Association between Pruritus and Psychosocial Well-being: A Population-based Study among 6,809 Subjects

ORIGINAL ARTICLE

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Pruritus has an extensive impact on functional, social and psychosocial behaviour. The association between pruritus and psychological well-being has mostly been studied among selected patient groups, whereas population-based studies are lacking. The aim of this study was to determine the association between pruritus and insomnia, quality of life, depression and anxiety at the population level in the general population. A cross-sectional population-based study was conducted in 2012 to 2013. Study subjects (n = 6,809) belonging to the Northern Finland Birth Cohort 1966 Study participated in a large follow-up study at the age of 45-47 years. They completed an extensive health questionnaire including questions on pruritus and several previously validated questionnaires regarding symptoms of psychosocial well-being. Pruritus affected 19.9% of the study subjects weekly, being more common in women than in men (p < 0.001). A significant association was found between both localized and generalized pruritus and symptoms of insomnia, depression, anxiety and decreased quality of life. The association was seen even in those with mild psychological symptoms/ insomnia, and it affected both sexes. The severity of psychological symptoms increased with increasing frequency of pruritus. In conclusion, pruritus has a multiple effect on psychosocial well-being. Physicians should consider possible psychosocial symptoms in patients with pruritus.

Key words: pruritus; depression; anxiety; insomnia; quality of life; general population.

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By definition, pruritus is an unpleasant skin sensation that leads to scratching. Pruritus is a common symptom and, in population-based studies, the lifetime prevalence of chronic pruritus (duration over 6 weeks) is reported to be up to 26% (1, 2). Pruritus affects more females than males and its incidence increases with age (1). There are many aetiological factors behind pruritus (3). Pruritus is the major symptom in many dermato-

SIGNIFICANCE

Pruritus, "itching", is an uncomfortable sensation that leads to scratching. Pruritus has been linked with psychiatric symptoms. However, previous studies have mostly examined the relationship between pruritus and psychosocial health among selected patient groups (such as dermatological patients), whereas studies focusing on the general population are scarce. This study examined the relationship between pruritus with symptoms of depression, anxiety, insomnia and quality of life in the general population of Northern Finland Birth Cohort 1966 Study (n = 6,809). The study found that those with pruritus had increased risk of sleeping difficulties, depressive and anxiety symptoms, and decreased quality of life.

logical conditions, such as atopic eczema, psoriasis and chronic urticaria. Besides dermatological diseases, pruritus can be caused by many other factors, such as systemic diseases (e.g. renal failure) or medications (opioids); however, sometimes the underlying disease cannot be found (3).

Pruritus is a distressing symptom with extensive impact on functional, social and psychosocial behaviour (4). The association between pruritus and depression (5–8), anxiety (7, 8), insomnia (6, 9–11) and quality of life (QoL) (12, 13) has been demonstrated previously in many studies. However, earlier reports have focused mostly on selected patient samples, such as those from dermatology or specified pruritus clinics (6, 8) or specific patient groups (e.g. renal patients with pruritus) (14), whereas general population studies concerning the association with pruritus and psychosocial well-being are scarce (1).

Although pruritus can derive from different origins and the underlying reasons need to be clarified, the symptom itself requires independent consideration and attention. To address this gap, the aim of this study was to determine the prevalence of pruritus in the general population and the association between pruritus and psychosocial well-being at population level in middle-aged subjects (n=6,809) in the Northern Finland Birth Cohort 1966 (NFBC1966). More precisely, the associations between pruritus and insomnia, depression, anxiety and QoL were studied using standardized questionnaires.

MATERIALS AND METHODS

Study population

The study data originated from the NFBC1966, a longitudinal research programme in the 2 northernmost provinces in Finland. Initially, the NFBC1966 included all 12,058 children in the 2 northernmost provinces of Finland whose expected dates of birth fell in the year 1966 (covering 48% of Finnish territory and 13.2% of the population in 1966) (15). The whole cohort has been evaluated regularly since birth by means of health questionnaires and clinical examinations. When the subjects whose expected date of birth was in 1966 reached the age of 45–47 years, a large health study including questionnaires and clinical examinations was conducted in 2012 to 2013. The questionnaires covered comprehensive items about health, including psychosocial well-being and pruritus.

Assessment of pruritus

The presence of pruritus was self-reported in the 46-year follow-up study. The subjects were asked: "How often do you have pruritus? (never, seldom, every month, weekly, or daily" (to evaluate the frequency of pruritus). The more frequently pruritus presented the more severe it was considered to be. To evaluate the extent of pruritus, subjects were also asked at the time of the study: "Do you have pruritus on limited skin areas of the body?" (localized) or "Do you have generalized pruritus?".

Psychological questionnaires

Athens Insomnia Scale. The question regarding sleep disturbance was addressed with the modified Athens Insomnia Scale (AIS) including the following items: 1: Sleep induction; 2: Awakenings during the night; 3: Final awakening; 4: Total sleep duration; and 5: Sleep quality (16). Sleep disturbance was rated from 0 (meaning that the item in question has not been a problem) to 3 (indicating more acute sleep difficulties). The total score of insomnia ranges from 0 to 15. Higher scores indicate higher severity of insomnia (16).

Hopkins Symptom Checklist-25. Participants were screened for common psychiatric symptoms using the Hopkins Symptom Checklist-25 (HSCL-25) (17). An individual's total score was calculated as the mean score of all 25 items, ranging from 1.00 to 4.00. A high total score is shown to correlate highly with severe emotional distress and to indicate the presence of psychiatric disorder (17, 18). In the HSCL-25 a score <1.55 referred to no symptoms; 1.55–1.75 to mild symptoms; and >1.75 to moderate/severe symptoms.

Beck Depression Inventory—II. Current depression was assessed using the Beck Depression Inventory II (BDI-II) (19, 20). Scores <14 referred to no symptoms of depression; 14—20 to mild symptoms; and >20 to moderate to severe symptoms of depression (19, 20).

Generalized Anxiety Disorder Screener. The Generalized Anxiety Disorder Screener (GAD-7) was used as a measure of generalized anxiety disorder (GAD). A score <7 referred to no symptoms of GAD, 7–10 to mild symptoms and >10 to moderate/severe symptoms (21, 22).

15-dimensional measure of health-related quality of life (15D HRQoL). This questionnaire is a generic, standardized, well-validated, self-administered measure of health-related QoL (HRQoL) (23). Possible total scores range from 0 (death) to 1 (full health). State-Trait Anxiety Inventory. The State-Trait Anxiety Inventory (STAI) is a commonly used measure of trait and state anxiety (24). It can be used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. The higher the score, the more severe the symptoms.

Previous skin disease

Patient records (history of predefined skin disease in which chronic itching occurs particularly frequently and which were diagnosed before the 46-year follow-up study) were obtained from the Finnish Institute of Health and Welfare's statutory Care Register of Health Care (CRHC) and selected by all International Classification of Diseases 10th revision (ICD-10) codes: L20 atopic dermatitis, L28 prurigo, L30 eczemas, L40 psoriasis, L43 lichen ruber planus, L23 contact dermatitis, and L50 urticaria. The CRHC contains inpatient data from all state-administered Finnish hospitals and from the largest private hospitals from 1987 onwards. Each record contains the identification numbers of the patient and hospital, primary and subsidiary diagnoses, and duration of hospital stay. The Care Register covers outpatient visits from 1998 onwards. In Finland, the ICD-10 has been used since 1996.

Confounding factors

Smoking (25), alcohol use (26), body mass index (BMI) (27), physical activity (28), socioeconomic status (29), and a history of skin disease with pruritus (30) were considered as possible confounders because of their known association with psychological symptoms.

Ethics statement

The Ethics Committee of the Northern Ostrobothnia Hospital District approved the study (§94/2011), which was performed according to the principles of the Declaration of Helsinki 1983. Subjects participated on a voluntary basis and signed an informed consent. Data were handled on the group level only, personal information being replaced by identification codes, resulting in complete anonymity.

Statistical analyses

The lifetime prevalence of pruritus was calculated. Distributions of continuous variables were expressed as mean and standard deviation (SD) and categorical variables as numbers and percentage of proportions. Categorical variables were tested by χ^2 test and continuous variables using the Mann–Whitney U test. Multivariate logistic and linear regression analyses were used to estimate association between pruritus and different self-reported psychological measurements. The following variables were used in the adjusted multivariate model: Smoking, alcohol use, BMI, physical activity, socioeconomic status (SES) and history of skin disease. To correct for multiple comparisons, the false discovery rate (FDR) was controlled at 0.05 using the Benjamini-Hochberg method, and p < 0.05 was considered statistically significant. Statistical analyses were conducted using the R software package version 4.0.2 (https://cran.rstudio.com).

RESULTS

Health questionnaires were sent to all cohort members who were alive and whose postal address was known at the age of 45–47 years (n=10,282). A total of 6,809 subjects (66.2%) answered the question about pruritus in limited skin areas and 6,744 (65.6%) answered the question about generalized pruritus. The following numbers completed the questionnaires concerning psychosocial well-being: AIS (n=6,809), HSCL (n=6,436), STAI (n=5,405), GAD-7 (n=5,439) and 15D HRQoL (n=5,295). The baseline characteristics of the study subjects are shown in Tables SI and SII.

Table I. Prevalence of pruritus by sex (n = 6,809)

	Males n=3,111	Females n = 3,698	
	n (%)	n (%)	<i>p</i> -value ^a
Pruritus in limited areas $n = 6,809$			< 0.001
Never	751 (24.1)	715 (19.3)	
Seldom	1,413 (45.4)	1,624 (43.9)	
Monthly	500 (16.1)	585 (15.8)	
Every week	307 (9.87)	487 (13.2)	
Daily	140 (4.50)	287 (7.76)	
Generalized pruritus $n = 6,744^{b}$			< 0.001
Never	1,718 (55.9)	1,812 (49.3)	
Seldom	1,005 (32.7)	1,309 (35.6)	
Monthly	169 (5.50)	257 (7.00)	
Every week	117 (3.81)	182 (4.96)	
Daily	63 (2.05)	112 (3.05)	

 a p-values tested by χ^2 test. b There is some missing data because not all cohort members answered the question on generalized pruritus.

Pruritus affected 19.9% of subjects (including those with weekly pruritus; either localized or generalized). **Table I** shows the prevalence of pruritus by sex. Both pruritus in limited areas and generalized pruritus were more common in females than in males (p<0.001). Increasing frequency of pruritus was significantly associated with depression, anxiety, insomnia and HRQoL. This association was seen with both pruritus limited to small areas and generalized pruritus (**Table II**) and was found similarly in both sexes.

In an adjusted model in multivariate logistic regression analyses (adjusted with SES, smoking, alcohol use, body mass index, physical activity and the history of skin disease), those reporting daily generalized pruritus had over 3-fold (odds ratio (OR) 3.30, 95% confidence interval (CI) 1.65–6.59) risk of generalized anxiety measured by GAD-7 (score > 10 referring to moderate/severe symptoms). Correspondingly, daily pruritus (generalized) increased the risk of depressive symptoms (measured by BDI-II, those with > 20 value) over 4-fold (OR 4.27, 95% CI 2.22–8.19). However, the association between pruritus and depression and anxiety was seen even in those with mild symptoms (GAD-7 score 7–10 and BDI-II score 14–20) (**Table III**).

There was also a significant association between severe emotional distress (measured by HSCL-25) and pruritus (Table III). The association of sleep disturbance (measured by AIS), anxiety (measured by STAI) and QoL (measured by 15D HRQoL) with pruritus (both localized and generalized) was evaluated using linear regression analyses, and the association between pruritus and these factors remained statistically significant after adjusting (Table SIII). The more frequently pruritus presented the more severe were the symptoms of insomnia, anxiety, distress, and the worse was the subject's OoL.

Table II. Association between pruritus and psychosomatic symptoms in limited skin areas, n = 6,809 and generalized pruritus, n = 6,744

	Never n = 1,466	Seldom n = 3,037	Monthly n = 1,085	Weekly n = 794	Daily n = 427	<i>p</i> -value
Limited skin areas						
Athens Insomnia Scale, mean (SD)	2.35 (2.34)	2.77 (2.52)	3.29 (2.70)	3.58 (2.84)	3.69 (3.11)	< 0.001
State-Trait Anxiety Inventory, mean (SD)	9.85 (2.74)	10.3 (2.71)	10.9 (2.89)	11.0 (3.05)	11.4 (3.17)	< 0.001
15D HRQoL, mean (SD)	0.95 (0.05)	0.93 (0.06)	0.92 (0.07)	0.91 (0.08)	0.90 (0.08)	< 0.001
Beck Depression Inventory-II, n (%)						< 0.001
<14	1,072 (92.7)	2,297 (92.0)	788 (87.9)	555 (83.5)	300 (84.3)	
14-20	56 (4.84)	113 (4.52)	74 (8.26)	54 (8.12)	32 (8.99)	
> 20	29 (2.51)	88 (3.52)	34 (3.79)	56 (8.42)	24 (6.74)	
Hopkins Symptom Checklist-25, n (%)						< 0.001
< 1.55	1,224 (87.9)	2,334 (81.6)	759 (74.9)	524 (70.3)	262 (65.3)	
1.55-1.75	89 (6.39)	250 (8.74)	115 (11.4)	82 (11.0)	52 (13.0)	
>1.75	79 (5.68)	278 (9.71)	139 (13.7)	139 (18.7)	87 (21.7)	
Generalized Anxiety Disorder Screener, n (%)						< 0.001
< 7	1,022 (92.9)	2,183 (91.0)	746 (87.8)	542 (85.6)	290 (84.3)	
7–10	55 (5.00)	146 (6.08)	68 (8.00)	55 (8.69)	25 (7.27)	
>10	23 (2.09)	71 (2.96)	36 (4.24)	36 (5.69)	29 (8.43)	
Generalized pruritus						
Athens Insomnia Scale, mean (SD)	2.52 (2.43)	3.17 (2.62)	3.76 (2.90)	3.64 (3.03)	4.31 (3.45)	< 0.001
State-Trait Anxiety Inventory, mean (SD)	10.1 (2.75)	10.7 (2.76)	11.1 (3.14)	11.0 (3.10)	11.6 (3.56)	< 0.001
15D HRQoL, mean (SD)	0.94 (0.06)	0.92 (0.07)	0.90 (0.07)	0.91 (0.07)	0.87 (0.09)	< 0.001
Beck Depression Inventory-II, n (%)						< 0.001
< 14	2,673 (92.9)	1,685 (88.6)	288 (80.4)	214 (85.6)	111 (79.3)	
14-20	126 (4.38)	125 (6.57)	42 (11.7)	21 (8.40)	11 (7.86)	
>20	78 (2.71)	92 (4.84)	28 (7.82)	15 (6.00)	18 (12.9)	
Hopkins Symptom Checklist-25, n (%)						< 0.001
<1.55	2,843 (85.3)	1,658 (76.2)	272 (68.9)	184 (65.9)	101 (60.5)	
1.55-1.75	249 (7.47)	241 (11.1)	41 (10.4)	31 (11.1)	18 (10.8)	
>1.75	242 (7.26)	278 (12.8)	82 (20.8)	64 (22.9)	48 (28.7)	
Generalized Anxiety Disorder Screener, n (%)	` ,	` ,	, ,	, ,	` ,	
<7	2,529 (92.0)	1,627 (89.2)	288 (83.7)	198 (84.3)	97 (75.2)	< 0.001
7–10	142 (5.17)	132 (7.24)	28 (8.14)	25 (10.6)	17 (13.2)	
>10	78 (2.84)	64 (3.51)	28 (8.14)	12 (5.11)	15 (11.6)	

Categorical variables were tested by χ^2 test and continuous variables using the Mann–Whitney U test. SD: standard deviation; 15D HRQoL: 15-dimensional measure of health-related quality of life.

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Table III. Association between pruritus and psychological symptoms in adjusted multivariate logistic regression analyses

Pruritus	Never	Seldom Adjusted OR (95% CI)	Monthly Adjusted OR (95% CI)	Weekly Adjusted OR (95% CI)	Daily Adjusted OR (95% CI)
Generalized Anxiety Disorder Screener-7	Ref				
Pruritus in limited areas					
7–10		1.32 (0.92-1.88)	1.82 (1.22-2.73)	2.01 (1.32-3.07)	1.50 (0.88-2.56
>10		1.55 (0.91-2.66)	2.13 (1.18-3.87)	2.46 (1.34-4.51)	3.69 (1.95-7.01)
Generalized pruritus					
7–10		1.36 (1.04-1.78)	1.47 (0.93-2.31)	1.95 (1.19-3.18)	2.46 (1.35-4.48)
>10		1.18 (0.81-1.71)	2.62 (1.60-4.28)	2.04 (1.07-3.87)	3.30 (1.65-6.59)
Beck Depression Inventory-II	Ref				
Pruritus in limited areas					
14-20		0.82 (0.58-1.17)	1.67 (1.14-2.44)	1.58 (1.05-2.38)	1.68 (1.05-2.70)
>20		1.68 (1.00-2.81)	1.81 (1.00-3.26)	3.61 (2.07-6.28)	2.88 (1.51-5.52)
Generalized pruritus					
14-20		1.30 (0.99-1.71)	2.66 (1.81-3.91)	1.72 (1.04-2.86)	1.43 (0.72-2.86)
>20		2.02 (1.41-2.88)	2.64 (1.57-4.44)	2.67 (1.45-4.94)	4.27 (2.22-8.19)
Hopkins Symptom Checklist-25	Ref				
Pruritus in limited areas					
1.55-1.75		1.48 (1.10-1.99)	1.87 (1.33-2.62)	1.94 (1.35-2.78)	2.33 (1.54-3.51)
>1.75		1.77 (1.29-2.41)	2.45 (1.73-3.47)	3.52 (2.48-5.00)	3.89 (2.62-5.78)
Generalized pruritus					
1.55-1.75		1.45 (1.18-1.80)	1.31 (0.88-1.93)	1.44 (0.92-2.24)	1.28 (0.70-2.33)
>1.75		1.82 (1.47-2.26)	2.91 (2.10-4.04)	3.65 (2.55-5.24)	3.94 (2.52-6.16)

Multivariate logistic regression analyses, adjusted with the following confounder factors: smoking, alcohol use, body mass index (BMI), physical activity, socioeconomic status, and the history of skin disease. OR: odds ratio; 95% CI: 95% confidence interval.

DISCUSSION

This study comprehensively examined the prevalence of pruritus and its association with psychosocial wellbeing in a general population of middle-aged subjects (n=6,809) in a large birth cohort. The study demonstrated that pruritus has a multidimensional impact on subjects' health. There was a significant association between pruritus and symptoms of insomnia, depression, anxiety, HROoL and psychological stress. It is noteworthy that this association was seen even in the group including those with mild/milder psychosocial symptoms, and not only in those who had severe symptoms. The association affected both sexes and was independent of dermatological diseases.

This study demonstrates that frequently occurring pruritus is a common symptom in the middle-aged population; pruritus affected 19.9% of the study subjects weekly and 7.2% daily. There is only 1 previous general population study of pruritus: in a German study (n=1,190) Matterne et al. (2) reported a lifetime prevalence of pruritus of 25.0%. The current study is thus in line with this German study, confirming that pruritus is a common symptom. There are many aetiological factors behind pruritus (3), which need to be identified; however, the symptom itself should be noticed.

This study found that the QoL in subjects with either localized or generalized pruritus was significantly decreased compared with those without pruritus. In addition, the cohort members with pruritus reported more sleeping problems than those without. Moreover, the severity of insomnia increased with the severity of pruritus. Many itching patients experience nocturnal pruritus, which may result in sleep disturbances (31), and a recent Korean study (n=91) also demonstrated the

association between pruritus and insomnia (6). Pruritus has multiple effects on OoL and the burden caused by pruritus is probably even higher than previously thought (4). Factors mediating the impact of pruritus on QoL are variable; pruritus can cause impairment in activities of daily living and sleep, distress, and psychological symptoms (32). In a study performed in Georgia the impact of pruritus on QoL was shown to correlate with that of chronic pain and to be higher than of some malign skin diseases (33). Insomnia is one of the symptoms that has a strong impact on people's QoL, self-satisfaction, well-being and occupational and social functioning (34).

Pruritus has been linked with psychiatric symptoms (1, 4, 6, 7, 35). Interestingly, the current study found the relationship between pruritus and psychiatric symptoms to be present even in the group that also included those with mild/milder symptoms, and not only in those with severe symptoms. A study performed in the University of Münster among dermatology patients (n=109) found that over 70% of patients with pruritus presented with at least 1 psychiatric illness (35). Furthermore, in a German general population study a relationship was found between chronic pruritus and anxiety and depression (n=1,190) (1). The significant effect of pruritus on well-being has been shown particularly in patients with dermatological diseases characterized by intense itching (36). Subjects with atopic dermatitis reported itching as the most burdensome symptom of the disease (37). Furthermore, patients with itching skin diseases have been reported to have increased suicide risk (38). The relationship between pruritus and psyche is probably bidirectional: Pruritus causes one to scratch, which can affect mood, further increase distress and anxiety in addition to causing difficulty falling sleep. In turn, stress and psychological symptoms may have a direct effect on the skin through several mechanisms, such as increased release of histamine, proinflammatory cytokines and vasoactive neuropeptides, and haemodynamic-related changes, which may lead to pruritus (6, 39).

Unlike previous studies, the current study found no sex-specific differences in the relationship between pruritus and psychosocial symptoms (7, 40). In a German study, Stumpf et al. (7) reported that female subjects with pruritus had more anxiety than males. Correspondingly, in another study females with pruritus had more psychosomatic diseases and emotional factors in relation to pruritus than did men (40). This difference between the current study and others may originate from the fact that the current study population represented the general population, whereas other studies have focused mainly on selected dermatological patients. In general, men are slower than women to seek medical help, and this could be the reason why previous studies performed in medical clinics have not found a relationship between pruritus and psychological symptoms in men.

The major strength of this study is that is based on a wide (over 6,800 subjects) general population of the NFBC1966. To the best of our knowledge, this is by far the largest epidemiological study at the population level about pruritus and psychological symptoms, insomnia and OoL. The participation rate of the study was satisfactory (66%) and comparable with the participation rates in other cross-sectional European health examination surveys (15, 41). Many previous studies concerning pruritus and psychological symptoms have used questionnaire settings focused specifically on pruritus. In the current study psychological questionnaires had no such direct link to pruritus, which probably led to a more objective evaluation (questionnaires were part of the large 46-year collection of birth cohort data). In addition, due to the study design, we were able to evaluate psychosocial symptoms from diverse viewpoints by using comprehensive, previously standardized questionnaires whose results have been shown to correlate moderately well with psychiatric diagnoses (17).

Study limitations

This study has some limitations. Since the study was not longitudinal we cannot exclude the possibility of a bidirectional association between pruritus and psyche. In addition, the study included a narrow age cohort of Caucasian subjects, which may limit generalization of the results to other age groups or nationalities. Furthermore, even though there were 2 questions about pruritus, describing both the extent and frequency of pruritus at the time of the study, the questions were not validated and do not directly show the chronicity of pruritus. Recall bias might also affect the study results, while, for example, pruritus at any time in small areas might be difficult to remember. Due to the study design we did

not have objective measurements for the evaluation of pruritus, and thus the findings rely on self-reporting only, which may have also caused bias. Finally, not all invited cohort members participated in the study, which may have led to some bias: in the current 46-year follow-up study, participants were more often employed and from higher social class and more likely to be married and have children than non-participants (15).

Conlcusion

This study highlights the significant impact pruritus has on people's lives. It is noteworthy that not all subjects with pruritus seek medical help, which makes population-based studies like this important. In this study, the more severe the pruritus, the stronger the relationship with well-being in both localized and generalized pruritus. Awareness of the effect of pruritus on QoL should be increased. In addition, although the treatment of pruritus is often challenging, different kinds of treatment options should be explored. Based on these findings, we recommend that physicians seeing patients with pruritus should also consider possible psychosocial symptoms.

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Data referral. https://etsin.fairdata.fi/dataset/716939c3-7a2a-4b6a-91f3-92aca09bc52d.

Data available. NFBC data are available from the University of Oulu, Infrastructure for Population Studies. Permission to use the data can be applied for research purposes via electronic material request portal. In the use of data, we follow the EU general data protection regulation (679/2016) and Finnish Data Protection Act. The use of personal data is based on cohort participant's written informed consent at their latest follow-up study, which may cause limitations to its use. More information is available from NFBC project centre (NFBC projectcenter(at)oulu.fi) and the cohort website.

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