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ORIGINAL ARTICLE

Discharge Information About Adverse Drug Reactions Indicates Lower Self-Reported Adverse Drug Reactions and Fewer Concerns in Patients After Percutaneous Coronary Intervention

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Aim There are discrepancies between the information patients desire about adverse drug reactions (ADRs) and the information they receive from healthcare providers; this is an impediment to shared decision-making. This study aimed to establish whether patients received information about ADRs resulting from prescribed pharmacotherapy, before hospital discharge, after percutaneous coronary intervention (PCI) and to determine whether receiving information about ADRs was associated with incidence of self-reported ADRs or concerns related to prescribed pharmacotherapy.

Methods CONCARD[PCI], a prospective multicentre cohort study including 3,417 consecutive patients after PCI, was conducted at seven high-volume referral PCI centres in two Nordic countries. Clinical data were collected from patients' medical records and national quality registries. Patient-reported outcome measures were registered 2 months (T1), 6 months (T2), and 12 months (T3) after discharge. Covariate-adjusted logistic regression yielded adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

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Results At discharge, 38% of participants had been informed about potential ADRs. For these patients, the incidence of self-reported ADRs was significantly lower at T1 (aOR 0.61, 95% CI 0.50–0.74; p<0.001), T2 (aOR 0.60, 95% CI 0.49–0.74; p<0.001), and T3 (aOR 0.57, 95% CI 0.46–0.71; p<0.001). Those who were not informed reported higher levels of concern about prescribed pharmacotherapy at all measuring points (p<0.001 for all comparisons). Those living alone (aOR 0.73, 95% CI 0.57–0.92; p=0.008), who were female (aOR 0.57, 95% CI 0.44–0.72; p<0.001), and with three or more versus no comorbidities (aOR 0.61, 95% CI 0.44–0.84; p=0.002) were less likely to receive information.

Conclusion A substantial proportion of patients were not informed about potential ADRs from prescribed pharmacotherapy after PCI. Patients informed about ADRs had lower incidences of self-reported ADRs and fewer concerns about prescribed pharmacotherapy.

Keywords Adverse drug reactions • Concerns • Patient education • Patient-reported outcome measures

Introduction

Adverse drug reactions (ADRs), defined as "a noxious and unintended response to a medicine" [1], are common in patients with coronary artery disease and contribute to worse outcomes [2,3]. Perceived ADRs may arise from the fear of ADRs themselves; this is known as the nocebo effect, a phenomenon where negative expectations of inert exposure cause noxious symptoms, which is solely a result of psychological mechanisms [4].

Studies have found that informing patients about ADRs significantly increases self-reporting of ADRs [5]; there is also contradictory evidence [6,7]. Reducing information about ADRs has nevertheless been advocated as a strategy for reducing both ADR expectations and subsequent ADR experiences [8]. This is concerning because withholding information is in direct conflict with patient autonomy and legislation [9]. There are discrepancies between the information patients desire about ADRs and the information they receive from clinicians [10]. Thus, new evidence from larger confirmatory studies is needed to determine whether providing information about ADRs is associated with the incidence of ADRs [6,7].

Therefore, this study aimed to: 1) establish whether patients received information about ADRs resulting from prescribed pharmacotherapy before hospital discharge after PCI; and 2) determine whether receiving information about ADRs is associated with the incidence of self-reported ADRs or concerns related to prescribed pharmacotherapy.

Methods

Study Design and Setting

CONCARD^{PCI} [11] is an international prospective multicentre cohort study based on real-world data from 3,417 consecutive patients after PCI, including three measuring time points during one year of follow-up. The study was conducted at seven high-volume referral PCI centres in Norway and Denmark between June 2017 and May 2020. The PCI centres were selected based on the presence of a committed research team, prior research experience, and size. The included centres performed on average 1,700 (range 900 to >2,000) PCI procedures annually, had 629–1,400 beds (mean 943), and were referral centres for coronary angiography and PCI for 37 local hospitals. Furthermore, CONCARD was organised in four thematic projects, of which one was related to adherence to treatment. Participating centres were included stepwise [11].

Study Population

The study population comprised all patients included in CONCARD^{PCI} (n=3,417). To identify potentially eligible patients, daily admission records and operating programs were reviewed. Dedicated study nurses prospectively screened all adult patients undergoing PCI at the seven centres (n=5,608) for eligibility during the index hospitalisation after PCI prior to hospital discharge. Patients were deemed eligible to participate if they gave informed consent, had undergone PCI, were aged ≥18 years, and community-dwelling. Exclusion criteria were patients who: did not speak Norwegian/Danish; were unable to complete the questionnaires due to reduced capacity; had a life expectancy of <1 year; or had undergone PCI without stent implantation, in connection with transcatheter aortic valve implantation or MitraClip examination. Furthermore, those who had previously been enrolled in CONCARD^{PCI} (readmissions within the 12-month follow-up period) were excluded from a second enrolment (Figure 1). If cognitive impairment was suspected, patients were screened using The Confusion Assessment Method [12] and the 4AT [13] to determine whether they needed to be excluded. Clinically unstable or delirious patients who would otherwise be eligible for inclusion were reassessed for inclusion before hospital discharge.

Patient-Reported Outcomes Measures

Self-reported adverse drug reactions

De novo questions were used to determine whether patients reported ADRs resulting from prescribed pharmacotherapy between the three measuring time points (Supplementary Table A1), and where the ADRs originated (Figure 2). In addition, patients could provide a written description of the experienced ADRs. Two of the authors (JS, clinical

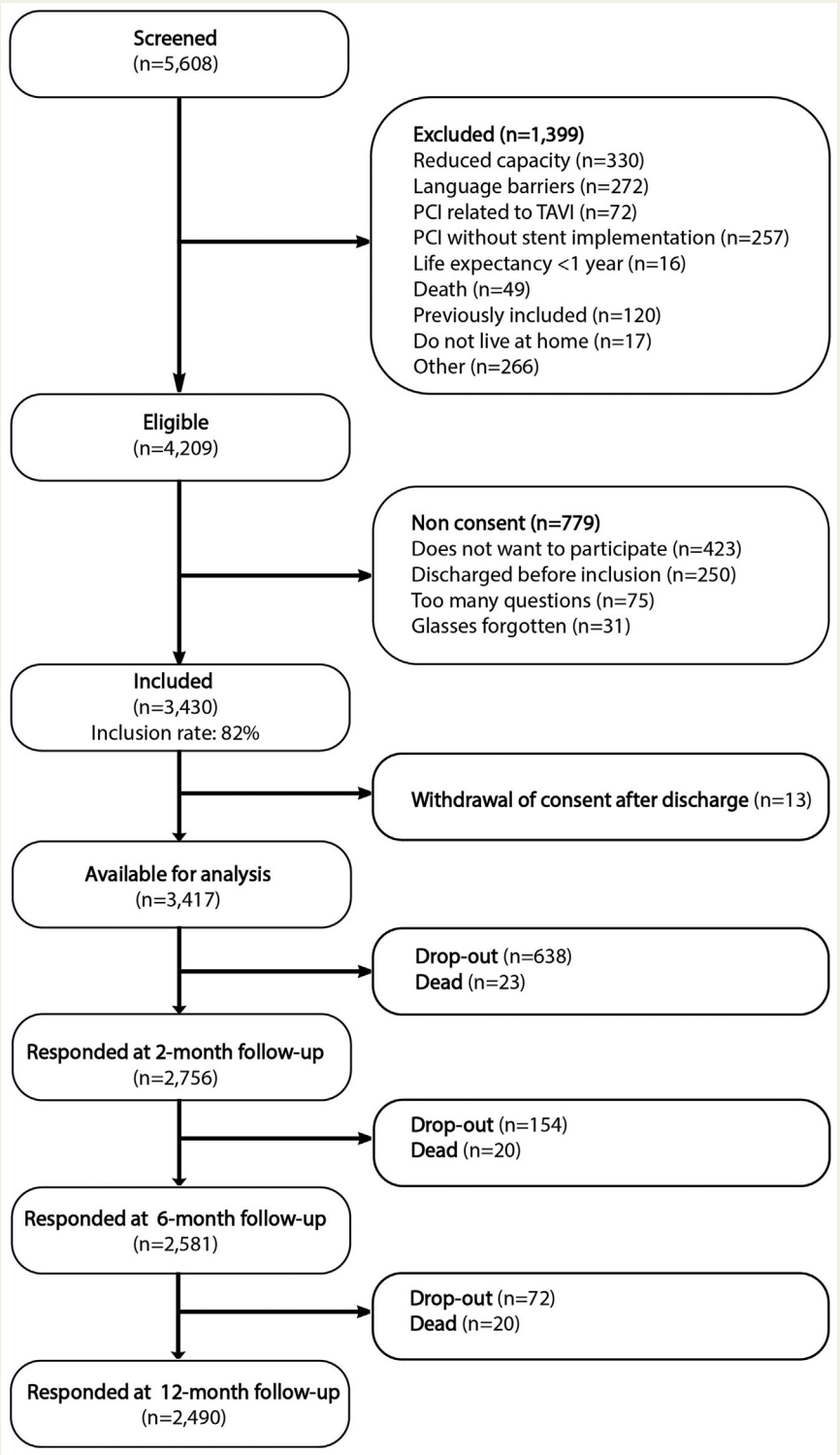

Figure 1 Patient flow in the CONCARD[PCI] study.

pharmacologist and leader of a regional pharmacovigilance centre, and SR, interventional cardiologist) examined a random sample (10%) of the self-reported ADRs and their descriptions with the patients' prescribed drugs at each measuring time point to determine whether the ADRs could be drug-related or not.

Heart Continuity of Care Questionnaire

The Heart Continuity of Care Questionnaire (HCCQ) comprises 33 items and assesses three domains of perceived continuity of care among cardiac patients: informational, relational, and management [14]. Each item is scored on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), with a not applicable option. Two questions related to information about ADRs were used in this study: "I was informed of the potential side-effects that could occur as a result of taking my heart medications" and "I was told what to do if I experienced any side-effects as a result of taking my heart medications". The instrument does not distinguish whether information about ADRs is provided for different types of heart medications (e.g., beta blockers or statins), but investigates information about ADRs in general. To be able to compare clearly defined categories, those reporting strongly agree or somewhat agree were categorised as having received information about ADRs. Those reporting strongly disagree or somewhat disagree were categorised as not having received such information. To reduce recall bias, those reporting hard to decide or not applicable were excluded from the analyses. The HCCQ is reported to be a comprehensive, valid, and reliable instrument for measuring continuity of care from a patient perspective [14,15]. The questionnaire has been translated into Norwegian [16] and Danish, and has shown satisfactory psychometric properties.

Beliefs About Medicines Questionnaire

The Beliefs about Medicines Questionnaire (BMQ) comprises 19 items and is divided into two sections: BMQ-Specific and BMQ-General [17]. Further, it comprises a five-item scale assessing the perceived necessity of prescribed pharmacotherapy (Specific-Necessity) and a six-item scale assessing concerns related to prescribed pharmacotherapy (Specific-Concerns). Each item is scored on a Likert scale ranging from strongly disagree to strongly agree. Thus, total scores range from 5–25 and 6–30 for the Specific-Necessity and Specific-Concerns scale, respectively. Higher scores on the Specific-Necessity scale indicate a higher perceived need for the prescribed medicines, whereas lower scores on the Specific-Concerns scale indicate fewer concerns related to prescribed medicines. This study used the Specific-Concerns scale to determine the level of concerns related to prescribed pharmacotherapy. The instrument has shown satisfactory psychometric properties [17], and has previously been translated and validated for the Norwegian [18] and Danish [19] populations. The internal consistency of the Specific-Concerns scale was satisfactory at 2-month (α=0.82), 6-month (α=0.83), and 12-month follow-up (α=0.84).

Data Collection

A detailed description of the data collection can be found elsewhere [11]. In brief, patient-reported outcomes were collected at baseline registration after PCI (T0), and 2 month (T1), 6 months (T2), and 12 months (T3) after discharge. Sociodemographic characteristics were self-reported during index hospitalisation. Clinical data were collected from medical records and national quality registries upon baseline registration. Data on prescribed pharmacotherapy were collected from medical records and included number and class of both cardiovascular and non-cardiovascular drugs. A comprehensive data dictionary and case report form ensured standardisation of the collected data. Vital status was identified from national registries before follow-up to avoid sending questionnaires to deceased patients or their families. Non-responders received one reminder.

Statistical Analysis

Values are presented as means, standard deviations (SD), and percentages, as appropriate. All the regression models were estimated both with and without adjustment for sex, age, education, cohabitation status, comorbidities, polypharmacy (five or more medications), and index hospital. Covariate-adjusted logistic regression analyses, reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs), were performed. This was performed to determine whether receiving information about ADRs as the independent variable was associated with the incidence of self-reported ADRs as the dependent variable. Whether sociodemographic characteristics as independent variables were associated with receiving information about ADRs as the dependent variable was also examined.

Mean scale scores were computed for the Specific-Concerns Scale of the BMQ. In the event of missing data, the "half rule" was applied, whereby scale scores were computed based on the means of valid items if at least half the items were valid. Thus, patients were excluded from the scale scores if more than three items were missing from the Specific-Concerns scale. Linear regression analysis was performed to determine associations between concerns about prescribed pharmacotherapy as the dependent variable and information about ADRs as the independent variable. For the linear regression analysis, the scale was converted to a 0–100 scale, with higher scores indicating more concerns about prescribed pharmacotherapy. The following subgroup analysis was performed: a logistic regression analysis to investigate whether sex, age and indication for PCI were related to participation. Sex and age distributions in the study sample were compared with data from the Norwegian Registry of Invasive Cardiology (NORIC) [20]. The study population percentages of drug-related ADRs were estimated using Blaker CIs. Statistical significance was set at a $p<0.05$. Analyses were conducted using SPSS Version 26 (IBM corp. SPSS Statistics for Windows, Armonk, NY, USA) and the R package BlakerCI [21].

Ethics

The study complied with the Declaration of Helsinki (2008), and was approved by the Norwegian Regional Committee

for Ethics in Medical Research in Western Norway (REK 2015/57) and the Data Protection Agency in the Zealand region (REG-145-2017) in Denmark. Written informed consent was obtained from all participants, including that participants could withdraw from the study at any time without any explanation.

Results

Patient Characteristics

Of 4,209 eligible patients, 3,430 gave informed consent to participate (inclusion rate 82%). Thirteen patients withdrew their consent after hospital discharge, leaving 3,417 patients available for analysis at baseline (Figure 1). Patients were predominantly male (78%) and 66 years (SD 11, range 20–96 years). A sizeable proportion had previous cardiovascular comorbidities, including hypertension (52%) and hypercholesterolaemia (47%). Most admissions for PCI were due to acute coronary syndrome (62%). Patient characteristics are presented in Table 1.

Information About Potential Adverse Drug Reactions Resulting From Pharmacotherapy

At T1, 2,659 of the included patients responded to the questions from the HCCQ. Of these, 1,019 patients (38%) reported having been informed of ADRs resulting from prescribed pharmacotherapy before discharge, 1,075 patients (40%) reported not having been informed, 511 patients (19%) reported hard to decide, and 51 (2%) reported not applicable (Supplementary Table A2). Patients reporting hard to decide or not applicable were excluded from further analysis. Those living alone (aOR 0.73, 95% CI 0.57–0.92; p=0.008), who were female (aOR 0.57, 95% CI 0.44–0.72; p<0.001), and with three or more versus no comorbidities (aOR 0.61, 95% CI 0.44–0.84; p=0.002) were less likely to receive information about ADRs. A large variation in the percentage of patients reporting that they had been informed was found at the hospital level (33%–77%). In addition, the index hospital was significantly associated with provision of information (overall p<0.001). No significant associations were found for age, education, or polypharmacy (Table 2).

Incidence of Self-Reported Adverse Drug Reactions

At T1, 2,574 of the included patients responded to the question "After PCI, have you experienced ADRs as a result of your drugs?". Of these, 1,089 patients (42%) reported experiencing ADRs within 2 months of discharge. The ADRs related to airways, the gastrointestinal tract, circulatory system, muscle/skeletal system, and skin or hair were most frequently reported (Figure 2). Incidences of self-reported ADRs were significantly lower for those who were informed of ADRs than for those who were not (aOR 0.61, 95% CI 0.50–0.74; p<0.001) (Table 3).

At T2, 2,524 of the included patients responded to the question "Within the last four months, have you experienced ADRs as a result of your drugs?". Of these, 1,236 patients (49%) reported experiencing ADRs between 2 and 6 months after discharge. As at T1, most ADRs were related to airways, the gastrointestinal tract, circulatory system, muscular/skeletal system, and skin or hair (Figure 2). Incidences of self-reported ADRs were significantly lower for those who were informed of ADRs than for those who were not (aOR 0.60, 95% CI 0.49–0.74; p<0.001) (Table 3).

At T3, 2,343 of the included patients responded to the question "Within the last six months, have you experienced ADRs as a result of your drugs?". Of these, 941 patients (40%) reported experiencing ADRs between 6 and 12 months after discharge. Self-reported ADRs were similar to previous measuring points (Figure 2). Incidences of self-reported ADRs were significantly lower for those who were informed of ADRs than for those who were not (aOR 0.57, 95% CI 0.46–0.71; p<0.001) (Table 3).

Validation of Self-Reported Adverse Drug Reactions

The subsamples used to validate patient-reported ADRs consisted of 113, 106, and 96 patients at T1, T2, and T3, respectively. Almost all ADRs in the subsamples were regarded as drug related. At all measuring time points, the lower confidence limit for the population percentage of ADRs regarded as drug related was at least 96%.

Concerns Related to Prescribed Pharmacotherapy

For the total study population, the mean score on the BMQ Specific-Concerns Scale (0–100) was 45.0 (T1), 44.7 (T2), and 44.1 (T3). After adjusting for sociodemographic and clinical variables, patients who were not informed of ADRs scored higher than those who were informed at all measuring points, indicating increased concerns about prescribed pharmacotherapy (p<0.001 for all comparisons) (Table 4, Supplementary Table A3).

Discussion

In this prospective, multicentre cohort study of patients after PCI, a substantial proportion of the patients reported that they were not informed about potential ADRs from prescribed pharmacotherapy. Incidences of self-reported ADRs were significantly lower at all measuring time points for those who were informed of ADRs at discharge compared with those who were not informed. In addition, those not informed reported significantly more concerns related to prescribed pharmacotherapy. Those less likely to receive information about ADRs were female, living alone, and had three or more comorbidities. Figure 3 presents a graphical abstract of this study and its findings.

A sizeable proportion of patients recalled experiencing ADRs between hospital discharge and 2 months, 6 months,

Table 1 Baseline characteristics of patients undergoing percutaneous coronary intervention.

Characteristics	Total study sample (n=3,417)[a]	Informed about ADRs (n=1,019)[b]	Not informed about ADRs (n=1,075)[c]	Excluded from analyses (n=562)[d]
Sex, men	2,671 (78)	847 (83)	786 (73)	421 (82)
Age, years, mean (SD)	66 (11)	66 (10)	66 (10)	67 (10)
Living alone	750 (24)	181 (19)	247 (25)	105 (22)
Ethnicity				
Native born	2,829 (92)	880 (93)	928 (93)	444 (93)
Born of immigrant parents	114 (4)	38 (4)	32 (3)	18 (4)
Immigrant	135 (4)	32 (3)	35 (4)	14 (3)
Education				
Primary school	640 (20)	176 (18)	199 (19)	95 (19)
Vocational school	1,375 (43)	446 (46)	428 (42)	211 (43)
Upper secondary school	298 (9)	90 (9)	96 (9)	47 (10)
University college or university, <4 years	488 (15)	146 (15)	167 (16)	87 (18)
University college or university, ≥4 years	380 (12)	122 (12)	142 (14)	50 (10)
Employment				
Full-time work	1,056 (31)	336 (33)	342 (32)	145 (28)
Part-time work	162 (5)	55 (5)	45 (4)	33 (7)
Retired	1,615 (47)	508 (50)	528 (49)	279 (55)
Other	366 (17)	104 (12)	160 (15)	105 (10)
Total household gross income (Euros)				
≤15,000	68 (2)	17 (2)	20 (2)	25 (5)
15,000^{+}–22,000	255 (8)	77 (8)	69 (7)	35 (7)
22,000^{+}–33,000	449 (15)	138 (15)	123 (12)	73 (15)
33,000^{+}–44,000	425 (14)	127 (13)	128 (13)	80 (17)
44,000^{+}–60,000	507 (17)	143 (15)	169 (17)	89 (19)
66,000^{+}–77,000	448 (15)	153 (16)	154 (16)	69 (15)
77,000^{+}–93,000	307 (10)	108 (11)	103 (10)	42 (9)
>93,000	590 (19)	185 (20)	223 (23)	82 (17)
Smoking status				
Never smoker	943 (30)	311 (32)	302 (29)	142 (29)
Former smoker	1,712 (54)	542 (55)	567 (55)	278 (57)
Current smoker	529 (17)	134 (14)	159 (16)	67 (14)
Indication for PCI				
Stable coronary artery disease	1,023 (30)	281 (28)	359 (33)	157 (31)
Unstable angina pectoris	441 (13)	109 (11)	149 (14)	72 (14)
Non-ST-segment elevation myocardial infarction	916 (27)	273 (27)	289 (27)	136 (27)
ST-segment elevation myocardial infarction	742 (22)	257 (25)	193 (18)	113 (22)
Other	294 (9)	99 (10)	85 (8)	33 (7)
Previous PCI	875 (26)	235 (23)	282 (26)	123 (24)
Previous CABG	312 (9)	86 (9)	101 (10)	59 (12)
Previous cardiovascular comorbidities				
Atrial fibrillation/flutter	406 (12)	122 (12)	125 (12)	73 (15)
Coronary artery disease	1,156 (34)	305 (30)	385 (36)	175 (35)
Chronic heart failure	264 (8)	86 (9)	68 (6)	42 (8)
Hypercholesterolemia	1,569 (47)	478 (47)	505 (47)	225 (45)
Hypertension	1,773 (52)	499 (49)	561 (53)	273 (54)
Myocardial infarction	704 (21)	176 (17)	243 (23)	96 (19)
Peripheral artery disease	205 (6)	39 (4)	75 (7)	29 (6)
Previous medical comorbidities				
Anxiety and depression	333 (10)	85 (8)	100 (9)	42 (8)
Cancer	395 (12)	117 (12)	129 (12)	51 (10)

Table 1. (continued).

Characteristics	Total study sample (n=3,417)[a]	Informed about ADRs (n=1,019)[b]	Not informed about ADRs (n=1,075)[c]	Excluded from analyses (n=562)[d]
Cerebrovascular disease	215 (6)	59 (6)	60 (6)	39 (8)
Chronic obstructive pulmonary disease	247 (7)	75 (7)	69 (7)	29 (6)
Chronic renal failure	156 (5)	36 (4)	48 (5)	21 (4)
Diabetes (insulin)	210 (6)	52 (5)	57 (5)	24 (5)
Diabetes (tablets)	495 (15)	130 (13)	130 (12)	67 (13)
Number of comorbidities				
No comorbidity	366 (11)	136 (14)	102 (10)	55 (11)
One comorbidity	471 (14)	154 (15)	144 (14)	70 (14)
Two comorbidities	500 (15)	157 (16)	153 (15)	80 (16)
Three or more comorbidities	1,994 (60)	551 (55)	647 (62)	293 (59)
Medications at discharge				
ACE-inhibitors	925 (27)	266 (26)	280 (26)	141 (28)
Anticoagulants	715 (21)	216 (21)	216 (20)	123 (24)
ARBs	805 (24)	228 (22)	265 (25)	127 (25)
Acetylsalicylic acid	3,285 (96)	980 (96)	1,045 (97)	488 (96)
Beta-blockers	1,790 (53)	525 (52)	575 (53)	259 (51)
Calcium channel blockers	700 (21)	189 (15)	233 (22)	117 (23)
Clopidogrel	1,596 (47)	440 (43)	531 (49)	245 (48)
Diuretics	613 (18)	196 (19)	198 (18)	111 (22)
Prasugrel	89 (3)	28 (3)	25 (2)	9 (2)
Lipid-lowering agents	3,151 (92)	1,019 (100)	1,071 (99)	503 (98)
Ticagrelor	1,613 (47)	514 (50)	494 (46)	232 (45)
≥5 medications	2,084 (61)	608 (74)	645 (68)	315 (62)

Data are shown as n (%) or mean (SD).

[a]The total study sample also includes those with missing items on the Heart Continuity of Care Questionnaire.

[b]Those reporting strongly agree or somewhat agree to receiving information about adverse drug reactions on the Heart Continuity of Care Questionnaire.

[c]Those reporting strongly disagree or somewhat disagree to receiving information about adverse drug reactions on the Heart Continuity of Care Questionnaire.

[d]Those who answered hard to decide or not applicable to receiving information about adverse drug reactions on the Heart Continuity of Care Questionnaire.

Abbreviations: ACE-inhibitors, angiotensin-converting-enzyme inhibitors; ADRs, adverse drug reactions; ARBs, angiotensin II receptor blockers; CABG, coronary artery bypass grafting; CAD, coronary artery disease; PCI, percutaneous coronary intervention; SD, standard deviation.

and 12 months after discharge. This was expected because ADRs as a result of cardiovascular drugs are common [2,3]. Adverse drug reactions resulting from cardiovascular drugs also more often result in hospitalisation compared with other drugs [22]. Although this study validated self-reported ADRs in a randomly selected subsample at all measuring time points, the results provide a consistent response that almost all self-reported ADRs were drug related. Given the increased propensity to experience ADRs from cardiovascular drugs, providing evidence-based information is particularly important for this patient group.

Studies investigating the impact of informing patients about ADRs have produced conflicting results [5,6]. Those informed about ADRs reported significantly fewer ADRs than those not informed in the current study. This is consistent with results from a systematic review of 17 randomised controlled studies (RCTs), where only four of the included studies reported significantly more ADRs in those who were informed [6]. However, all but two of the included studies had a relatively small study sample (n≤249) and the methods for delivering information were heterogeneous, warranting further research. Furthermore, reporting of ADRs is often biased in RCTs due to heterogeneous disease definitions, different reporting thresholds, and incomplete reporting [23]. Thus, results from the current cohort study, with a large and representative study sample, add important information to the existing literature. Several methods have been proposed to frame ADR information, including numerical information (e.g., "common, 1 in 10 are affected") [24]. Positively framing this information (e.g., "uncommon, 9 in 10 are not affected") upholds informed consent and does not infringe on patient autonomy [25]. The current study did not investigate how the information about ADRs was provided, the content of the information, or which drugs patients were informed about (e.g., specific drug classes,

Table 2 Association between sociodemographic and clinical characteristics and receiving information about potential adverse drug reactions resulting from prescribed pharmacotherapy.

	OR	95% CI	p-value
Female sex	0.57	0.44–0.72	<0.001
Age	1.01	1.00–1.02	0.151
Education			[a]0.901
Primary school (reference)			
Vocational school	0.94	0.72–1.22	0.636
Upper secondary school	1.01	0.69–1.47	0.977
College/university <4 years	0.86	0.62–1.19	0.358
College/university ≥4 years	0.92	0.65–1.30	0.648
Living alone	0.73	0.57–0.92	0.008
Polypharmacy*	1.08	0.87–1.34	0.481
Comorbidities			[a]0.005
No comorbidities (reference)			
One comorbidity	0.88	0.61–1.28	0.511
Two comorbidities	0.78	0.54–1.13	0.195
Three or more comorbidities	0.61	0.44–0.84	0.002
Hospital			[a]<0.001
Hospital 1 (reference)			
Hospital 2	1.54	1.12–2.13	0.008
Hospital 3	1.13	0.82–1.55	0.465
Hospital 4	1.97	1.41–2.76	<0.001
Hospital 5	2.99	2.13–4.19	<0.001
Hospital 6	3.12	2.20–4.42	<0.001
Hospital 7	3.05	2.21–4.21	<0.001

*Currently using five or more medications.
[a]Overall p-values for education, comorbidities, and hospital.
Abbreviations: CI, confidence intervals; OR, odds ratio.

new drugs vs previously prescribed drugs). However, regardless of the method utilised, and the content of the information, those recalling being informed reported significantly fewer ADRs.

Concerns about ADRs are a known barrier to medication adherence [26,27]. After PCI, medication adherence is pivotal to avoid future cardiac events and worsened patient outcomes. Thus, patient education and counselling about warning signs of ADRs, how to cope with transient ADRs, and when and who to contact if complications arise, could increase patient satisfaction and adherence. The current study did not investigate whether information about ADRs affected medication adherence; however, it demonstrated that those recalling being informed reported fewer concerns about prescribed pharmacotherapy.

Associations between sociodemographic and clinical variables and receiving information about ADRs appear to be under-investigated. This study found that those living alone, females, and patients with three or more comorbidities were less likely to receive information about ADRs. The likelihood of receiving information about ADRs differed between hospitals, indicating that there are structural differences, such as the time available for patient education and counselling, and the amount of information provided to patients. However, after adjusting for index hospital in the regression models, the results were similar. Sex-specific differences in cardiovascular pharmacotherapy related to body composition and physiology, drug pharmacokinetics and pharmacodynamics are well known [28]. In addition, women are more prone to experience and report ADRs as a result of prescribed pharmacotherapy [29]. Further, patients with cardiovascular diseases are particularly vulnerable to ADRs due to comorbidity and age-related physiological changes. Multiple comorbidities are one explanatory factor, as this inevitably leads to polypharmacy, which increases the risk of drug-to-drug interactions and the subsequent risk of experiencing ADRs [30]. Given the increased propensity to experience ADRs, special attention should be given to providing comorbid patients with information about ADRs, including involving next of kin and collaborating with primary care services. Moreover, shared decision-making is particularly important in older comorbid patients, since cognitive and functional status, polypharmacy, and heterogeneous care goals complicate decision-making [31].

Informing patients about ADRs resulting from prescribed pharmacotherapy is especially important in the present digital era. There are numerous health information sources on the internet; however, the quality greatly varies [32]. This is concerning because patients often seek health information on the internet, including information about ADRs, which they do not discuss with clinicians [33]. In addition, the mass media, including social media, constantly bombard consumers with health information of varying quality, making it difficult for patients to find trustworthy sources and reliable guidance when they need it. Further, the communication of disputed research in the mass media may have adverse consequences [34].

With that in mind, informing patients about ADRs does not necessarily prevent ADRs. However, being informed about ADRs might help patients prevent and tolerate transient ADRs, such as headaches and nausea, and to seek medical attention for ADRs that are more serious, such as an increased bleeding tendency [6]. This underlines the importance of patient education and counselling on all aspects of prescribed pharmacotherapy to alleviate concerns and reduce the incidence of ADRs.

Study Limitations

The use of serial measures of patient-reported outcomes in this prospective multicentre cohort study was a major strength since patient-reported outcome measures are increasingly recognised by policymakers as an important tool that aids decision-making. Furthermore, it achieved a high inclusion rate (82%) and a large study sample (n=3,417) derived from seven high-volume referral PCI centres, thereby strengthening the transferability of the results. Moreover, high response rates at T1 (78%), T2 (74%), and T3 (69%) were achieved. To ensure the relevance of the research questions and choice of questionnaires, patient representatives were involved in all aspects of the study.

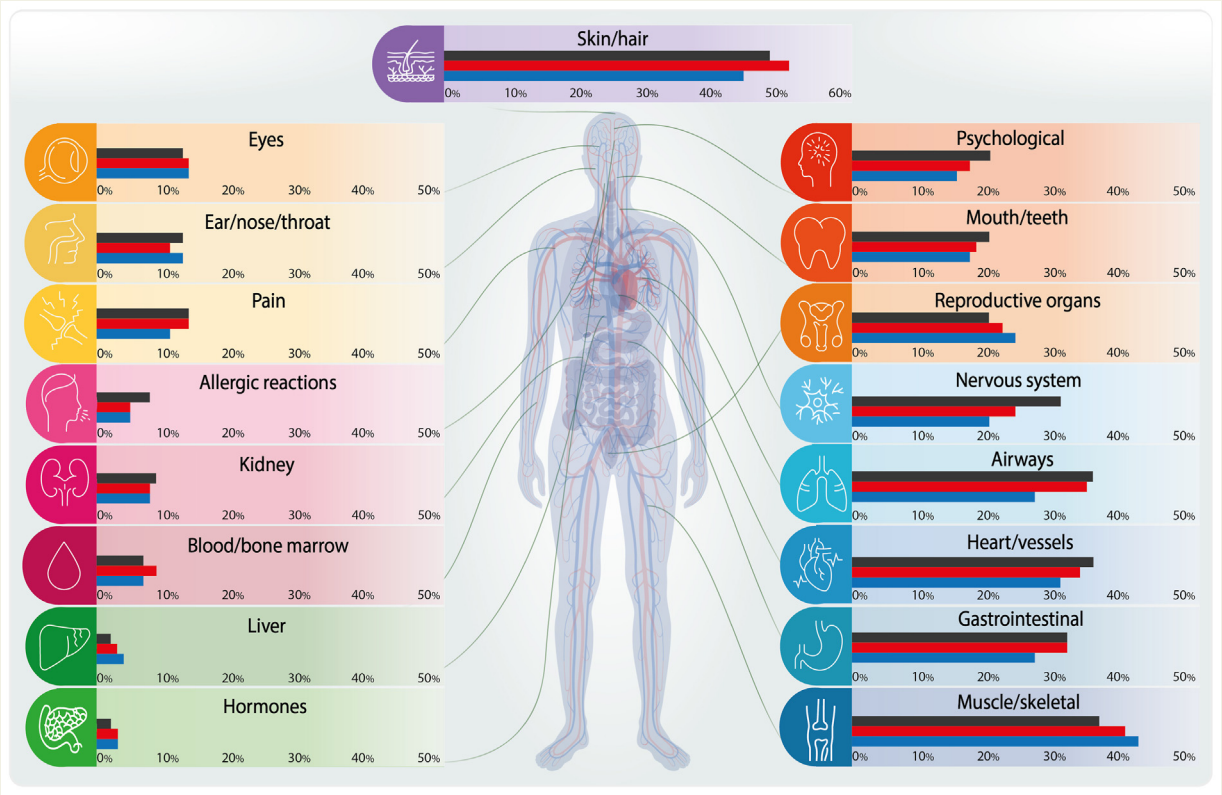

Figure 2 Self-reported adverse drug reactions and the origin of these. Black bar: 2-month follow-up. Red bar: 6-month follow-up. Blue bar: 12-month follow-up.

This study did have some limitations. First, drugs may have been deprescribed or changed during follow-up. As a result, those reporting ADRs at T1 may not have reported ADRs at T3, and those reporting ADRs at T3 may have started a new drug. This also raises the possibility of adverse drug events, unrelated to the prescribed pharmacotherapy at discharge but with temporal association to the study period, being reported as ADRs. However, due to restructuring of the Norwegian Prescription Database, data on prescribing among the study participants are currently unavailable. Second, recall bias may have been introduced as patients completed the HCCQ 2 months after discharge. Patients who were unsure about whether they had received information about ADRs were therefore excluded from the analyses. Third, large variation in the provision of information was found between participating centres. Index hospital was therefore added as an adjustment variable in the regression models (Supplementary Table A4). Fourth, the content of the patient physician post-care conversation was not recorded and it is therefore unknow whether ADRs were key in this conversation. However, regardless of the method utilised to inform patients about ADRs, and the content of such conversations, those who were informed reported significantly fewer ADRs and concerns regarding prescribed pharmacotherapy at all measuring time points. Furthermore, the study was not designed to assess or compare information practices among clinicians, but to provide a patient perspective on the information provided about potential ADRs. Finally,

Table 3 Self-reported adverse drug reactions (ADRs) in those informed of potential ADRs compared with those who were not.

	Unadjusted			Adjusted[a]		
	OR	95% CI	p-value	OR	95% CI	p-value
Two-month follow-up	0.54	0.45–0.65	<0.001	0.61	0.50–0.74	<0.001
Six-month follow-up	0.56	0.46–0.67	<0.001	0.60	0.49–0.74	<0.001
Twelve-month follow-up	0.51	0.42–0.63	<0.001	0.57	0.46–0.71	<0.001

[a]Adjusted for age, sex, education, polypharmacy (currently using five or more medications), comorbidities, cohabitation status, and index hospital.
Abbreviations: CI, confidence interval; OR, odds ratio.

Table 4 Concerns regarding prescribed therapy in those not informed of potential adverse drug reactions compared with those who were.[a]

	Difference[b]	95% CI	p-value
Two-month follow-up	7.33	5.34–9.33	<0.001
Six-month follow-up	5.90	3.66–8.14	<0.001
Twelve-month follow-up	4.08	1.87–6.28	<0.001

[a]Adjusted for age, sex, education, cohabitation status, polypharmacy (currently using five or more medications), comorbidities, and cohabitation status.

[b]Mean score on the Specific-Concerns Scale of the Beliefs About Medicines Questionnaire (0–100). Higher scores indicate higher levels of concern.

Abbreviations: CI, confidence interval.

Norwegian patients who declined to participate in the study were older and more often had other indications for PCI than those participating (Supplementary Table A5). However, the propensity to complete the questionnaire at follow-up increased with age for those remaining in the study (Supplementary Table A6). Adding additional sociodemographic and clinical variables in the models would have been preferable and might have influenced the findings. However, the regional ethics committees only allowed comparison of participants with non-participants on a limited number of factors. Nevertheless, sex and age distributions were comparable with data provided from NORIC [20] for this patient population, where the proportion of men undergoing PCI was 77% with an average age of 68 years, strengthening the generalisability of the results.

Conclusion

A substantial proportion of patients reported that they were not informed about potential ADRs from prescribed pharmacotherapy after PCI. Those informed about ADRs had a lower incidence of self-reported ADRs and fewer concerns about prescribed pharmacotherapy at all measuring time points. Thus, patient education about ADRs seems to be key in improving patient outcomes. Furthermore, these results show that women, those living alone, and those with multimorbidity may be at higher risk of not being informed about ADRs as well as experiencing ADRs. Therefore, it is suggested that special attention should be paid to these subgroups. Future studies should assess whether tailored and structured information about ADRs will further improve patient outcomes. A prerequisite is more specific self-reporting of ADRs with updated prescribing data.

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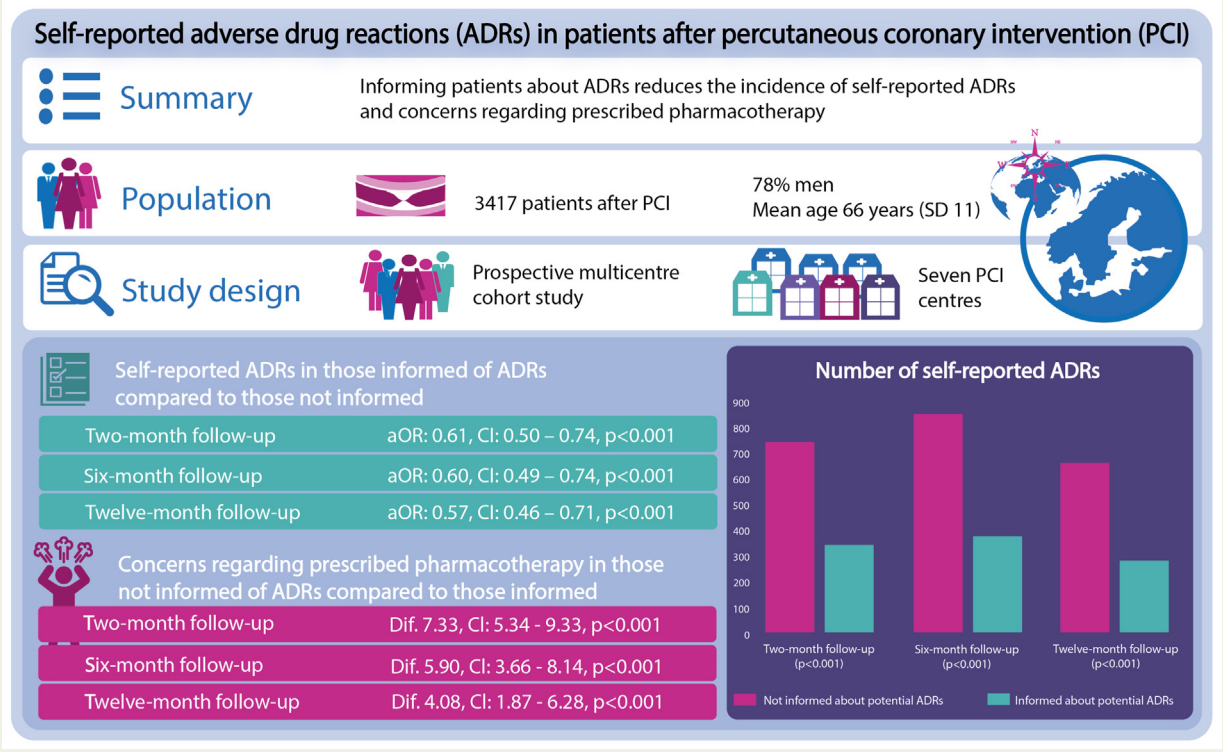

Figure 3 Self-reported adverse drug reactions (ADRs) after percutaneous coronary intervention (PCI).

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Authors' Contributions

TMN, TRP, and JS contributed to the study design. HA is chairing the Scientific Advisory Board in CONCARD^{PCI}, and provided advice on the study design and statistical analyses. TWL and TRP analysed and interpreted the data. JS and SR examined a random sample of the self-reported ADRs and their descriptions with the patients' prescribed drugs. TRP wrote the first draft of the paper. All authors critically revised the manuscript, and read and approved the final draft. The corresponding author attests that all listed authors meet authorship criteria and no others meeting the criteria have been omitted.

Data Availability

No additional data available.

Conflict of Interest

None.

Appendices

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2023.12.005.

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