [27]

April 2024

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**India:** “All infants should be immunized except in these situations: High fever (>38.5°C). Do not give a vaccine if the caregiver objects to immunization for a sick infant after explanation that mild illness is not a contraindication. Ask the caregiver to come back when the infant is well.”[29] 2018

**Switzerland:** “It is recommended to defer vaccinations in case of severe acute illness ».[28] March 2024

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