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Symptom Expectations and Subsequent Symptom Reporting Following COVID-19 Vaccination: A Prospective Naturalistic Study of Nocebo-Related Processes

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Research Article

Keywords: nocebo, response expectancy, symptom perception, symptom reporting, vaccination

Posted Date: October 30th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10436096/v1

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Additional Declarations: No competing interests reported.

Abstract

Purpose.

Response expectancies are central to nocebo models, but naturalistic studies cannot readily distinguish expectancy-related symptom reporting from biological reactions. We tested whether pre-intervention symptom expectations prospectively predicted subsequent reports.

Methods.

Adults awaiting AstraZeneca or Pfizer-BioNTech vaccination in Poland completed a pre-vaccination assessment in the first half of 2021 (N = 244); 197 completed telephone follow-up about two weeks later. The primary outcome was the number of reported symptoms. A multivariable negative-binomial model adjusted for vaccine type, sex, and age. Symptom-specific logistic models were adjusted for the same covariates and controlled using the Benjamini-Hochberg false-discovery rate. Attrition-weighted and alternative-model analyses assessed robustness.

Results.

The expected and reported symptom counts were positively correlated (rho = .34, 95% CI [.22, .46]). In the adjusted count model, each additional expected symptom was associated with an 11% higher expected number of reported symptoms (incidence rate ratio = 1.11, 95% CI [1.02, 1.20], p = .011). Vaccine type was not independently associated with symptom count (incidence rate ratio = 0.91, 95% CI [0.61, 1.36]). Of five symptom-specific models, only expected headache remained associated with reported headache after adjustment and false-discovery-rate correction (adjusted odds ratio = 4.06, 95% CI [1.52, 10.88], q = .027). Attrition-weighted analysis produced a similar estimate for expected symptom count.

Conclusions.

Pre-intervention symptom expectations were independently associated with later symptom reporting in a real-world medical context. The temporal ordering and adjusted analyses are consistent with nocebo-related processes, but the observational design does not establish an expectancy-induced nocebo effect.

1 Introduction

Nocebo effects refer to adverse experiences arising or worsening through negative expectations and the psychosocial context of treatment [1, 2]. They are clinically important because many treatment-related complaints are nonspecific, subjectively experienced, and influenced by attention, interpretation,

previous experience, and communication [2–5]. Such complaints affect adherence, the assessment of treatment efficacy, and the quality of care, so nocebo carries practical weight across clinical settings [5]. Nonspecific adverse effects are common during active drug treatment and often track expectations, attention to the body, and prior experience more than pharmacology alone [6, 7]. The distinction between a nocebo effect and a nocebo response is especially relevant in observational research: symptoms reported after an active intervention may reflect biological effects, ordinary background symptoms, attribution processes, and expectancy-related amplification in varying proportions [1].

Response expectancy theory proposes that anticipating a particular internal response can influence the subsequent experience and report of that response [8, 9]. Contemporary accounts additionally emphasize learning, verbal suggestion, social observation, and predictive interpretation of bodily signals [10, 11]. Response expectancies, which concern the anticipated experience of a symptom itself, most directly shape later sensations and form the theoretical axis of the present study [9]. Anxiety and selective attention to the body offer plausible mechanisms, directing perception toward expected sensations [2]. Prospective measurement is therefore important. When expectations are measured only after symptoms occur, recollection of the expectation may be reconstructed in light of the outcome. However, temporal ordering alone is not sufficient for causal inference, because people with stronger expectations may differ in prior symptoms, affect, health beliefs, exposure to information, or characteristics of the intervention received.

The neurobiological basis is clearest in pain research, where anxiogenic suggestions produce hyperalgesia through anxiety-related mechanisms [12] and expectation can even abolish the analgesic action of a potent opioid [13]. Placebo and nocebo thus form one family, in which expectation, anxiety, and learning converge on the circuits that shape bodily experience [7, 14].

Nocebo expectations arise through direct experience, verbal suggestion, and observational learning [10]. Observation matters because expectations can be acquired without direct experience: watching another person's reaction can change one's own, with expectations carrying the effect [15], and the order of conditioning and suggestion shapes the size of placebo hypoalgesia and nocebo hyperalgesia [16]. Seeing someone gain relief or express pain can induce placebo or nocebo responses in the observer [17, 18], and social modeling can raise later reporting [19]. This shared reliance on expectations makes mass health programs, where adverse-effect information circulates widely, a useful field for studying nocebo [11].

Vaccination provides a useful naturalistic setting for studying these processes. It is an active medical intervention with genuine immunological reactogenicity, yet common post-vaccination complaints such as fatigue, headache, and muscle pain are also nonspecific and sensitive to contextual influences. Placebo-arm data from vaccine trials demonstrate that symptoms can be reported without an active vaccine, but they do not identify how much of an individual vaccinated participant's experience is expectancy-related [20]. In a meta-analysis of more than 45,000 trial participants, about 35% of placebo-group recipients reported systemic symptoms after the first dose, most often headache and fatigue, and

roughly three-quarters of first-dose systemic symptoms were attributed to nocebo mechanisms [20]. Expectations therefore contribute even when an intervention has genuine biological action. Prospective studies have shown that pre-vaccination expectations, psychosocial factors, prior adverse experiences, vaccine hesitancy, and social communication predict later symptom burden [21–25]. These studies establish that expectations matter, while also making clear that no single observational association constitutes a direct measure of a nocebo effect.

The pandemic also created an intense exchange of information about adverse effects through media and personal contacts, so many people formed expectations before vaccination from their own and others' accounts. This uncontrolled social transmission is hard to reproduce in the laboratory, which makes a real vaccination campaign a valuable setting for studying how expectations form and act.

Several gaps remain in this literature. Much of the evidence rests on retrospective measurement, where expectations are recorded only after symptoms appear, so genuine expectations are hard to separate from later reinterpretation [26]. Many vaccine studies compare preparations directly without accounting for the fact that recipients of different preparations may already differ in age, sex, fear, or expectations, so an apparent biological difference can be psychological in origin [27]. Studies that do measure expectations prospectively rarely test whether expecting a specific symptom predicts that same symptom, as distinct from predicting an overall count.

Two further gaps motivate the present analysis. First, the individual nocebo model is seldom connected to the wider social context in which pandemic expectations formed, even though media and interpersonal communication shaped both expectations and their later report [21, 28, 29]. Second, knowledge about nocebo translates only partly into practice, despite consensus on limiting unnecessary nocebo responses while conveying full risk information [30] and evidence that framing and brief education can lower reporting [31, 32]. A prospective design that measures expectations before an active intervention, separates overall from symptom-specific correspondence, and adjusts for demographic and psychological differences addresses these gaps.

The present study provides an independent prospective test in a Polish naturalistic sample in which two vaccine groups differed markedly in their pre-intervention expectations. It extends a simple overall association by examining (a) expected and reported symptom counts using a multivariable count model, (b) symptom-specific correspondence after adjustment for age, sex, and vaccine type with control for multiple testing, and (c) the sensitivity of the primary estimate to selective follow-up. The primary hypothesis was that a larger expected symptom count would be associated with a larger reported symptom count after adjustment for vaccine type, sex, and age. Secondary analyses examined whether expecting a specific symptom was associated with reporting the same symptom. Comparisons between vaccine groups and associations with symptom intensity and duration were treated as secondary or exploratory.

2 Methods

2.1 Design and participants

This prospective observational study comprised two assessments and was conducted in Poland during the first half of 2021. At baseline, a researcher approached adults waiting at a COVID-19 vaccination point, introduced the study and the institution represented, briefly explained the aims and procedure, emphasized that participation was voluntary, and explained that the second stage required providing a telephone number and agreeing to a follow-up conversation. Individuals who agreed completed the questionnaire before vaccination. Approximately two weeks later, they were contacted by telephone and asked about symptoms and well-being experienced after vaccination. Reporting was prepared with reference to the STROBE statement [33].

The analytic cohort comprised adults who completed the pre-vaccination assessment and received either AstraZeneca or Pfizer-BioNTech. Baseline data were available for 244 participants: 115 AstraZeneca recipients and 129 Pfizer-BioNTech recipients. The sample included 123 men and 121 women, with a mean age of 47.25 years (SD = 11.87; range 18–90). Follow-up data were available for 197 participants (80.7%): 102 AstraZeneca and 95 Pfizer-BioNTech recipients. The follow-up sample included 96 men and 101 women, with a mean age of 45.56 years (SD = 11.88). Analyses involving post-vaccination outcomes were based on these 197 participants.

The study was approved by an Institutional Review Board in Poland (approval codes KB-256/2021 and 42/2022). It was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

2.2 Measures

All variables were self-reported and assessed using brief study-specific items rather than multi-item validated scales. For variables rated on 0–100 scales, higher values indicated a higher level of the construct.

Pre-vaccination variables included age, sex, vaccine type, fear of COVID-19 (0–100), concern about post-vaccination symptoms (0–100), general expectation that symptoms would occur (0–100), expected vaccine efficacy (0–100), predicted duration of feeling unwell in hours, and a separately elicited expected symptom count (range 0–9). Participants also indicated whether they expected fatigue, headache, muscle pain, nausea, fever, and chills. The expected symptom count was not calculated as the sum of these six checklist items; it was a distinct overall estimate and could therefore exceed six.

At follow-up, participants reported whether any post-vaccination symptoms had occurred, a separately elicited total symptom count (range 0–8), overall symptom intensity on a five-point scale (0–4), time of onset, duration of feeling unwell in hours, and whether they experienced the same six specific symptoms. The total reported symptom count was not limited to the six-item checklist. The primary predictor was expected symptom count and the primary outcome was reported symptom count. The symptom-specific expectation and report pairs were secondary outcomes.

2.3 Statistical analysis

Baseline characteristics were summarized using means and standard deviations or counts and percentages. AstraZeneca and Pfizer-BioNTech groups were compared using Mann-Whitney U tests for continuous or ordinal variables and chi-square tests for categorical variables. Within-person differences between expected and reported symptom frequencies were assessed with exact McNemar tests; expected versus reported total counts and predicted versus reported duration were compared using Wilcoxon signed-rank tests.

The primary analysis used negative-binomial regression with maximum-likelihood estimation and heteroskedasticity-consistent (HC0) standard errors. The dependent variable was reported symptom count. Predictors were expected symptom count, vaccine type (AstraZeneca versus Pfizer-BioNTech as reference), sex (woman versus man as reference), and age in years. Results are reported as incidence rate ratios (IRRs) with 95% confidence intervals. Negative-binomial regression was selected because an adjusted Poisson model showed overdispersion (Pearson chi-square/degrees of freedom = 1.75). Model fit was summarized using Akaike's information criterion and McFadden's pseudo-R-squared.

Each symptom-specific logistic model included the corresponding baseline symptom expectation, vaccine type, sex, and age. Adjusted odds ratios (aORs) with 95% confidence intervals were estimated. Nausea was omitted because only three follow-up events produced unstable estimates. Benjamini-Hochberg correction controlled the false-discovery rate across the remaining five symptom models.

Exploratory associations were estimated using Spearman correlations with percentile bootstrap 95% confidence intervals from 5,000 resamples; Benjamini-Hochberg correction was applied across nine correlations. Robustness analyses included (a) an unadjusted negative-binomial model, (b) an adjusted Poisson model with robust standard errors, (c) an expanded negative-binomial model additionally including general symptom expectation, pre-vaccination concern, and fear of COVID-19, and (d) a stabilized inverse-probability-of-follow-up weighted negative-binomial model. Follow-up probabilities were estimated from baseline age, sex, vaccine type, and expected symptom count. Two-sided p values below .05 were considered statistically significant. Analyses were conducted in Python 3.13 using SciPy 1.17 and statsmodels 0.14.6.

3 Results

3.1 Participant flow, baseline differences, and attrition

The baseline sample (N = 244) had a mean age of 47.25 years (SD = 11.87; range 18–90); 121 participants (49.6%) were women. The follow-up sample (n = 197) had a mean age of 45.56 years (SD = 11.88), and 101 participants (51.3%) were women. As shown in Table 1, the two vaccine groups were not comparable before vaccination. AstraZeneca recipients were younger, more often women, and expected

substantially more symptoms and a longer period of feeling unwell. Fear of COVID-19 and general concern about post-vaccination symptoms did not differ between groups.

Follow-up completers were younger than non-completers (M = 45.56 versus 54.32 years, p < .001) and reported stronger general symptom expectations (M = 46.09 versus 30.43, p = .002), a larger expected symptom count (M = 2.87 versus 1.64, p < .001), and a longer predicted duration of feeling unwell (M = 21.31 versus 8.00 hours, p = .001). They did not differ in fear of COVID-19, concern about symptoms, or sex distribution (Supplementary Table S4). Thus, attrition was related to the primary expectancy construct.

3.2 Expected and reported symptoms

Among follow-up participants, 178 (90.4%) expected at least one symptom and 155 (78.7%) reported at least one symptom (exact McNemar p < .001). Expected frequencies exceeded reported frequencies for fatigue, headache, muscle pain, fever, and chills, but not nausea (Supplementary Table S1). The mean expected symptom count was 2.87 (SD = 2.27), compared with a mean reported count of 1.85 (SD = 1.86; Wilcoxon p < .001). Participants also predicted a longer duration of feeling unwell than they later reported (M = 21.31, SD = 30.89 versus M = 11.51, SD = 20.45 hours; p < .001).

3.3 Primary adjusted count model

Expected and reported symptom counts were positively correlated (Spearman rho = .34, bootstrap 95% CI [.22, .46], p < .001). In the primary multivariable negative-binomial model, each additional expected symptom was associated with an 11% higher expected reported symptom count (IRR = 1.11, 95% CI [1.02, 1.20], p = .011; Table 2). Vaccine type was not independently associated with the symptom count (AstraZeneca versus Pfizer-BioNTech: IRR = 0.91, 95% CI [0.61, 1.36], p = .643). Estimates for sex and age were also imprecise and did not meet the .05 threshold. The estimated dispersion parameter was 0.41 (p < .001), the model AIC was 709.97, and McFadden's pseudo-R-squared was .032.

The primary estimate was similar in the unadjusted negative-binomial model (IRR = 1.14, 95% CI [1.07, 1.21], p < .001), adjusted robust Poisson model (IRR = 1.11, 95% CI [1.02, 1.21], p = .014), expanded negative-binomial model (IRR = 1.10, 95% CI [1.00, 1.20], p = .044), and attrition-weighted negative-binomial model (IRR = 1.11, 95% CI [1.02, 1.20], p = .019; Supplementary Table S3). Stabilized weights among completers ranged from 0.82 to 3.54.

3.4 Symptom-specific and exploratory analyses

Only headache showed a robust symptom-specific association after covariate adjustment and false-discovery-rate correction: participants who expected headache had higher odds of reporting headache (aOR = 4.06, 95% CI [1.52, 10.88], raw p = .005, q = .027; Table 3). The estimate for muscle pain was positive but imprecise (aOR = 2.75, 95% CI [0.99, 7.65], q = .130). Fatigue, fever, and chills were not associated with their corresponding expectations in adjusted models.

Exploratory analyses showed that expected symptom count correlated with symptom intensity (rho = .21, 95% CI [.07, .33], q = .004), duration of feeling unwell (rho = .26, 95% CI [.12, .39], q < .001), and post-vaccination concern (rho = .42, 95% CI [.29, .54], q < .001). General symptom expectation and predicted duration also correlated with reported symptom count, whereas fear of COVID-19 did not (Supplementary Table S2).

Table 1
Baseline characteristics by vaccine group

Variable	**AstraZeneca (n = 115)**	**Pfizer-BioNTech (n = 129)**	**p**
Age, years	41.53 (11.53)	52.35 (9.67)	< .001
Women, n (%)	71 (61.7%)	50 (38.8%)	< .001
Fear of COVID-19 (0–100)	48.09 (28.80)	49.84 (31.84)	.711
Concern about post-vaccination symptoms (0–100)	35.22 (28.17)	32.64 (27.00)	.544
General expectation of symptoms (0–100)	58.61 (29.41)	29.22 (23.34)	< .001
Expected vaccine efficacy (0–100)	62.61 (24.57)	48.37 (29.42)	< .001
Expected number of symptoms	4.10 (2.26)	1.33 (1.06)	< .001
Predicted duration of feeling unwell, h	34.90 (34.63)	4.36 (9.21)	< .001

Note. Values are mean (SD) unless otherwise indicated. Continuous and ordinal variables were compared with Mann-Whitney U tests; sex distribution was compared with a chi-square test.

Table 2
Multivariable negative-binomial model predicting reported symptom count (n = 197)

Predictor	**IRR**	**95% CI**	**p**
AstraZeneca vs Pfizer-BioNTech	0.91	0.61–1.36	.643
Woman vs man	1.27	0.95–1.68	.104
Age, per year	0.99	0.97–1.00	.059
Expected symptom count, per symptom	1.11	1.02–1.20	.011

Note. IRR = incidence rate ratio. Model used HC0 robust standard errors. Dispersion alpha = 0.41 (p < .001); AIC = 709.97; McFadden pseudo-R-squared = 0.032.

Table 3
Adjusted symptom-specific logistic regressions (n = 197)

Symptom	Expected n	Reported n	aOR	95% CI	Raw p	FDR q
Fatigue	101	76	1.60	0.81–3.17	.173	.289
Headache	64	42	4.06	1.52–10.88	.005	.027
Muscle pain	61	33	2.75	0.99–7.65	.052	.130
Fever	76	34	0.75	0.25–2.28	.617	.667
Chills	64	26	1.24	0.46–3.32	.667	.667

Note. Each model included the corresponding baseline symptom expectation plus vaccine type, sex, and age. aOR = adjusted odds ratio; FDR = Benjamini-Hochberg false-discovery-rate correction across five models. Nausea was omitted because only three follow-up events produced unstable estimates.

4 Discussion

In this prospective naturalistic study, the number of symptoms expected before vaccination was associated with the number reported afterward. The association remained after adjustment for vaccine type, sex, and age and was similar across alternative count models and an attrition-weighted analysis. The adjusted effect was modest: each additional expected symptom corresponded to an approximately 11% higher expected reported count, and the model explained limited overall variation. The findings therefore support expectations as one contributor to symptom reporting rather than a dominant explanation of post-vaccination reactions. Among the covariates, the adjusted estimate for sex was positive but imprecise (IRR = 1.27, 95% CI [0.95, 1.68]; Table 2). Women tend to report stronger symptom expectations, so expectations may account for part of any sex difference, although the present data cannot establish this.

The size of the association deserves comment. An 11% increase in the expected count per additional anticipated symptom is small for a single symptom, yet it accumulates across the several symptoms that many recipients anticipated, and it sits alongside associations with symptom intensity and with the duration of feeling unwell. Participants also expected more symptoms than they later reported, a pattern in which anticipation runs ahead of experience while still ordering it, since those who expected most reported most [8, 9]. This dissociation is informative, since expectations shaped relative differences between people even where they overpredicted symptoms in absolute terms.

This result is consistent with response expectancy theory and with prospective studies showing that expectations, psychosocial factors, prior experiences, vaccine attitudes, and social communication predict subsequent vaccine-related symptoms [8–11, 21–25]. Information about possible adverse effects is therefore not neutral, since it can direct attention toward bodily sensations and shape how they are interpreted [4, 5]. The present study is best understood as an independent replication and extension

rather than the first demonstration of this relationship. Its contribution lies in combining an overall expected symptom burden with an appropriate multivariable count model, testing symptom-specific correspondence under covariate adjustment and false-discovery-rate control, and examining a cohort in which vaccine groups had markedly different expectations before the intervention.

These findings sit within a larger population literature. Vaccine beliefs shaped both the occurrence and the perceived severity of common adverse effects [24], vaccine hesitancy prospectively predicted nocebo side effects [23], and prior expectations and experiences were associated with later adverse effects in a large cohort [25]. Media evidence points two ways: after publicized reports of myocarditis following one vaccine, reporting of the named symptoms rose while unnamed symptoms stayed near baseline [29], whereas a broad comparison found little correspondence between media attention and persistent somatic symptoms in the general population [28]. These results are reconcilable, since nocebo reporting grows where a message concentrates attention on a single salient signal and weakens against a dispersed narrative. By measuring expectations before vaccination, the present study locates the mechanism at the individual level.

The symptom-specific findings were selective rather than universal. Expected headache was associated with approximately fourfold higher adjusted odds of reported headache, whereas the remaining symptom models did not survive correction. This pattern is compatible with the possibility that expectations focus attention on, or influence the attribution of, a salient nonspecific sensation. Headache is common in everyday life and was widely communicated as a vaccine effect, so recipients held a ready template for noticing and labeling ambiguous sensations [10]. Response expectancy theory predicts this correspondence, because expecting a specific symptom raises the probability of experiencing and reporting it through anticipation and bodily monitoring [9]. It also cautions against assuming that every named adverse effect produces a corresponding nocebo-related report. Low event counts, biological reactogenicity, measurement error, and differences in symptom specificity may all influence symptom-level estimates. The broad confidence interval for headache further indicates that its magnitude requires replication.

A predictive account integrates these findings: perceived symptoms arise from the brain's combination of prior expectations with incoming sensory signals, so strong expectations bias perception toward anticipated sensations [34]. This explains both the overall association and the sharper correspondence for a salient, frequently communicated symptom such as headache, and it predicts that expectations matter most when sensory evidence is ambiguous, as with nonspecific post-vaccination complaints.

The vaccine comparison should be interpreted conservatively. AstraZeneca recipients reported more symptoms in unadjusted analyses, but they were also younger, more often women, and had much stronger symptom expectations at baseline. In the adjusted negative-binomial model, the AstraZeneca-versus-Pfizer estimate was close to the null and imprecise. This attenuation does not demonstrate that the vaccines were equivalent, that expectations mediated the difference, or that biological differences were absent. Vaccine assignment was nonrandom, the groups had limited covariate overlap, and the

confidence interval was compatible with effects in either direction. Because a large share of early systemic symptoms is attributable to nocebo mechanisms [20], genuine differences between preparations can be assessed only after adjustment for psychological and demographic factors, as this analysis illustrates.

The findings have potential relevance for risk communication, though they do not test a communication intervention. Experimental work shows that how side-effect information is framed changes how many symptoms people later report [35], that a brief explanation of the nocebo mechanism dampens reporting while alarming information amplifies it [36], and that educating patients about nocebo reduces adverse symptoms [32]. Listing side effects on a consent form can itself raise later reporting [37], and a sizeable share of adverse effects attributed to active drugs may reflect nocebo processes [38]. A review of framing strategies indicates that presenting the same risk positively can lower nocebo reporting while preserving needed information [31], consistent with expert consensus favoring full, honest, and supportive communication that limits unnecessary nocebo responses [1, 30]. Communication should not be assumed to eliminate symptoms produced by an active intervention. Future randomized studies should manipulate ethically acceptable framings, measure expectations before and after communication, record a baseline symptom inventory with daily diaries, and add objective indicators where feasible, so as to separate expectancy-related reporting from reactogenicity.

These processes extend beyond vaccination. The same expectancy pathway operates in pharmacotherapy and general medical care, where nonspecific adverse effects sometimes reflect expectation together with pharmacology [2, 5]. COVID-19 vaccination therefore serves as a convenient model of a broader psychosomatic phenomenon in which biological, cognitive, and social processes shape how people report bodily change [4, 10].

Strengths of the study include prospective assessment before a real medical intervention, temporal separation of expectations and outcomes, use of a model appropriate for overdispersed count data, covariate-adjusted symptom-specific analyses, control of multiple testing, and a sensitivity analysis addressing selective follow-up. Several limitations are substantial. First, the observational design cannot distinguish expectancy-induced symptoms from biological reactions, background symptoms, or reporting and attribution processes. Second, the study did not include a placebo or comparison intervention, objective biological measures, or a baseline inventory of the same symptoms. Third, key constructs were assessed with study-specific single items, and the separate total symptom counts were broader than the six-item checklists. Fourth, symptoms were recalled approximately two weeks later rather than recorded daily, and information on vaccine dose and previous-dose status was not available. Fifth, attrition was associated with stronger expectations; weighting yielded a similar estimate but cannot remove bias from unmeasured determinants of completion. Sixth, the vaccine groups were nonrandom and strongly imbalanced at baseline. Finally, media exposure, previous adverse reactions, health status, affective symptoms, and other plausible confounders were not directly measured.

5 Conclusion

In this prospective naturalistic study, participants who anticipated a greater number of symptoms before vaccination subsequently reported a greater symptom burden, even after adjustment for vaccine type, sex, and age. Although the magnitude of the association was modest, the estimate remained similar across alternative statistical models and an analysis accounting for selective follow-up. Expectations also showed selective symptom-specific correspondence: expecting headache was associated with later headache reporting, whereas comparable associations for the remaining symptoms were not robust after correction for multiple testing.

Taken together, these findings suggest that response expectancies contribute to, but do not fully explain, symptom reporting during an active medical intervention. The results are consistent with nocebo-related processes involving attention, symptom perception, and attribution, but the observational design cannot distinguish these processes from biological reactogenicity, background symptoms, or other unmeasured influences and therefore does not establish a causal nocebo effect.

Nevertheless, the findings support treating expectations and risk communication as clinically relevant components of medical care. Honest, balanced, and supportive communication may help limit the unnecessary amplification of nonspecific symptoms without withholding information or compromising informed consent. Vaccination serves here as a naturalistic model of a broader phenomenon relevant to pharmacotherapy and other medical interventions. Randomized studies using validated expectancy measures, baseline symptom assessment, daily symptom recording, and objective indicators are needed to determine whether modifying expectations changes subsequent clinical experience.

Declarations

Conflict of Interest:

The authors declare that they have no conflict of interest.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

Funding:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contribution

An.P. conceived the study, developed the methodology, conducted the investigation, curated the data, performed the formal analysis, wrote the original draft, and reviewed and edited the manuscript. A.M.-K.

contributed to the conceptualization, methodology, investigation, formal analysis, project administration, and writing of the original draft. Ad.P. performed the formal analysis, curated the data, developed the software, and reviewed and edited the manuscript. A.K. contributed to the conceptualization and formal analysis and supervised the study. All authors reviewed and approved the final manuscript.

The authors thank all participants who volunteered to take part in this study.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request. The dataset contains health-related information collected in the context of COVID-19 vaccination and is therefore shared in deidentified form, subject to conditions that protect participant confidentiality.

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