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ORIGINAL ARTICLE

The impact of including a medication review in an integrated care pathway: A pilot study

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Abstract

Aim: The objective of the present study was to measure the impact of the intervention of combining a medication review with an integrated care approach on potentially inappropriate medications (PIMs) and hospital readmissions in frail older adults.

Methods: A cohort of hospitalized older adults enrolled in the French PAERPA integrated care pathway (the exposed cohort) was matched retrospectively with hospitalized older adults not enrolled in the pathway (unexposed cohort) between January 1st, 2015, and December 31st, 2018. The study was an analysis of French health administrative database. The inclusion criteria for exposed patients were admission to an acute care department in a general hospital, age 75 years or over, at least three comorbidities or the prescription of diuretics or oral anticoagulants, discharge alive and performance of a medication review.

Results: For the study population (n = 582), the mean ± standard deviation age was 82.9 ± 4.9 years, and 380 (65.3%) were women. Depending on the definition used, the overall median number of PIMs ranged from 2 [0;3] on admission to 3 [0;3] at discharge. The intervention was not associated with a significant difference in the mean number of PIMs. Patients in the exposed cohort were half as likely to be readmitted to hospital within 30 days of discharge relative to patients in the unexposed cohort.

Conclusion: Our results show that a medication review was not associated with a decrease in the mean number of PIMs. However, an integrated care intervention including the medication review was associated with a reduction in the number of hospital readmissions at 30 days.

KEYWORDS
hospital readmission, integrated care, older adults, potentially inappropriate medications

1 | BACKGROUND

Potentially inappropriate medications (PIMs) and suboptimal care trajectories that lead to hospital readmission are challenging problems in older people with comorbidities and polypharmacy.[1] According to the literature data, the prevalence of PIMs among hospitalized adults aged 65 years and older ranges from 25% to 56%.[2,3] PIMs are associated with comorbidities, polypharmacy, geriatric syndrome and thus an elevated risk of adverse drug reactions, falls, hospital readmission and death.[4–7] In older adults, the rate of hospital readmission 1 month after the initial discharge can vary from 10% to 24%, depending on the type of readmission and the patient's characteristics (age, comorbidities, frailty, etc).[8] Hospital readmission is associated with an elevated risk of subsequent hospital readmissions and death.[8–10]

Medication reviews have been developed to help prescribers improve the quality of prescriptions in older adults with polypharmacy and multiple comorbidities, and thus decrease the prevalence of PIMs.[7,11–13] The results of many randomized, controlled trials (RCTs) have shown that medication reviews are effective for reducing PIMs.[14–17] However, RCTs and systematic reviews have failed to provide evidence of effectiveness with regard to reducing hospital readmission.[18–21] For example, a recent large European multicenter RCT did not find an effect of medication review on drug-related hospital readmission.[22,23] Integrated care has been shown to improve the continuity of care among frail older adults by increasing coordination and communication between healthcare professionals.[24–26] Integrated care effectively improves outcomes for the hospital and the patient (reduced hospital readmissions, a shorter length of stay, etc).[25] Including medication review in integrated care pathways might therefore help to reduce PIMs and hospital readmission rates among older adults.

The French nationwide Personnes Agées En Risque de Perte d'Autonomie (PAERPA) project was set up in 2014 with the goal of optimizing care pathways and notably reducing hospital readmissions for frail adults aged over 75 years.[27] In the Hauts-de-France area, a medication review was combined with an integrated care approach. The objective of the present study was to measure the impact of this intervention on PIMs and hospital readmissions in frail older adults. We hypothesized that the inclusion of a medication review would reduce the numbers of PIMs and hospital readmissions per hospital stay.

What is already known about this subject

- Medication review is effective in randomized clinical trials of potentially inappropriate medications. The implementation of integrated care improves the nursing of older patients, but its impact on hospital readmissions has not been proven.

What this study adds

- Our study shows that the introduction of integrated care on hospital admission is correlated with a reduction in hospital readmission. We used the difference-in-difference method to make up for the absence of randomization of patients. We also included an evaluation of usual care practices within the framework of a project developed by regional health agencies.

2 | METHOD

2.1 | Study design, setting, intervention and data sources

We analysed a cohort of older adults enrolled in the PAERPA project (ie, the exposed cohort) matched with a retrospective, control cohort of hospitalized adults not enrolled in the intervention (ie, the unexposed cohort). The study period ran from 1 January 2015 to 31 December 2018 in the Valenciennois-Quercitain area of France. To measure the effect of the intervention, we used data extracted from the French health administrative database to retrospectively build a 1:1-matched unexposed cohort for comparison with the exposed cohort.

This intervention was part of an innovative integrated care programme that included actions at the macro, meso and micro levels.[28,29] For example, the macro-level actions included specific governmental decrees, the meso-level actions included support from the regional health agency and from the PAERPA project team for the corresponding geographic area (Valenciennois-Quercitain) and the micro-level actions included specific funding and reimbursements for healthcare professionals. The PAERPA programme also included integrated care with an in-hospital medication review and then structured follow-up in the community by the patient's family physician (FP) and community pharmacist.[30] Both components were evaluated in the present study. A care coordinator coordinated the actions of the in-hospital team and the community professionals.[31] The hospital-based team (comprising a geriatrician, a pharmacist and a nurse) conducted a medication review first on hospital admission and then again on discharge. The medication review included suggesting medication changes to the attending physician's team if necessary, a medication plan, counselling and patient education on medication use.[32] Furthermore, the patient's FP and community pharmacist were informed of the medication review's recommendations. Determination of FP and community pharmacist agreement to participate came before approaching the patient.

For all participating older adults, data on age, sex, date of hospital admission and date of hospital discharge were recorded in a specific PAERPA implementation database. The French health administrative database is formed by linking a health insurance database (the SNIIRAM database), a hospital database (the PMSI database) and a death register indicating the cause of death (the CépiDC database). The database

collects information on out-of-hospital events (eg, physician and pharmacist visits, drug prescriptions) and in-hospital events (eg, hospital stays, diagnoses, drug prescriptions, surgical and other medical procedures).[33] Under French regulations, individual-level linkage between the health administrative database and the PAERPA implementation database through a person's unique identifier, name or date of birth is not allowed because these items of information are not accessible for research purposes. Probabilistic linkage through the hospital admission date and the discharge date is, however, allowed. Hence, probabilistic linkage is the recommended procedure for analyses of the health administrative database.[34] The extracted data were converted into the Observational Medical Outcomes Partnership format.[35]

2.2 | Study population

2.2.1 | Inclusion and exclusion criteria in the exposed cohort

Patients admitted to an acute care department via the emergency department at Denain General Hospital (Denain, France) were eligible if they met all the following criteria: (i) age 75 or over, (ii) residence in the Valenciennois-Quercitain area, (iii) at least three comorbidities or the prescription of diuretics or oral anticoagulants, (iv) discharge alive and (v) registration with an FP and a community pharmacist who agreed to participate in the study. Cognitive disorder was not an exclusion criteria and informed consent could be provided by the next of kin, family caregivers or legal guardian of an older person with cognitive disorder. Each patient could be enrolled in the PAERPA project once a year.

2.2.2 | Data extraction for the exposed cohort

For each patient in the exposed cohort, we extracted the year of birth, sex, date of hospital admission and date of hospital discharge from the PAERPA implementation database. Hospital stays by the adults in the exposed cohort were linked probabilistically to hospital stays in the health administrative database. The probabilistic linkage was based on the year of birth, sex, date of hospital admission and date of discharge.[34] Hospital stays for which no medication was delivered in the 90 days prior to admission (according to the health administrative database) or that could not be linked to a hospital stay by a member of the exposed cohort were excluded from the analysis.

2.2.3 | Inclusion and exclusion criteria in the unexposed cohort

Each hospital stay by a person in the exposed cohort was matched with a hospital stay by a person in the unexposed cohort according to the following criteria: year of birth in classes (1910-1925, 1926-1930, 1931-1935, 1936-1945), sex, semester of hospital admission (eight semesters, from 2015 to 2018), the Charlson Comorbidity Index (CCI) in classes (0-2, 3-4, 5-6, >6),[36,37] the number of medications in classes (0-5, 6-10, >10) and the number of hospitalizations in the previous year. We considered these parameters because they are known to be associated with polypharmacy, PIMs and hospital readmissions. The semester was included because it takes account of the training given to the region's healthcare professionals during the study period. Indeed, the information provided to the healthcare professionals was disseminated more intensively at the beginning of the study period than at the end of the study period. Because of work organization in France, where physicians work on the same ward continuously, training needs decrease over time. All stays ending in the patient's death, in hospitals where a medication review was part of routine care or in hospitals which had a multidisciplinary geriatrics team were not considered in the matching process.

2.2.4 | Data extraction for the exposed and unexposed cohorts

Using the administrative database, we extracted the year of birth, sex, date of hospital admission, date of discharge, CCI, drugs delivered during the 90 days before hospital admission and the 90 days after discharge, and the number of hospitalizations 1 year before admission and 1 year after discharge.

2.2.5 | Primary outcome

The primary outcome was the number of PIMs per hospital stay in the 90 days after discharge. Medications were coded using the Anatomical Therapeutic Chemical classification. Medications with codes J01 and J02 (antibacterials and antimycotics for systemic use) were not considered because they are often given for short time periods. We also measured the number of PIMs per hospital stay in the 90 days prior to hospital admission. PIMs were defined according to the French Laroche list, the Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) criteria and the EU(7)-PIM list.[38–40]

2.2.6 | Secondary outcomes

Hospital readmission was defined as hospitalization within 30 days of discharge from hospital. For hospital stays that occurred before the intervention, we recorded the number of hospitalizations less than 30 days apart in the year prior to the intervention-related hospital stay.

2.3 | Analysis

The unit of analysis was the hospital stay. Qualitative variables were described as the frequency (percentage). Continuous quantitative

variables were described as the mean (standard deviation, SD) when distributed normally (according to Henry's line and the Kolmogorov test) or as the median (interquartile range, IQR) if not. Discrete quantitative variables were described as the median (IQR).

The exposed and unexposed cohort were matched on six different criteria: year of birth in classes (1910-1925, 1926-1930, 1931-1935, 1936-1945), sex, semester of hospital admission (eight semesters, from 2015 to 2018), the CCI in classes (0-2, 3-4, 5-6, >6), the number of medications in classes (0-5, 6-10, >10) and the number of hospitalizations in the previous year.

We used a difference-in-differences estimation to evaluate the association between the intervention and the outcomes.[41–43] This approach is recommended for nonrandomized interventions and strengthens causal inferences based on observational data by disentangling the intervention's impact from (i) permanent differences between unexposed and exposed cohorts (ie, potential confounding factors) and (ii) time trends in the outcome that are unrelated to the intervention. Hence, a difference-in-differences estimation compares the outcomes before and after the intervention in the exposed *versus* unexposed cohorts.

Conditional logistic regression was used as a sensitivity analysis to compare the risk of hospital readmission after having received the intervention *versus* not having received the intervention, ie in the 1:1-matched exposed and unexposed cohorts.[44,45]

2.4 | Ethical approval

In France, routine care does not require written informed consent from patients (ie, consent for research), as it falls outside the scope of the French Law on Research on the Human Person (Jardé law). Consent for routine care was sought as it should be in any care, and it was traced in the framework of the PAERPA experimentation. All the older adults in the exposed cohort gave their verbal, informed consent. Data on the unexposed and exposed cohorts were extracted by the Hauts-de-France Regional Health Authority after the study database had been registered with the French National Data Protection Commission (Commission Nationale de l'Informatique et des Libertés, Paris, France). All data were anonymized. In line with French legislation on retrospective studies of routine clinical practice, approval by an investigational review board was neither required nor sought.

3 | RESULTS

3.1 | Characteristics of the exposed and unexposed cohorts

Between 1 January 2015 and 31 December 2018, 328 hospital stays were considered for inclusion in the exposed cohort (Figure 1). The selection of patients exposed to the intervention is provided in Data S1. Probabilistic matching with hospital stays in the administrative database was feasible for 291 (88.7%) of these 328 stays, corresponding to 273 older adults and thus forming the exposed cohort. The unexposed cohort comprised 291 older adults identified in the administrative database and matched with the older adults in the exposed cohort.

In the exposed cohort, the mean (SD) age was 83.10 (4.60) years and 190 of the patients (65.30%) were women. In the unexposed cohort, the mean age was 82.70 (5.21) years and 190 of the patients (65.30%) were women (Table 1). The two cohorts were similar in

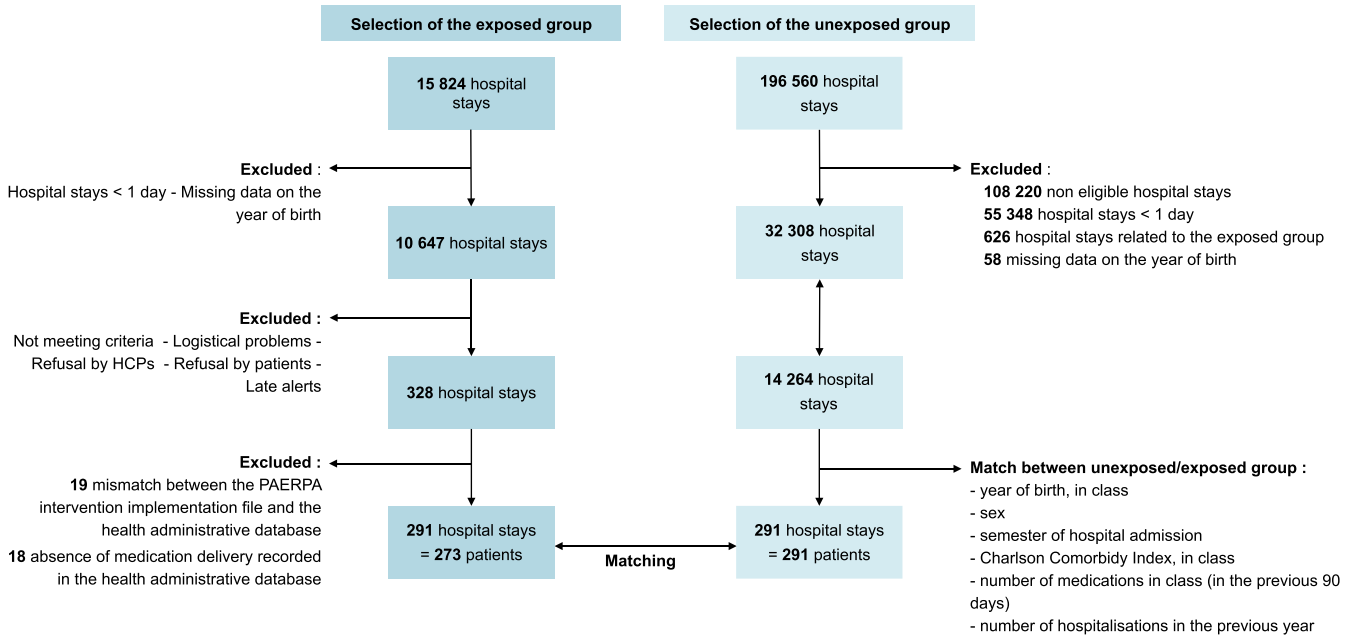

FIGURE 1 Flow chart for the exposed and unexposed cohorts (n = 582)

TABLE 1 Characteristics (matching criteria and mean number of PIMs per hospital stay) in the exposed and unexposed cohorts

Matching criteria	Exposed cohort (n = 291 hospital stays) Mean (SD)	Unexposed cohort (n = 291 hospital stays) Mean (SD)	*P* value
Age (years)	83.10 (4.60)	82.70 (5.21)	
Women	190 (65.30)	190 (65.30)	
CCI	2.80 (2.57)	2.76 (2.77)	
Mean number of hospitalizations in the previous year	0.58 (1.00)	0.58 (1.00)	
Mean number of drugs delivered during the previous 90 days	13.30 (5.39)	12.70 (4.54)	
Length of stay (days)	8.82 (5.13)	7.44 (7.50)	.09
PIMs on hospital admission			
Laroche list	0.42 (0.72)	0.36 (0.60)	.32
EU(7)-PIM list	2.80 (1.90)	2.75 (1.89)	.71
STOPP criteria	2.77 (1.96)	2.58 (1.96)	.25

Abbreviations: CCI, Charlson Comorbidity Index; PIM, potentially inappropriate medication; STOPP, Screening Tool of Older Persons' Potentially Inappropriate Prescriptions.

TABLE 2 Outcomes and estimated effects on PIMs and hospital readmission

	Exposed cohort (n = 291 hospital stays) Mean (SD)	Unexposed cohort (n = 291 hospital stays) Mean (SD)	Difference-in-differences estimate	
			Estimate (SD)	*P* value
PIMs in the 90 days following discharge				
Laroche list	0.39 (0.62)	0.33 (0.61)	0.02 (0.08)	*.82*
EU(7)-PIM list	2.98 (1.88)	2.80 (1.89)	0.14 (0.22)	*.53*
STOPP criteria	2.73 (1.96)	2.68 (2.16)	−0.17 (0.23)	*.46*
Hospitalization within 30 days	0.10 (0.32)	0.20 (0.47)	−0.21 (0.06)	0.0002

Abbreviations: PIM, potentially inappropriate medication; STOPP, Screening Tool of Older Persons' Potentially Inappropriate Prescriptions.

terms of the matching criteria: CCI, number of drugs delivered in the 90 days before hospitalization and mean number of hospitalizations in the previous year. The length of stay was longer for the exposed cohort than the unexposed cohort (8.82 *vs* 7.44 days, respectively). The mean numbers of PIMs (according to the Laroche list, the EU(7)-PIM list and the STOPP criteria) per hospital stay on hospital admission were similar in the two cohorts (Table 1).

3.2 | Potentially inappropriate medications in the 90 days after discharge

The intervention was not associated with a statistically significant difference in the mean number of PIMs (according to the Laroche list, the EU(7)-PIM list and the STOPP criteria) in the 90 days following discharge (Table 2 and Figure 2).

The difference-in-difference estimate (−0.21) suggested that the medication review was associated with a significantly lower incidence of hospital readmission within 30 days of discharge ($P = .0002$) (Table 2).

Figure 3 shows the change in the number of hospitalizations before admission and in the 30 days after discharge for each cohort.

In the sensitivity analysis using logistic regression, patients exposed to the intervention were less likely (risk ratio [RR] [95% confidence interval, CI] 0.45 [0.26-0.74]) to be readmitted to hospital within 30 days of discharge than patients not exposed to the intervention.

4 | DISCUSSION

We evaluated the inclusion of a medication review in the PAERPA integrated care pathway in the Valenciennes-Quercitain area of France. Our results showed that the in-hospital medication review as a part of integrated care was not associated with a decrease in the mean number of PIMs but was associated with a two-fold reduction in the number of hospital readmissions within 30 days of discharge from hospital.

Many studies (including a number of RCTs) have shown that medication reviews can reduce the number of PIMs.[11,46,47] However, the

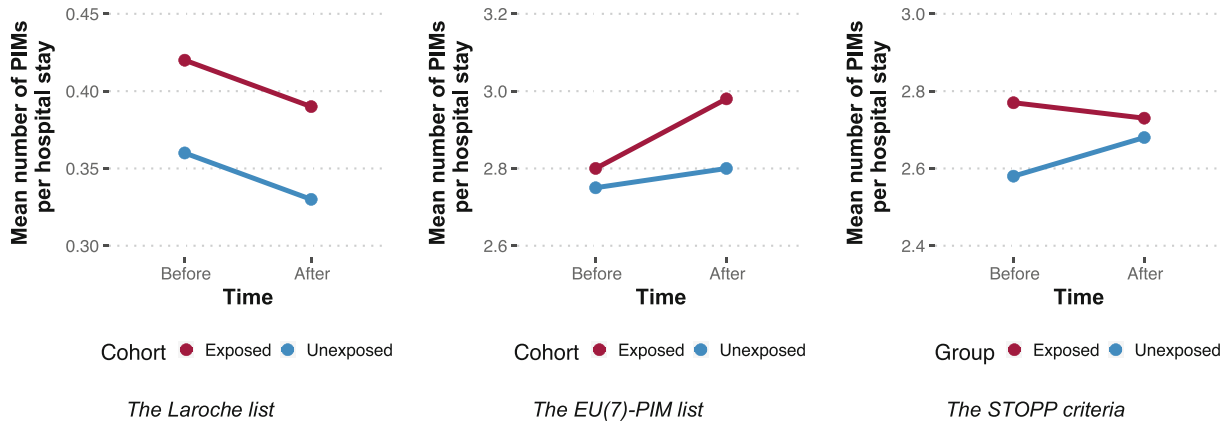

FIGURE 2 The number of PIMs (according to the Laroche list, the EU(7)-PIM list and the STOPP criteria) in the 90 days before admission *vs* the 90 days after discharge for the exposed and unexposed cohorts

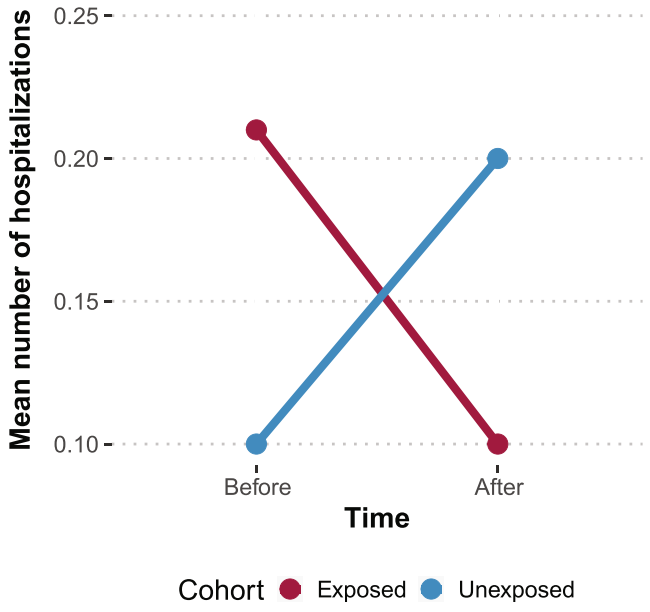

FIGURE 3 The number of readmissions in the 30 days before admission and in the 30 days after discharge for the exposed and unexposed cohorts

data from nonrandomized studies of the effects of medication reviews are discordant.[48–50] In the study of primary care by Sloeserwij et al, a medication review by a nondispensing pharmacist did not improve most of the prescription quality indicators. The researchers suggested that "prescribing indicators might not capture the full effect of non-dispensing pharmacists integrated in primary care teams, when interventions are not specifically targeted upon these indicators".[50]

First, our results are in line with Sloeserwij et al's findings because our medication review included the suggestion of medication changes to the medical team if necessary, a medication plan, educational programmes for prescribers or patients, and counselling. However, the prescribers in our study did not necessarily apply standardized procedures like the EU(7)-PIM list or the STOPP/START criteria. Second, our medication review was initiated in hospital by a multidisciplinary geriatrics team that comprised a geriatrician, a pharmacist and a nurse. The team acted in an advisory capacity, and so the attending physician was not obliged to follow the team's recommendations. Thus, it is possible that physicians did not withdraw PIMs, and so the intervention may have lacked an effect. Given that the multidisciplinary team in charge of the intervention relied on its members' preferences and expertise, the lack of standardization might have decreased the effectiveness of the medication review. Indeed, randomized studies usually promote well-structured evidence-based interventions and then evaluate the change in medication appropriateness (as measured by an implicit tool), the change in inappropriately prescribed medications (as measured by an explicit tool) or the change in prescribing omissions (as measured by an explicit tool).[51] Guidelines on medication review in older adults with multiple comorbidities have been published but these were not available when the project was initiated in 2014.[52] These observations suggest that the real-life implementation of medication review must be based on clear, validated procedures. The team in charge of medication optimization should be able to modify prescriptions directly.

We observed a significant reduction in hospital readmissions in the 30 days following discharge. However, most RCTs and systematic reviews failed to identify an effect of medication review on the risk of hospital readmission in general[18] and drug-related hospital readmission in particular.[22,23] This could suggest that the risk reduction observed in the present study was related to the integrated care pathway and not to the medication review. Indeed, it is possible that the reduction in hospital readmission was related to dedicated, standardized management after discharge by the FP and the community pharmacist, with the support of a care coordinator.[31] Several studies have shown that the initiation of integrated care on hospital admission is associated with a reduction in hospital readmission.[53,54] Other studies have shown that posthospital follow-up by FPs and pharmacists can reduce the number of medication-related problems.[55–57]

The extent to which our results can be generalized depends on the possibility of implementing the procedures and getting healthcare professionals (HCPs) to commit to the integrated care project. In a qualitative study with 75 different HCPs, we identified four categories of barriers or facilitators influencing the readiness of HCPs to implement integrated care pathways for older patients, regardless of whether or not the HCPs had agreed to participate in the PAERPA programme.[31] Barriers and facilitators included communication aspects (about the project and between HCPs), benefits for the patients and HCPs, interest in team working and in geriatric medicine, and the presence of a care coordinator (CC). Indeed, the procedures developed in the PAERPA programme involved a CC without a medical background. In a dedicated study, we have shown that the programme's overall workload was greater than expected.[58] During the study, the CC became more extensively involved in three areas: administration, coordination and communication. These care coordination needs were confirmed by the HCPs included in interviews. Despite the help of the CC, the level of interest in integrated care for frail older people was highly variable among FPs: some FPs were naturally interested in the PAERPA programme, whereas others were strongly opposed. Conversely, nearly all pharmacists accepted participation in the PAERPA programme. These issues should be considered when designing medication optimization programme projects for older people.

Our study had several strengths: integrated care with macro-, meso- and micro-level actions,[29,31,59] a real-life context, matching exposed patients with unexposed patients, an intervention by a multidisciplinary geriatrics team, the use of large national health insurance databases and the application of difference-in-differences causal inference methods.[42,60–62]

However, our study also had several limitations. First, the evaluation part of study was not designed at the time of the intervention. The evaluation required complex procedures for accessing data on medications delivered before and after the intervention in the intervention cohort (probabilistic linkage) and for emulating a comparable control cohort (via matching in the administrative database). Moreover, as data collection closed in January 2019, we do not have data on hospital readmission at 60 days, 90 days and 1-year postintervention for all patients. The results obtained at 30 days could not be extrapolated and compared to 60 days, 90 days and 1 year postintervention. It was therefore not possible to know the impact of the intervention over time. Second, the administrative databases were not set up for research purposes. Some data may have been missing or poorly recorded, which compromised their use.[63,64] Even though the control cohort was created by matching patients for several factors known to be associated with PIMs and re-hospitalization, other (unknown) confounders might have been present. For example, the older adults included in the intervention cohorts had FPs and pharmacists who were willing to participate in the integrated care. This was not true for the unexposed cohort, and so this introduced selection bias in our estimation of the intervention's impact (especially for 30-day readmission) and might have increased the strength of the association measured. Older people who were not able to provide informed consent and who had no next of kin were not included, which could represent a selection bias. However, they represented a low proportion of eligible patients (lower than 0.3% on the basis of local data collected between 2015 and 2017; see Supporting Information Data S1). In our study, the difference in length of stay between the exposed and unexposed cohorts was slightly different but not statistically significant. So, the effect of length of stay on the risk of hospital readmission could be discussed. Furthermore, studies that investigated the association between length of stay and risk of hospital readmission has shown conflicting results in the literature.[8,65–68] Because of our study design, we could not check the parallel trend assumption, ie, that the trend of hospitalizations before intervention was parallel between the two groups. This may be important because violation of parallel trend assumption can lead to biased estimation of the causal effect. Lastly, the study was conducted in a single, medium-sized general hospital located in an area of France with a high prevalence of PIMs and social disadvantage.[69] Caution should be taken when extrapolating these results to other settings. The intervention effects observed in our study were not solely dependent on the medication optimization intervention. Our results were also related to the procedures implemented at the meso and macro levels of the integrated care organization,[59] notably the implementation of a CC.[31] These procedures are not always available in all territories and countries, which may limit the reproducibility of our results. However, many barriers and facilitators are common to integrated care projects[59] and need to be addressed with existing or innovative support. Our study can thus alert HCPs and researchers to the importance of these aspects when developing integrated care in relation to medication optimization.

In conclusion, medication review by a multidisciplinary geriatric team with an advisory role only was not associated with a reduction in the number of PIMs among hospitalized older adults. However, the medication review was part of a standard integrated care procedure associated with a significant decrease in the 30-day hospital readmission rate.

CONTRIBUTORS

David Verloop, Marie-Marguerite Defebvre, Corinne Dupont and Delphine Dambre supported the project with the Hauts-de-France Regional Health Agency. Julien Soula and Antoine Lamer were involved in data management and data analysis. Anaïs Payen, Claire Godard-Sebillotte, Jean-Baptiste Beuscart and Nadia Sourial contributed to study conception and design. Anaïs Payen, Claire Godard-Sebillotte and Jean-Baptiste Beuscart drafted the manuscript. All authors approved the manuscript.

COMPETING INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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