




BMJ Open Loss to 5-year follow-up in the population-based Telemark Study: risk factors and potential for bias

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ABSTRACT

Objectives This study aimed to characterise participants lost to follow-up and identify possible factors associated with non-participation in a prospective population-based study of respiratory health in Norway. We also aimed to analyse the impact of potentially biased risk estimates associated with a high proportion of non-responders.

Design Prospective 5-year follow-up study.

Setting Randomly selected inhabitants from the general population of Telemark County in south-eastern Norway were invited to fill in a postal questionnaire in 2013. Responders in 2013 were followed-up in 2018.

Participants 16 099 participants aged 16–50 years completed the baseline study. 7958 responded at the 5-year follow-up, while 7723 did not.

Main outcome measures χ^2 test was performed to compare demographic and respiratory health-related characteristics between those who participated in 2018 and those who were lost to follow-up. Adjusted multivariable logistic regression models were used to assess the relationship between loss to follow-up, background variables, respiratory symptoms, occupational exposure and interactions, and to analyse whether loss to follow-up leads to biased risk estimates.

Results 7723 (49%) participants were lost to follow-up. Loss to follow-up was significantly higher for male participants, those in the youngest age group (16–30 years), those in lowest education level category and among current smokers (all $p < 0.001$). In multivariable logistic regression analysis, loss to follow-up was significantly associated with unemployment (OR 1.34, 95% CI 1.22 to 1.46), reduced work ability (1.48, 1.35 to 1.60), asthma (1.22, 1.10 to 1.35), being woken by chest tightness (1.22, 1.11 to 1.34) and chronic obstructive pulmonary disease (1.81, 1.30 to 2.52). Participants with more respiratory symptoms and exposure to vapour, gas, dust and fumes (VGDF) (1.07 to 1.00–1.15), low-molecular weight (LMW) agents (1.19, 1.00 to 1.41) and irritating agents (1.15, 1.05 to 1.26) were more likely to be lost to follow-up. We found no statistically significant association of wheezing and exposure to LMW agents for all participants at baseline (1.11, 0.90 to 1.36), responders in 2018 (1.12, 0.83 to 1.53) and those lost to follow-up (1.07, 0.81 to 1.42).

Conclusion The risk factors for loss to 5-year follow-up were comparable to those reported in other population-based studies and included younger age, male gender,

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study used a longitudinal design to follow-up 16 099 participants from the general population of Telemark County, Norway.
- ⇒ Baseline data were available on all participants lost to follow-up.
- ⇒ We used occupations reported by the participants and coded them using the International Standard Classification of Occupations in combination with an asthma-specific job-exposure matrix to reduce recall bias.
- ⇒ The use of self-reported questionnaires is a limitation of this study.
- ⇒ The study population may not be representative of the Norwegian population.

current smoking, lower educational level and higher symptom prevalence and morbidity. We found that exposure to VGDF, irritating and LMW agents can be risk factors associated with loss to follow-up. Results suggest that loss to follow-up did not affect estimates of occupational exposure as a risk factor for respiratory symptoms.

INTRODUCTION

Prospective population-based surveys are a valuable source of evidence for disease prevention and treatment possibilities. They have the advantage of yielding incidence rates, which allow conclusions to be drawn about causal relationships.¹ However, there is an increasing problem of declining participation in these studies. This may lead to systematic errors, making it challenging to draw valid conclusions.^{2–3} A recent study of loss to follow-up found that estimates of either the exposure or the outcome can be affected, due to selection bias.⁴ Other studies have shown that loss to follow-up does not have a major influence on risk estimates.^{5–7}

There are various reasons for non-participation in population-based studies. Some of these include refusal, death or lack



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of contact. Some previous studies have provided evidence that non-response is increasing due to an inability to locate individuals.^{8 9} Conversely, another similar study did not obtain the same result.¹⁰ Other risk factors for non-participation in population-based surveys include male gender, young age, lower socioeconomic status and current smoking.^{10–14}

In studies of exposure–disease relationships, it is crucial to investigate whether loss to follow-up is related to both exposure and outcome. If this occurs, it can lead to systematic bias in the measurement of exposure–outcome associations.⁴ Thus, it is important that the number of participants lost to follow-up is as low as possible. Furthermore, it is important to assess possible risk factors that may lead to loss to follow-up, so that appropriate approaches for preventing loss of participants can be discussed and new strategies can be implemented.

The Telemark Study was initiated in 2013 as a prospective longitudinal cohort study, with the aim of providing data on the impact of occupational, environmental and individual factors on respiratory health.^{14 15} Telemark County is in south-eastern Norway and is one of the most important industrial centres in Norway with a high proportion of industrial and craft workers. In the last decade, data from national statistics have shown that people living in Telemark County have higher rates of disability (6.9%) and sick leave (5.8%) than people living in other parts of Norway.¹⁶ Telemark County is, thus, considered an important geographical location to investigate the association between occupational, environmental and individual risk factors, and obstructive lung diseases. The first 5-year follow-up of the Telemark Study, which had the objective of providing updated knowledge regarding the incidence and causes of respiratory disease, was completed in 2018.

Our hypothesis was that male gender, younger age, lower socioeconomic status, smoking habits, respiratory symptoms and occupational exposure as determined at the baseline survey could be risk factors for loss to follow-up. The aim of this study was to characterise those lost to 5-year follow-up in the Telemark Study. We also aimed to analyse the impact of potentially biased risk estimates associated with a high proportion of non-responders at follow-up.

METHODS

Baseline study design and population

In 2013, a baseline cross-sectional survey was conducted with a target random sample of 50 000 people aged 16–50 years living in Telemark (figure 1). The sample was drawn by using The National Population Register (Folkeregister). Of this sample, 63% lived in the urban and 37% in the rural parts of the county. The questionnaire was sent by post and the participants were asked to mail it back in a prepaid envelope. Two reminders were sent. At the end of the survey, we had collected data from 16 099 participants resulting in a response rate of 33%.

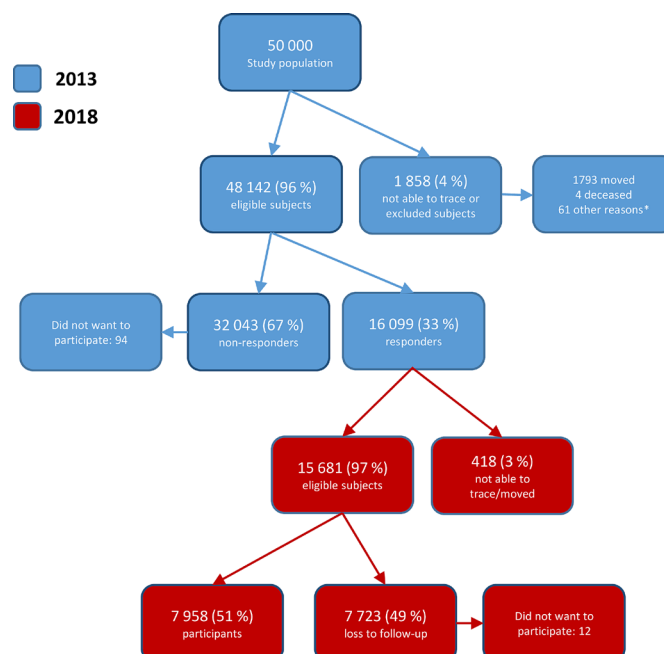


Figure 1 Flowchart of the Telemark Study, showing number of responders and non-responders in 2013 and loss to follow-up in 2018. *Unable to answer due to disease of disability (13), language problems (23).

Follow-up study design and population

In 2018, the first of three planned follow-up studies of the baseline cohort was conducted. All participants (16 099) in the baseline study were asked to complete a postal questionnaire. We continued to use the same questionnaire as that used in the baseline study in 2013. Information about the sample from The National Population Register included names, addresses and unique national ID numbers. At follow-up, the participants were given the opportunity to answer and send the questionnaire back by mail in a prepaid envelope. As an alternative, the participants could also answer the questionnaire by logging onto a secure internet webpage with a unique ID. Two reminders were sent to increase response rate. Any further efforts to contact non-answering participants were restricted by the Regional Committee for Medical and Health Research Ethics (REC).

Questionnaire

We based our questionnaire on the European Community Respiratory Health Survey (ECRHS) questionnaire, which was designed to compare the occurrence of respiratory symptoms and diseases among adults in European countries. The questionnaire contains questions addressing obstructive lung disease and respiratory symptoms and has been assessed for validity.¹⁷ In accordance with ECRHS and a previous study in Sweden,¹⁸ physician-diagnosed asthma and chronic obstructive pulmonary disease (COPD) were defined as positive responses to the questions: ‘Have you been diagnosed by a physician as having bronchial asthma?’ and ‘Have you been diagnosed by a physician as having COPD?’, respectively. Work ability

was assessed using the first single-item question in the Work Ability Index questionnaire, the Work Ability Score (WAS).¹⁹ Participants were asked to grade their current work ability on a scale from 0 ('I cannot work at all') to 10 ('my work ability is at its best right now'). The WAS was then categorised into normal (score ≥ 8) and reduced (score < 8) work ability.²⁰

Occupational exposure

The questionnaire also asked participants to list their occupational history. Responders and non-responders at follow-up were classified according to their current self-reported occupation in the baseline survey. All occupations were first classified according to the 1988 International Standard Classification of Occupations (ISCO-88).²¹ ISCO-88 classifies occupations into the following 10 major groups that are related to formal education/qualification: legislators, senior officials and managers (ISCO 1), professionals (ISCO 2), technicians and associated professionals (ISCO 3), clerks (ISCO 4), service workers and shop and market sales workers (ISCO 5), skilled agricultural and fishery workers (ISCO 6), craft and related workers (ISCO 7), plant and machine operators and assemblers (ISCO 8), elementary occupations (ISCO 9) and armed forces (ISCO 10). The ISCO codes were then connected to an asthma-specific job-exposure matrix (JEM) developed for the northern European countries (N-JEM).^{22 23} The N-JEM assigned participants to six main exposure groups as follows: high-molecular weight agents, low-molecular weight agents (LMW), irritants, accidental peak exposure to irritants, uncertain or low exposure and an unexposed reference group.

Statistical analysis

To identify predictors of loss to follow-up, that is, risk factors for non-response in 2018, univariable analyses were performed using data collected at baseline in 2013 (16 099 responders). The demographic characteristics at baseline of participants in 2018 and those lost to follow-up were compared using χ^2 tests. Respiratory health-related characteristics and occupational risk factors were also compared using χ^2 tests (online supplemental table 1). The largest percentage of missing data (6%) was for the variable describing employment during the past 12 months. Other demographic and disease-related factors (physician-diagnosed asthma and smoking) all had less than 4% of values missing. Missing values were merged with the group 'other' for education level, and with the group 'never' or 'no' for smoking, respiratory and occupational risk factors. Baseline characteristics with statistically significant associations ($p < 0.05$) with loss to follow-up at 5 years were included in all the multivariable models. An exception was education, which was not included because it was strongly correlated with occupational exposure. Education is also the basis of the ISCO-88 classification of blue-collar and white-collar occupations and was, thus, not included as an adjustment variable in the subsequent analyses.

Multivariable logistic regression models adjusted for identified baseline risk factors (gender, age, area of residence and smoking habits) were fitted to investigate whether loss to follow-up was related to the outcome (respiratory symptoms) and exposure (occupational factors). The (adjusted) ORs for loss to follow-up were reported with 95% CIs. A sensitivity analysis was performed excluding participants with missing values for smoking (data not shown). We fitted a multivariable regression model with interaction terms for wheezing, a symptom that has high predictive value for asthma and different occupational exposures (ever exposed to vapour, gas, dust and fumes (VGDF), LMW agents and irritants) to determine whether these combinations had a greater association with non-response than either factor alone.

All statistical analyses were performed using SPSS V.26 (IBM, Armonk, New York).

Patient and public involvement

We involved user representatives in the study planning, design and transfer of knowledge. We held regular meetings with the patient organisation group, Norges Astma- og Allergiforbund (NAAF). User representatives were engaged in the dissemination of results to the public, policymakers and healthcare workers through various platforms (newspapers, the internet, radio and television). A representative from NAAF served on the steering committee and contributed to the development of questionnaires.

RESULTS

The demographic characteristics of the participants and risk factors for non-response at baseline have been described in a separate paper.¹⁴ Out of 16 099 participants who completed the baseline study, almost half ($N=7958$) responded to the 5-year follow-up, while 7723 did not (figure 1). A total of 418 baseline participants did not receive the questionnaire at the 5-year follow-up because they had moved out of the county and were, thus, excluded from further analysis. The population characteristics of responders and non-responders (loss to follow-up) in 2018 are shown in table 1. The relationship between gender and responder status was significant, with male participants less likely to respond than female participants ($p < 0.05$), and the response rate was significantly lower in urban residents than in rural residents. Non-response was significantly higher in the younger age groups (16–30 years) and in participants who reported lower education (elementary school) at baseline. Employment in the past 12 months was also significantly related to a lower frequency of non-response. In addition, non-response was more common among current smokers.

Multivariable relationships

The adjusted ORs of respiratory symptoms or diseases among non-responders compared with responders are shown in table 2. Respiratory symptoms,

Table 1 Characteristics of responders and non-responders (loss to follow-up) in 2018

	Non-responder N=7723 (49%)	Responder N=7958 (51%)	P
<i>Gender</i>			<0.001
Females	4063 (46.6)	4653 (53.4)	
Males	3660 (52.5)	3305 (47.5)	
<i>Area of residence</i>			0.003
Urban	2874 (50.8)	2779 (49.2)	
Rural	4849 (48.4)	5179 (51.6)	
<i>Age group (years)</i>			<0.001
16–30	3149 (62.8)	1863 (37.2)	
31–40	1993 (49.2)	2055 (50.8)	
41–50	2581 (39.0)	4040 (61.0)	
<i>Education</i>			<0.001
Elementary+1–2	1558 (62.2)	948 (37.8)	
Upper secondary and certificant	3283 (53.4)	2862 (46.6)	
University/college	2515 (39.4)	3865 (60.6)	
Other/missing	367 (56.5)	283 (43.5)	
<i>Ever employed</i>			<0.001
Yes	6993 (48.0)	7574 (52.0)	
No	683 (65.5)	359 (34.5)	
<i>Employed past 12 months</i>			<0.001
Yes	6124 (47.0)	6918 (53.0)	
No	1599 (60.6)	1040 (39.4)	
<i>Smoking habits</i>			<0.001
Never	4216 (48.4)	4486 (51.6)	
Past	1450 (44.8)	1784 (55.2)	
Current	1985 (54.7)	1644 (45.3)	

physician-diagnosed asthma and COPD had increased odds of non-response that were statistically significant, while nasal allergies and other lung diseases did not.

We also investigated which occupational risk factors were associated with 5-year loss to follow-up, as shown in [table 3](#). Loss to follow-up was positively associated with reduced work ability (OR: 1.48, 95% CI 1.35 to 1.60) and being unemployed during the past 12 months (OR: 1.34, 95% CI 1.22 to 1.46). Participants with occupational exposure to VGDF (OR: 1.07, 95% CI 1.00 to 1.15), irritants (OR: 1.15, 95% CI 1.05 to 1.26) and LMW agents (OR: 1.19, 95% CI 1.00 to 1.41) were more likely to be lost to follow-up.

[Table 4](#) shows the association between occupational exposure to VGDF, LMW agents or irritants and loss to follow-up controlling for wheezing, and interaction between wheezing and exposure to these agents.

Table 2 Respiratory risk factors predicting loss to follow-up

	Non-responder N=7723 (49%)	Responder N=7958 (51%)	Non-responder OR adj* (95% CI)
<i>Wheezing past 12 months</i>			1.21 (1.12 to 1.32)
Yes	1667 (53.3)	1460 (46.7)	
No	6056 (48.2)	6498 (51.8)	
<i>Woken with chest tightness</i>			1.22 (1.11 to 1.34)
Yes	1192 (53.2)	1047 (46.8)	
No	6531 (48.6)	6911 (51.4)	
<i>Woken with dyspnoea</i>			1.27 (1.21 to 1.44)
Yes	601 (53.0)	532 (47.0)	
No	7122 (49.0)	7426 (51.0)	
<i>Physician-diagnosed asthma</i>			1.22 (1.10 to 1.35)
Yes	971 (53.9)	832 (46.1)	
No	6752 (48.7)	7126 (51.3)	
<i>Asthma attack last 12 months</i>			1.38 (1.17 to 1.63)
Yes	350 (55.4)	282 (44.6)	
No	7373 (49.0)	7676 (51.0)	
<i>Current use medication</i>			1.19 (1.05 to 1.35)
Yes	590 (52.3)	539 (47.7)	
No	7133 (49.0)	7419 (51.0)	
<i>Nasal allergies</i>			0.99 (0.93 to 1.07)
Yes	2277 (48.4)	2423 (51.6)	
No	5446 (49.6)	5535 (50.4)	
<i>COPD</i>			1.81 (1.30 to 2.52)
Yes	96 (60.8)	62 (39.2)	
No	7627 (49.1)	7896 (50.9)	
<i>Other lung diseases</i>			1.19 (0.92 to 1.54)
Yes	7591 (49.2)	7835 (50.8)	
No	132 (51.8)	123 (48.2)	

Bold typeface indicates $p < 0.05$.

*Adjusted for age, gender, area of residence and smoking habits, with one respiratory risk factor per model.

COPD, chronic obstructive pulmonary disease.;

Wheezing during the past 12 months and exposures to VGDF, LMW agents and irritants were associated with loss to follow-up ([table 4](#), model 1). Participants exposed to VGDF had 1.05 (95% CI 0.98 to 1.13, $p=0.05$) times the risk of being lost to follow-up than those not exposed to VGDF, adjusted for the baseline variables (residence, gender, age and smoking) and wheezing during the past 12 months. Participants exposed to LMW agents had 1.18 (95% CI 1.00 to 1.41) times the risk, and those exposed to irritants had 1.15 (95% CI 1.05 to 1.26) times the

Table 3 Work ability and occupational risk factors predicting loss to follow-up

	Non-responder N=7723 (49%)	Responder N=7958 (51%)	Non-responder OR adj*† (95% CI)
Reduced work ability‡			1.48 (1.35 to 1.60)
Reduced (WAS 0–7)	1558 (55.2)	1264 (44.8)	
Normal (WAS 8–10)	5962 (47.6)	6574 (52.4)	
Employed past 12 months			1.34 (1.22 to 1.46)
Yes	6124 (47.0)	6918 (53.0)	
No	1599 (60.6)	1040 (39.4)	
Ever VGDF			1.07 (1.00 to 1.15)
Yes	3569 (49.5)	3637 (50.5)	
No	4154 (49.0)	4321 (51.0)	
Occupational groups			
HMW agents			0.89 (0.78 to 1.02)
Yes	439 (43.7)	565 (56.3)	
No	7284 (49.6)	7393 (50.4)	
LMW agents			1.19 (1.00 to 1.41)
Yes	309 (53.6)	267 (46.4)	
No	7414 (49.1)	7691 (50.9)	
Irritants			1.15 (1.05 to 1.26)
Yes	1324 (53.1)	1171 (46.9)	
No	6399 (48.5)	6787 (51.5)	
Peak exposure			0.93 (0.71 to 1.21)
Yes	113 (47.9)	123 (52.1)	
No	7610 (49.3)	7835 (50.7)	
Uncertain or low exposure			0.93 (0.80 to 1.08)
Yes	352 (47.0)	397 (53.0)	
No	7371 (49.4)	7561 (50.6)	

Bold typeface represents $p < 0.05$.

*Adjusted for age, gender, area of residence and smoking habits, with one risk factor per model.

†Reference category in each separate model was not exposed to that specific agent. For the variable 'employed past 12 months', the reference category was the individuals with employment in the past 12 months.

‡Work ability was treated as a dichotomous variable with a cut-off value of 8 (scale from 0 to 10). Scores under 8 were regarded as having reduced work ability, and scores equal to or greater than 8 as normal work ability.

HMW, high-molecular weight; LMW, low-molecular weight; VGDF, vapour, gas, dust and fumes; WAS, Work Ability Score.

risk of being lost to follow-up than those not exposed, controlling for wheezing and the other variables (table 4, model 2). Thus, the ORs changed little after controlling for wheezing, although the main effect of wheezing when controlled for all exposures was statistically significant. The interaction term indicated that there was not a statistically significant interaction between wheezing and the

exposure variables, with OR of 1.01 (95% CI 0.93 to 1.09) for interaction with VGDF, OR of 0.92 (95% CI 0.61 to 1.39) for interaction with LMW agents, and OR of 1.10 (95% CI 0.88 to 1.37) for interaction with irritants.

Finally, we analysed the relationship between wheezing during the past 12 months and exposure to LMW agents in the different responder groups at baseline. We conducted these analyses with baseline data to determine whether there was an indication that the effect of occupational exposure might be diminished in analyses limited to responders in the follow-up survey. For all responders and those lost to follow-up (N=15 681), the OR was 1.11 (95% CI 0.90 to 1.36). When we limited the analyses to responders (N=7958) and those lost to follow-up (N=7723) separately, the ORs were 1.12 (95% CI 0.83 to 1.53) and 1.07 (95% CI 0.81 to 1.42), respectively. Thus, the OR estimates varied little between the two groups and none of the associations was statistically significant.

DISCUSSION

In this 5-year follow-up study, the non-response rate from the baseline sample was 49%. The proportion of participants who were lost to follow-up differed by gender, age, area of residence, education level and smoking status. These findings are consistent with the results of other loss to follow-up studies from Scandinavia and elsewhere.^{2 3 24}

This study also showed that non-responders to follow-up were more likely to have respiratory symptoms and report more physician-diagnosed asthma and COPD. Few longitudinal studies have investigated these associations.

Most studies on occupation, respiratory symptoms and asthma as risk factors for non-participation were studies on non-response in cross-sectional surveys. Furthermore, the results of cross-sectional studies on how respiratory symptoms and asthma affect the risk of non-participation are divergent. Two previous studies on non-response and late response found lower response rates among participants with more respiratory symptoms and asthma.^{25 26} Wheezing (31% of non-responders), long-standing cough (26% of non-responders), sputum production, attacks of breathlessness, asthma and use of asthma medicines were significantly higher among non-responders.²⁶ Other similar studies found the opposite,^{27 28} with the prevalence of physician-diagnosed asthma and respiratory symptoms being higher among responders than among non-responders.^{14 29} Our results regarding respiratory symptoms such as wheezing in the past 12 months, waking up with chest tightness, waking with dyspnoea and non-response at follow-up are in line with the findings referred in a European loss to follow-up study.² Another apparent similarity is a higher participation rate of participants with nasal allergies in our study and rhinitis in that study. Interestingly, Johannessen *et al*² found that the respiratory symptom prevalence was higher among those who participated in both the screening and the clinical parts of the baseline survey than among those who participated only in the screening. Hence, the lack of clinical examinations

Table 4 ORs adjusted for non-response, with covariates for wheezing in the past 12 months, and occupational exposures in separate regression models, in the same models, and in the same models with interaction terms

Covariates for wheezing, occupational exposure and interaction*	Separate model for each covariate OR _{adj} (95% CI)	Models with covariates for wheezing and exposure OR _{adj} (95% CI)			Models with covariates for wheezing, exposure and interaction OR _{adj} (95% CI)		
Wheezing past 12 months	1.21 (1.12 to 1.31)	1.20 (1.10 to 1.31)	1.21 (1.11 to 1.31)	1.21 (1.12 to 1.31)	1.20 (1.06 to 1.34)	1.21 (1.12 to 1.32)	1.19 (1.09 to 1.30)
Occupational exposure							
Ever VGDF	1.07 (1.00 to 1.15)	1.05 (0.98 to 1.13)			1.04 (0.93 to 1.17)		
LMW agents	1.19 (1.00 to 1.41)		1.18 (1.00 to 1.41)			1.31 (0.77 to 2.24)	
Irritants	1.15 (1.05 to 1.26)			1.15 (1.05 to 1.26)			1.03 (0.77 to 1.36)
Interaction of wheezing and occupational exposure					1.01 (0.93 to 1.09)	0.92 (0.61 to 1.39)	1.10 (0.88 to 1.37)

Bold typeface represents $p < 0.05$.

*In addition to the covariates indicated, each model was adjusted for age, gender, area of residence, and smoking habits.

VGDF, vapour, gas, dust, and fumes; LMW, low-molecular-weight.

for all participants in our study could explain the low motivation of those with more respiratory symptoms and asthma to continue participating.

According to our results, being unemployed in the past 12 months was positively associated with loss to follow-up. Our results also showed that reduced work ability was associated with non-participation at follow-up. As shown in other studies, being unemployment and having reduced work ability are correlated with lower socioeconomic status and higher symptom prevalence or morbidity.^{30 31} Few studies have investigated work ability and employment in the past 12 months as potential risk factors for loss to follow-up.

Occupational exposure to VGDF, irritants and LMW agents was significantly associated with loss to follow-up in this study. Irritants may include a variety of exposures to VGDF that cause non-specific reactions in the upper respiratory tract on inhalation. Exposure to irritants can lead to the development of irritant-induced asthma.³² This was comparable with our findings which showed an increased risk of non-response in participants with asthma and respiratory symptoms.

A previous systematic review of 67 studies showed trends of underestimation of the smoking prevalence based on self-reported data.³³ Smoking is a socially undesirable and stigmatised behaviour and this can lead to not reporting smoking habits.³⁴ In our data set, we had a total of 116 participants with missing data on smoking. This led us to perform sensitivity analyses of the analyses shown in tables 2 and 3, with missing data on smoking excluded from the analysis, and the results were very similar (data not shown).

In a previous study, wheezing was shown to be one of the best single symptom predictor of an asthma diagnosis.³⁵ Our concern was that loss to follow-up may be more common in participants who were exposed to VGDF, LMW agents or irritants and reported wheezing in

the last 12 months. However, our analysis of interactions showed non-significant ORs for the interaction between these variables.

Our main concern was that loss to follow-up might have led to biased estimates. However, our data showed that there was no significant difference in the associations between respiratory symptoms and occupational exposure among responders in 2018 and those lost to follow-up.

Strengths and limitations

This study has several strengths. It had a large sample size and used a longitudinal study design. Few studies have been conducted on participants lost to follow-up in prospective studies of respiratory health and occupational exposure. Selection bias was previously assessed at baseline,¹⁴ and we had available baseline data on participants who were lost to follow-up. We used a web survey as an option to increase response among younger age groups. Confounders were assessed by adjusting for age, gender, area of residence and smoking habits.

While researchers attempt to obtain 100% participation rates, non-response is a common limitation of longitudinal population-based studies. In this study, strict requirements from the regional ethics committee regarding how many times (only two reminders were allowed) and the ways in which non-responders could be contacted made it difficult to obtain a high response rate. A systematic review of randomised control trials has shown that extensive questionnaires could lead to participants' decision not to participate in follow-up.³⁶ Our questionnaire consisted of 10 pages with 68 questions. This was needed in order to adhere to the standardised questionnaire for comparison with other studies. The same review found that the OR for response could be doubled using monetary incentives. According to Norwegian research standards, monetary incentives are not acceptable. Studies have also shown

that lottery incentives do not lead to higher response rates for postal questionnaires in observational studies.^{37 38} In the baseline Telemark Study, a lottery was performed with the permission from the REC, which included a drawing to potentially win one of two iPads. There were no incentives to participate in the 5-year follow-up. However, we took advantage of the similar representation of non-responders and responders and used it to investigate the risk factors for loss to follow-up.

The use of self-reported questionnaires in this study is a limitation. Self-reported questionnaires can introduce recall bias and selection bias regarding variables such as smoking, weight and exposure. In addition, misclassification may have occurred within exposure categories. Thus, results based on self-reported exposure should be interpreted with caution. However, we used self-reported occupation coded by the ISCO-88 system,²¹ in combination with JEM, an approach which is considered to reduce recall bias introduced by self-reported occupational exposures.

Regarding external validity, it is important to note that Telemark is a county with both urban and rural areas, including an area with a high level of industrial activity. It has a slightly lower level of education and of working-class population than the rest of the country. Therefore, our results may not be representative for the entire country of Norway.

By definition, it is not possible in the context of a longitudinal study, to measure the impact of occupational exposure among non-responders after the baseline survey. However, the analysis using baseline data suggests that the estimates of effect of the exposures of interest is unlikely to have been biased due to high non-response rate in the 5-year follow-up survey.

The findings highlight the importance of performing loss to follow-up studies in epidemiological research to better understand how a study sample changes over time.

CONCLUSION

In this 5-year follow-up, we found higher proportions of participants of male gender, younger age, lower educational level and current smokers among the non-responders. Having more respiratory symptoms, being unemployed in the past 12 months, and greater exposure to VGDF, irritants and LMW agents were associated with loss to follow-up. Our results also show that loss to follow-up is unlikely to have affected the estimates of occupational exposure as a risk factor for respiratory symptoms, which is important for our future research.

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Data availability statement Data are available upon reasonable request. This study is using de-identified data regarded as not anonymous data. The Project Steering Committee and The Regional Committee for Medical and Health Research Ethics do not allow data sharing, as they regard data as sensitive personal information, without further approval. If requests are received, this must be first approved by these two entities.

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