Effectiveness of a multicomponent pharmacist intervention at hospital discharge for drug-related problems: a cluster randomised cross-over trial.

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Principal Investigator statement : The authors confirm that the Principal Investigator for this paper is Xavier Pourrat and that he had direct clinical responsibility for patients.

Running head: Medication reconciliation and drug information sharing at discharge

Key words: Community pharmacist, hospital pharmacist, drug-related problem, communication, cluster randomised cross-over trial, hospital discharge, medication reconciliation

Words count: 3855

Tables count: 6

Figures count: 5

What is already known

-Medication reconciliation decrease number of errors at entrance

-Pharmacists are efficient to perform medication reconciliation

-medication reconciliation takes time

What this study adds

-Sharing drugs information between hospital and community pharmacists decrease patients exposition to drug-related problems

-Medication reconciliation at discharge is effectiveness and should be implemented in hospitals

-Medication reconciliation at discharge is more effective for patients discharge from surgery

Abstract

Aim: To assess whether a pharmacist intervention associating medication reconciliation at discharge with a link to the community pharmacist reduces drug-related problems (DRP) in adult patients during the 7 days after hospital discharge in 22 university or general hospitals in France.

Methods: We conducted a cluster randomised cross-over superiority trial with hospital units as the cluster unit. The primary outcome was a composite of any kind of DRP (prescription/dispensation, patient error or gap due to no medication available) during the 7 days after discharge, assessed by phone with the patient and community pharmacist. Among secondary outcomes, we studied self-reported unplanned hospitalisations at day 35 after discharge and severe iatrogenic problems.

Results: 1,092 patients were enrolled in 48 units (538 in the experimental periods and 554 in the control periods). Three patients refused to have their data analysed and were excluded from the analyses. As compared with usual care, the pharmacist intervention led to a lower proportion of patients with at least one DRP (44.0% vs 50.6%; odds ratio [OR] 0.77, 95% confidence interval [CI] 0.61 to 0.98) and severe iatrogenic problems (5.2% vs 8.7%; OR 0.57, 95% CI 0.35 to 0.93) but no significant difference in unplanned hospitalisations at day 35 (5.8% vs 4.5%; OR 1.46, 95% CI 0.91 to 2.35).

Conclusion: Medication reconciliation associated with communication between the hospital and community pharmacist may decrease patient exposure to DRP and severe iatrogenic problems but not unplanned hospitalisation. However, this intervention could be recommended in health policies to improve drug management.

Trial registration: NCT02006797 https://clinicaltrials.gov/ct2/show/NCT02006797

INTRODUCTION

Drug-related problems are defined as an "*event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes*" [1]. Studies suggest that at least 50% of patients experience drug-related problems after discharge, and 19% to 23% experience an adverse event that could be partially avoided [2,3]. The number of medication errors that occur in elderly patients due the discrepancies at discharge is about 1.5 per patient but can be very important from 0 to 11 [2]. Errors can be due to errors at admission (wrong regimen, drug omitted…) not being corrected properly, but also because of therapy changes not being documented.

In the United States, 19.6% of Medicare patients are readmitted to the hospital within 90 days of discharge. Most readmissions are avoidable, and only 10% are planned [4].

In France, drug dispensation combining medication review, drug delivery and information to patients is mandatory for in-patients. Medication reconciliation at admission and/or discharge occurs in few hospitals. At hospital discharge, the continuum of care includes any prescribing of medications if needed and ensuring that the patient has a full understanding of prescriptions. This is the purpose of medication reconciliation, defined as the formal process of checking the complete, accurate list of a patient's previous medications and comparing it with the prescriptions after a transition of care (on admission, after transfer to another medical unit, and at discharge), rectifying discrepancies and informing both the patient and his/her caregiver [5]. Medication reconciliation before discharge was found effective in decreasing drug-related problems by 50%, with higher efficiency when performed by a pharmacist versus a physician or nurse [6-10]. The US Joint Commission on Accreditation has recommended this process to prevent errors since 2005 [11]. In the UK NICE recommends that medicines reconciliation is carried out for people taking one or more medicines [12]. The recommendation 1.3.3 specifies that medication reconciliation should be carried out in primary care for all patients who have been discharged from hospital and before a new prescription or a new supply of medicines is issued.

However, deficits in communication and information transfer between hospital discharge and community care have been demonstrated in several studies [3]. Several experiments have been conducted in North America and Europe to increase the quality of patient's information at discharge, considering that well-informed patients can better manage their drug treatment

[13, 114]. However, few studies have focused on the role of the community pharmacist at discharge [15-17]. In France, many patients always go to the same community pharmacy, which offers a great opportunity for community pharmacists to play an important role.

Our trial investigated the impact of an intervention with two components: 1) a hospital pharmacist performing medication reconciliation at discharge and 2) the hospital pharmacist in charge of the medication reconciliation informing the community pharmacist of any drug modification. We assessed whether such an intervention affects the rate of drug-related problems in patients during the 7 days after discharge.

METHODS

This study was registered at ClinicalTrials.gov (NCT02006797) on December 5, 2013, and the protocol was previously published [18]. A complete description of the different steps is reported in Figure 1 using the Timeline cluster tool of Caille et al. [19]

Design

We designed a superiority cluster randomised cross-over controlled trial. Clusters were hospital units, each involved during two consecutive 14-day periods: an intervention and a control period. Randomising clusters rather than patients allowed us to provide differential information to patients according to the group they were recruited in. This process is described in the Figure 1. Randomizing patients would probably also have resulted in several patients refusing to be recruited because of the very nature of the intervention assessed (cf infra). The cross-over feature of the design was motivated by the gain in power and the expected benefit of a baseline characteristic balance between groups. It was considered possible because of minimal risk of a carry-over effect.

Settings and participants

Hospitals all over France — half of them being university hospitals — were involved. The recruitment of hospitals was as follows: all university hospitals were asked to participate and all those that accepted were retained. For non-university hospitals, the recruitment depended of their location (each area had to be represented) and their existing experience in clinical pharmacy. In each hospital, a hospital pharmacist was asked to select two units (one surgical

and one medical). Units that already had a medication reconciliation procedure led by a pharmacist at discharge were not eligible. All adult patients were eligible, except those who f stayed in the hospital longer than 21 days, who did not return home, who were in a moribund status, or who were not able to understand the topic of the study or complete a questionnaire. All French community pharmacists were informed of the study, but we included only those who typically dispensed drugs to at least one of the patients enrolled in the study.

Intervention

In each group, the intervention was applied at the patient level. For some hospitals, hospital pharmacists were recruited specifically for the study. To standardize this intervention over the different hospitals [20], hospital pharmacists received a 1-day training about the reconciliation procedure by an experienced clinical pharmacist accredited by the French Society of Clinical Pharmacy (SFPC). This trainer was a clinical pharmacist professor who had established medication reconciliation in his hospital 5 years ago and had participated in the High 5s MEDREC project [21].

Experimental intervention (Figure 2)

For patients included during experimental periods, hospital pharmacists performed the medication reconciliation at discharge. Of course, medication reconciliation at admission was performed as was drug dispensation for in-patients. Then hospital pharmacists completed a short form documenting the reason for hospitalisation, home medication modifications, new medication and laboratory results necessary for community pharmacists to understand and/or accept the prescription (estimated glomerular filtration rate, Na and K levels, coagulation results, etc.). They also checked the discharge prescriptions (drug added and/or omitted, different dosage, route or duration of treatment) and, if needed, made an intervention on physician's prescription according to SFPC standard (figure3) to change prescription [22]. Then, they explained to the patient the drug initiated and the modifications to the home medication. They phoned the patient's community pharmacist to explain the patient's inclusion in the study, the discharge time, and the modifications in treatment. They also sent the prescription sheet to the community pharmacist before patient discharge. The patient or caregiver as usual then visited the community pharmacist as usual.

Control intervention

For the control group, patients received usual care already implemented both at the hospital (classical drug dispensation by staff pharmacists) and by their community pharmacist (drug dispensation according the prescription sheet written by the hospital physician in addition to the general practitioner's sheet [if it existed]). For one hospital, medication reconciliation at admission was already implemented before the study.

Outcomes

The primary outcome was a composite outcome of drug-related problems occurring for any of the drugs the patient had to take, whatever the drug. Three types of problems were considered: 1) the drug was not the correct one (name, form, route, or dose) because of a prescription and/or dispensing error; 2) the patient did not take what was prescribed and/or took drugs that should have been stopped (patient error); and 3) the patient could not obtain the drug when visiting the pharmacy, which caused a gap in the continuity and duration of therapy (treatment gap). The primary outcome was assessed at day 7 (±2 days) after discharge. Two pharmacists specifically recruited for the study contacted all included patients (or their caregiver) by phone to identify any problem related to drugs observed during the 7 days after discharge. Community pharmacists were also called on day 7 (±2), to check that drugs had been delivered (third type of problem).

Each identified drug-related problem was secondarily assessed by an expert committee consisting of one nephrologist, one cardiologist, one gastroenterologist, and one clinical pharmacist. They assessed the potential medical impact of drug-related problems in terms of severity according to the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification [23], score 0 indicating "no potential harm"; 1, "low potentiality of harm"; 2, "significant potentiality of harm"; and 3, "potentially life-threatening". Physicians independently scored each identified problem. They also provided a general score to the patient, taking into account all the different problems identified for a patient. Discrepancies were discussed to reach a consensus.

Each component of the primary outcome (i.e., the three types of problems) was also individually considered as a secondary outcome. We also assessed the number of unplanned hospitalisations during the 35 days after discharge (declared by patients or their caregiver). Patient and community-pharmacist satisfaction were evaluated by using a four-point Likert scale. Finally, we assessed the duration of the intervention (medication reconciliation and communication to the community pharmacist) as self-reported by the hospital pharmacist and

the proportion of drugs initially prescribed by the physician at discharge and modified by the hospital pharmacist.

Blinding

The very nature of the assessed intervention did not allow for blinding, except for the members of the expert committee who assessed the potential medical impact of the identified problems. Pharmacists who contacted patients by phone at days 7 and 35 were not blinded. Indeed, we considered that blinding would have been compromised very easily during the phone contacts. However, although patients recruited during experimental periods were fully informed of the study, its aim, and the intervention assessed, patients recruited during control periods were just asked whether they would agree to be contacted by phone at days 7 and 35.

Randomisation

For each unit, we randomly assigned the order of the two periods. Randomisation was stratified by hospital, for logistical convenience. Because we expected to include two units per hospital, one unit was first included in the experimental period and the other in the control period. The randomisation sequence was generated by a statistician from INSERM CIC 1415 by using a computerized process. Units were randomised all at once. However, for logistical reasons, hospitals were activated sequentially, in an order that was randomly defined. Doing so allowed for the easiest implementation of the study in the different hospitals and easier management of outcome assessment, which was centralised and done by phone.

Ethical issues

The study was approved by the local ethics committee who agreed on a waiver of patient written consent. Thus, patients were informed in a different way according to the group they were recruited in, and were included after oral consent.

Sample size

We expected a reduction of drug-related problems from 60% [24] to 45%. Considering 90% power and a 5% two-sided alpha level, we needed 235 patients per group with a trial of two parallel, individually randomised groups (nQuery Advisor [2005] v6.0, Los Angeles, CA). We applied an inflation factor, taking into account that the trial was clustered and it was a cross-over trial [25-26]. We considered a high value for the intraclass correlation coefficient (ICC) because the primary outcome was a process and because of the expected incidence of about 50% [25]. Thus, we selected a 0.2 value for the ICC and further assumed a 0.1

correlation for the intra-cluster inter-period correlation, that is, half the intra-cluster intra-period correlation. We initially expected to involve 42 units, for a required number of 10.2 patients in each unit for each period. Because we aimed to perform a statistical analysis on the completer population, we planned to recruit 14 patients in each unit in each period, for a total of 1,176 patients.

Statistical analysis

Data are reported as median (interquartile range [IQR]), number (%) and odds ratios (ORs) or relative risk (RR), with 95% confidence intervals (CIs). Data analysis was based on an "intention-to-treat" strategy. Missing data were handled considering a best-case scenario (i.e., a missing outcome, meaning no problem). The number of problems was analysed by using a mixed logistic model with both the group and the period considered as fixed effects and the cluster and the interaction terms cluster*period as random effects. ICCs were estimated per group by using the Zou et al. approach [27]. We performed a sensitivity analysis excluding patients with missing data and also pre-specified subgroup analyses (medical vs surgical units; patients < 75 vs ≥ 75 years old; patients with < 5 vs ≥ 5 drugs prescribed at discharge). Secondary outcomes were analysed by using the same approach as for the primary outcome except for the number of problems per patients for which a mixed Poisson model was fitted. Analyses involved use of SAS v9.2 and R v3.1.2.

RESULTS

Participants

From January 2014 to March 2015, we enrolled 1,092 patients in 48 units from 22 hospitals: 538 in the intervention group and 554 in the control group (Figure 4). Twelve hospitals were university hospitals, nine were general hospitals and one was a military teaching hospital. Twenty-nine units were medical units and 19 were surgical ones. Three patients (two in the intervention group and one in the control group) refused their data to be used and were thus excluded from any analyses. The median number of patients per period per cluster in the intervention and control groups was 11.5 (IQR 7.0 to 15.0) and 11.5 (7.5 to 15.0) respectively. Patient characteristics are reported in Table 1. The median number of drugs at discharge in the intervention and control groups was 5 (IQR 3 to 8) and 5 (2 to 8) respectively.

Primary outcome

The number of patients with at least one drug-related problem in the intervention and control groups was 236 (44.0%) and 280 (50.6%) respectively (OR 0.77, 95% CI 0.61 to 0.98). The intervention reduced the frequency of prescription and/or dispensing errors, patient errors and treatment gaps (OR 0.52, 95% CI 0.29 to 0.93; 0.84, 0.66 to 1.07; and 0.65, 0.43 to 0.99, respectively; Table 2). Within-period and between-period intra-cluster correlation coefficients are reported in Table3. Sensitivity analyses excluded 39 patients (18 and 21 in the intervention and control groups) and led to consistent results. Subgroup analyses are reported in Figure 5. We found no significant interaction. The number of patient errors was significantly lower in the intervention than control group (RR 0.78, 95% CI 0.67 to 0.96) (Table 4).

Potential iatrogenic exposure

Considering severe iatrogenic drug-related problems (score 2 or 3 on the NCC MERP classification), 28 (5.2%) and 48 (8.7%) patients in the intervention and control groups had at least one severe iatrogenic problem (OR 0.57, 95% CI 0.35 to 0.93) (Table5 and Table6).

Secondary outcomes

Unplanned hospitalisations at day 35

At day 35, 31 (5.8%) versus 25 (4.5%) patients in the intervention and control groups had an unplanned hospitalisation (OR 1.46, 95% CI 0.91 to 2.35). For 9 patients, we could not conclude on a planned or unplanned hospitalisation.

Proportion of drug prescriptions modified by the hospital pharmacist at discharge

In the intervention group, hospital pharmacists modified the drug prescription at discharge for 99 patients (18.5%, 95% CI 12.8 to 25.1).

Time spent by hospital pharmacist

The median time dedicated by the hospital pharmacist for medication reconciliation at discharge and communication to the community pharmacist was 20 min (IQR 15 to 30). The estimated ICC was 0.493 (95% CI 0.419 to 0.577), which means that 49.3% of the variability in time spent was due to hospital pharmacists and the remaining 50.7% to heterogeneity in patient characteristics.

Satisfaction

Overall, 465/494 intervention patients who responded (94.1%, 95% CI 91.7 to 96.0) versus 494/524 control patients (94.3%, 95% CI 91.5 to 96.4) were very satisfied or satisfied with their medication management. Also, 439/447 intervention patients (98.2%, 95% CI 96.1 to 99.4) were very satisfied or satisfied that their prescriptions had been transmitted to their community pharmacist, and 391/397 (98.5%, 95% CI 96.0 to 99.8) were very satisfied or satisfied with the explanations given by the hospital pharmacist before their discharge. Among community pharmacists for the intervention group who responded, 390/409 (95.4%, 95% CI 92.8 to 97.2) were very satisfied or satisfied with the process.

DISCUSSION

In this cluster randomised superiority trial, association of medication reconciliation at discharge and communication from the hospital to the community pharmacist decreased drug-related problems and severe iatrogenic problems.

In terms of our composite outcome, we observed a significant effect of the intervention on prescribing/dispensing errors and treatment gap but not on patient errors. Although the proportion of patients with at least one home medication error did not significantly decrease, the overall number of errors significantly decreased by 22% (RR 0.78, 95% CI 0.67 to 0.96). When implementing a liaison from the hospital to community pharmacist associated with systematic medication reconciliation, Van Hollebeke et al. observed a large decrease in proportion of patients with at least one medication shortage during the 7 days after discharge (from 22% to 2%) [28]. However, this study was a single-centre trial, which limits its external validity. Duggan et al., conducted a similar study except that it was single-center and only for medical patients [29]. They demonstrated a decrease in discrepancies at discharge (32.2% vs 52.7% for prescribed drugs) when the patients received a copy of a letter listing their drugs prescribed at discharge and handed it to their regular community pharmacist. Walker et al. assessed an intervention including therapy assessment, medication reconciliation, counselling and education and finally post-discharge follow-up in patients with more than three prescribed drugs [24]. The authors observed a decrease from 59.6% to 33.5% in the proportion of patients with at least one discrepancy. Nevertheless, this study took place in the United States, whose health system differs from that in France where drugs are free of charge.

We observed a greater effect among surgical than medical hospital units (OR 0.64 vs 0.86), although the difference was not significant, probably because of lack of power. Sebaaly et al. identified more medication errors at discharge in surgical than medical units, although the difference was also not significant [30]. We also observed a smaller effect for patients ≥ 75 versus < 75 years old, although once again, the difference was not significant. Finally, the effect did not appear to be related to the number of drugs, with similar ORs for ≥ 5 and < 5 drug subgroups. These latter results do not fully agree with the Hias et al. study, that showed that the number of drugs at admission and patient age were associated with drug-related problems at admission [31].

Our trial shows a reduction in potential severe iatrogenic problems with the intervention. A similar result was observed in the Phatak et al. randomised trial assessing a complex intervention associating several clinical pharmacy activities: the proportion of adverse drug

events reduced from 12.8% to 8% [14]. Sebaaly et al. classified 6% of medication errors as serious or lethal in their study [32]. These results confirm the relevance of our intervention to decrease patient exposure to serious drug-related problems.

Concerning the time spent by the hospital pharmacist on the intervention, Zemaitis et al. found a mean of 10.1 min dedicated to medication reconciliation at discharge and 6.6 min to medication reconciliation at admission [4]. In our study, the median time spent by the hospital pharmacist was 20 min for the whole process, including communication with the community pharmacist. However, such a global median masks very different situations with high inter-hospital variability in time spent.

As in other studies [32; 35], we did not demonstrate a reduction in unplanned hospitalisations at day 35 after discharge. Overall, we observed a global rate of unplanned hospitalisations of 5.1% as compared with previously reported rates of 2.7% and 2.8% at 7 and 30 days, respectively, for all causes of hospitalisations (except recovery and psychiatric stays) in France [33-34]. The difference may be due to the way we assessed this outcome, directly from the patient. In their review, Christensen and Lundh explained the lack of evidence on unplanned hospitalisations as being due to low-quality trials and too-short follow-up: 1 year would be a better follow-up [36]. Arnold et al. observed a decrease from 19.5% to 9.2% in readmission rate at day 30 after discharge, but data were collected from physicians or pharmacists involved in clinical pharmacy, rather than from patients themselves [37].

Unlike other trials we didn't find a relationship between the number of drugs prescribed at discharge and the occurrence of DRPs, nor did we observe a relationship with age [38-39]. However, we observed a greater effect in surgical units as compared to medical ones, knowing that patients discharged from surgical wards are generally younger than those discharged from medical ones, and have fewer drugs. Therefore the type of unit (surgical/medical) may acts as a confounding factor when studying the relationship between the number of drugs or age and the number of DRPs.

Generalisability

Our study involved hospital pharmacists from 22 university and general hospitals. Units were representative of existing medical or surgical specialities, and eligibility criteria for patients were sufficiently extensive for intervention generalization in French hospitals. Community pharmacists were not "recruited" for the study: their involvement depended on whether the

patients they typically provide drugs to were recruited in the study. These elements offer good external validity to our trial. Moreover each cluster was its own comparator because of the cross-over design, which helped achieve good baseline balance in this non-blinded study, thus limited bias.

Limitations

Medication reconciliation at admission is considered good practice [40]; therefore, we did not exclude units in which it was usual care. Hence, we included one unit with medication reconciliation at admission. Nevertheless, because the study was cross-over, there is no reason to believe that this was source of bias.

We did not communicate the medication reconciliation synthesis to the patient's general practitioner, who was not involved in the present study. General practitioners receive a hospitalisation report with information about their patient's hospital stay, but generally at 1 to 4 weeks after hospital discharge. Our aim was to focus on the patient community pharmacist, who generally is the first healthcare person the patient meets after hospital discharge.

For logistical convenience, units were sequentially activated. Hence, when the last unit was activated, patient recruitment in the first unit had ended for more than 12 months. Such a situation may have induced between-unit contamination but this remains highly theoretical since units activated at different times were from different hospitals, with different hospital pharmacists. This sequential activation may have also affected how the intervention was applied, since hospital pharmacists were all informed together about the intervention, at the beginning of the study. To limit this problem, before activation of each unit, a phone meeting was organized to remind how the study had to be conducted and what were the intervention components.

Future research

Although we demonstrated the efficiency of our intervention for drug-related problems, we failed to observe a benefit for unplanned hospitalisation. As explained, this outcome was assessed in a non-optimal way (asking patients or their caregiver) and after a too-short follow-up. More work is undoubtedly needed on this outcome, relating it to severe iatrogenic problems, and considering a longer follow-up, as suggested by Christansen et al. [34].

Conclusion

Systematic medication reconciliation at discharge along with community-pharmacist contact is beneficial for patients. Since the end of this trial and the first results communicated in different meetings, medication reconciliation at discharge has become mandatory in French hospitals.

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Conflict of interest statement

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Martial Fraysse: none

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Clarisse Roux-Marson: none

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Xavier Pourrat guarantees accuracy of the above information.

Data availability: Data are available from the lead author on request.

References

1. Van Mil JW, Westerlund LO, Hersberger KE, Schaefer MA. Drug-related problem classification systems. Ann Pharmacother. 2004;38(5):859–867

2. Midlöv P, Bahrani L, Seyfali M, Höglund P, Rickhag E, Eriksson T. The effect of medication reconciliation in elderly patients at hospital discharge. Int J Clin Pharm. 2012 Feb;34(1):113-9

3. Kripalani S, Jackson AT, Schnipper JL, Coleman EA. Promoting effective transitions of care at hospital discharge: a review of key issues for hospitalists. J Hosp Med. 2007 Sep;2(5):314-23

4. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program.N Engl J Med. 2009 Apr 2;360(14):1418-28

5. Zemaitis CT, Morris G, Cabie M, Abdelghany O, Lee L Reducing Readmission at an Academic Medical Center: Results of a Pharmacy-Facilitated Discharge Counseling and Medication Reconciliation Program. Hosp Pharm. 2016 Jun;51(6):468-73

6. Durán-García E, Fernandez-Llamazares CM, Calleja-Hernández MA. Medication reconciliation: passing phase or real need? Int J Clin Pharm. 2012 Dec;34(6):797-802

7. Carter M., Allin D., Scott L.A., Grauer D. Pharmacist-acquired medication histories in a university hospital emergency department Am J Health Syst Pharm 2006; 63 (24): 2500-2503

8. Nester T., Hale L. Effectiveness of a pharmacist-acquired medication history in promoting patient safety Am J Health Syst Pharm 2002; 59: 2221-2225

9. Cohen J, Wilson C, Ward F. Improve drug history taking. Pharm Pract 1998;8:13-14,16,

10. Dawson P, Gray S. Clinical significance of pharmacist obtained drug histories. Pharm J 1981. 227120

11. Joint Commission. Sentinel Event Alert Using medication reconciliation to prevent errors. Issue 35 - January 25, 2006. 21. http://www.jointcommission.org/assets/1/18/SEA_35.PDF (27 december 2011)].

12. NICE. Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes. March 2015. Available at : https://www.nice.org.uk/guidance/ng5 (25 march 2020)

13. Kripalani S, LeFevre F, Phillips CO, Williams MV, Basaviah P, Baker DW. Deficits in communication and information transfer between hospital-based and primary care physicians: implications for patient safety and continuity of care. JAMA. 2007 Feb 28;297(8):831-41

14. Phatak, A., Prusi, R., Ward, B., Hansen, L. O., Williams, M. V., Vetter, E., ... & Postelnick, M. (2016). Impact of pharmacist involvement in the transitional care of high-risk patients through medication reconciliation, medication education, and postdischarge call-backs (IPITCH Study). Journal of hospital medicine, 11(1), 39-44.

15. Hugtenburg JG, Borgsteede SD, Beckeringh J. Medication review and patient counselling at discharge from the hospital by community pharmacists. J.Pharm World Sci. 2009 Dec;31(6):630-7

16. Jokanovic N, Tan EC, Sudhakaran S, Kirkpatrick CM, Dooley MJ, Ryan-Atwood TE, Bell JS. Pharmacist-led medication review in community settings: An overview of systematic reviews.Res Social Adm Pharm. 2017 Jul - Aug;13(4):661-685

17. Arnold ME, Buys L, Fullas F. Impact of pharmacist intervention in conjunction with outpatient physician follow-up visits after hospital discharge on readmission rate. Am J Health Syst Pharm. 2015 Jun 1;72(11 Suppl 1):S36-42

18. Pourrat X, Roux C, Bouzige B, Garnier V, Develay A, Allenet B, Fraysse M, Halimi JM, Grassin J, Giraudeau B. Impact of drug reconciliation at discharge and communication between hospital and community pharmacists on drug-related problems: study protocol for a randomised controlled trial. Trials. 2014 Jun 30;15:260

19. Caille A, Kerry S, Tavernier E, Leyrat C, Eldridge S, Giraudeau B. Timeline cluster: a graphical tool to identify risk of bias in cluster randomised trials. BMJ. 2016 Aug 16;354:i4291

20. Boutron I, Guittet L, Estellat C, Moher D, Hróbjartsson A, Ravaud P. Reporting methods of blinding in randomised trials assessing nonpharmacological treatments. PLoS Med. 2007;4:e61. doi: 10.1371/journal.pmed.0040061

21. https://www.who.int/patientsafety/topics/high-5s/en/

22. Allenet B, , Escofier L, Roubille R, Charpiat B, Juste M, Conort O. Validation of an instrument for the documentation of clinical pharmacists' interventions. Pharm World Sci (2006) 28:181–188

23. NCC MERP Taxonomy of Medication Errors. https://www.nccmerp.org/sites/default/files/taxonomy2001-07-31.pdf

24. Walker PC, Bernstein SJ, Jones JN, Piersma J, Kim HW, Regal RE, Kuhn L, Flanders SA: Impact of a pharmacist-facilitated hospital discharge program: a quasi-experimental study. Arch Intern Med 2009, 169:2003–2010

25. Donner A, Klar N, Zou G: Methods for the statistical analysis of binary data in split-cluster designs. Biometrics 2004, 60:919–925, Giraudeau B, Ravaud P, Donner A: Sample size calculation for cluster randomised cross-over trials. Stat Med 2008, 27:5578–5585

26. Gulliford MC, Adams G, Ukoumunne OC, Latinovic R, Chinn S, Campbell MJ: Intraclass correlation coefficient and outcome prevalence are associated in clustered binary data. J Clin Epidemiol 2005, 58:246–251

27. Zou G, Donner A. Confidence interval estimation of the intraclass correlation coefficient for binary outcome data. 2004. Biometrics. 60(3). 807-811

28. Van Hollebeke M, Talavera-Pons S, Mulliez A, Sautou V, Bommelaer G, Abergel A, Boyer A. Impact of medication reconciliation at discharge on continuity of patient care in France. Int J Clin Pharm. 2016 Oct;38(5):1149-56

29. C Duggan, R Feldman, J Hough, I Bates. Reducing Adverse Prescribing Discrepancies Following Hospital Discharge. Int J Pharm Pract 1998:6:77-82

30. Sebaaly J, Parsons LB, Pilch NA, Bullington W, Hayes GL, Easterling H. Clinical and Financial Impact of Pharmacist Involvement in Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. Hosp Pharm. 2015 Jun;50(6):505-13

31. Hias J, Van der Linden L, Spriet I, Vanbrabant P, Willems L, Tournoy J, De Winter S. Predictors for unintentional medication reconciliation discrepancies in preadmission medication: a systematic review. Eur J Clin Pharmacol. 2017 Jul 25. doi: 10.1007/s00228-017-2308-1. [Epub ahead of print]

32. Sebaaly J, Parsons LB, Pilch NA, Bullington W, Hayes GL, Easterling H. Clinical and Financial Impact of Pharmacist Involvement in Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. Hosp Pharm. 2015 Jun;50(6):505-13

33. Mercier G, Georgescu V., Bousquet J. Geographic Variation In Potentially Avoidable Hospitalizations In France. Health Aff May 2015 vol. 34: 5 836-843

34. DGOS-ATIH/Taux de réhospitalisation dans un délai de 1 à 7 jours - Outil d'accompagnement – 12 mai 2017 [Rehospitalisation rate 1 to 7 days after discharge in France]. download at URL http://solidarites-sante.gouv.fr/IMG/pdf/guide_indicateur_mco_rehospitalisations_1-7_jours_dgos-atih_2017_05_12.d.pdf

35. Caroff DA, Bittermann T, Leonard CE, Gibson GA, Myers JS. A Medical Resident-Pharmacist Collaboration Improves the Rate of Medication Reconciliation Verification at Discharge. Jt Comm J Qual Patient Saf. 2015 Oct;41(10):457-61

36. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality Cochrane Database Syst Rev. 2016 Feb 20;2:CD008986. doi: 10.1002/14651858.CD008986.pub3. Review.

37. Arnold ME, Buys L, Fullas F. Impact of pharmacist intervention in conjunction with outpatient physician follow-up visits after hospital discharge on readmission rate. Am J Health Syst Pharm. 2015 Jun 1;72(11 Suppl 1):S36-42

38. Climente-Martí, Mónica, et al. "Potential risk of medication discrepancies and reconciliation errors at admission and discharge from an inpatient medical service." Annals of Pharmacotherapy 44.11 (2010): 1747-1754.

39. Hellström, Lina M., et al. "Errors in medication history at hospital admission: prevalence and predicting factors." BMC Pharmacology and Toxicology 12.1 (2012): 9.

40. Mekonnen AB, McLachlan AJ, Brien JA. Pharmacy-led medication reconciliation programmes at hospital transitions: a systematic review and meta-analysis. J Clin Pharm Ther. 2016 Apr;41(2):128-44

Tables

Table 1: Characteristics of patients in intervention and control groups

Characteristics	Control/intervention sequence		Intervention/control sequence	
	Period 1: Control 24 units, n=307	Period 2: Intervention 24 units, n=258	Period 1: Intervention 24 units, n=278	Period 2: Control 24 units, n=246
No. of patients per cluster - median [Q1-Q3]	13.0 [9.0-15.0]	10.5 [7.0-14.5]	11.0 [2.0-14.0]	13.0 [7.5-15.5]
Men - n (%)	157 (51.1)	138 (53.5)	158 (56.8)	145 (58.9)
Age - mean (SD)	61.5 (17.0)	61.7 (16.1)	64.7 (17.0)	62.7 (16.4)
Autonomous patient - n(%)	278 (90.6)	239 (92.6)	250 (89.9)	237 (96.4)
No. of drugs at admission - median [Q1-Q3]	5.0 [3.0-8.0]	5.0 [2.0-8.0]	5.0 [3.0-9.0]	5.0 [2.0-8.0]
No. of drugs at discharge - median [Q1-Q3]	5.0 [2.0-8.0]	5.0 [3.0-8.0]†	5.0 [3.0-9.0]	4.0 [3.0-7.0]
Discharge before 1 pm - n (%)	85 (27.8)*	65 (25.2)	64 (23.0)	61 (24.8)

† n=1 missing value

Table 2: Drug-related problems observed during the 7 days after hospital discharge

Outcome	Control/Intervention sequence		Intervention/Control sequence		Risk difference (%) (95% CI)	Odds ratio (95% CI)
	Period 1: Control	Period 2: Intervention	Period 1: Intervention	Period 2: Control		
	24 units, n=307	24 units, n=258	24 units, n=278	24 units, n=246		
At least one drug-related problem (ITT)	160 (52.1)	115 (44.6)	121 (43.5)	120 (48.8)	-6.55 (-12.49;-0.60)	0.77 (0.61;0.98)
At least one prescription/dispensation problem	18 (5.9)	5 (1.9)	13 (4.7)	17 (6.9)	-3.19 (-5.71;-0.67)	0.52 (0.29;0.93)
At least one patient error	142 (46.3)	104 (40.3)	107 (38.5)	100 (40.7)	-4.27 (-10.1;1.59)	0.84 (0.66;1.07)
At least one treatment missing	36 (11.7)	25 (9.7)	16 (5.8)	27 (11.0)	-3.48 (-6.95;-0.01)	0.65 (0.43;0.99)
	24 units, n=263	24 units, n=233	24 units, n=242	24 units, n=233		
At least one drug-related problem (completers)	160 (60.8)	115 (49.4)	121 (50.0)	120 (51.5)	-6.64 (-12.9;-0.37)	0.77 (0.60;0.99)

Table 3: Within-period and between-period intra-cluster correlation coefficients

Outcome	Within-period correlation	Between-period correlation
At least one drug-related problem (ITT) n=1089	0.022 [0.000;0.051]	0.003 [0.000;0.012]
At least one prescription/dispensation problem	0.000 [0.000;0.019]	0.000 [0.000;0.014]
At least one patient error	0.019 [0.000;0.053]	0.002 [0.000;0.013]
At least one treatment missing	0.029 [0.000;0.070]	0.015 [0.000;0.037]
At least one drug-related problem (completers) n=971	0.030 [0.000;0.065]	0.004 [0.000;0.015]

ITT, intention to treat

Confidence intervals are obtained by a normal-based bootstrap approach with 10,000 replications

Table 4: Number of patient errors in the intervention and control groups.

		Control/intervention sequence		Intervention/control sequence	
		Period 1: Control 24 units, n=307	**Period 2: Intervention** 24 units, n=258	**Period 1: Intervention** 24 units, n=278	**Period 2: Control** 24 units, n=246
No. of patients with at least one medication error after discharge		142 (46.3)	104 (40.3)	107 (38.5)	100 (40.7)
No. of errors per patient					
	1	68 (47.9)	62 (59.6)	66 (61.7)	49 (49.0)
	2	46 (32.4)	24 (23.1)	25 (23.4)	27 (27.0)
	3	20 (14.1)	14 (13.5)	15 (14.0)	16 (16.0)
	4	4 (2.8)	2 (1.9)	1 (0.9)	5 (5.0)
	5	1 (0.7)	1 (1.0)	0 (0.0)	1 (1.0)
	6	3 (2.1)	0 (0.0)	0 (0.0)	2 (2.0)
	7	0 (0.0)	1 (1.0)	0 (0.0)	0 (0.0)
Total no. of errors		259	172	165	188

Table 5: Potential exposure to iatrogenic events by National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) classification [20] in the intervention and control groups.

NCC MERP score	Intervention	Control
0, exposure to at least one drug-related problem with no potential harm	66 (12.3)	65 (11.8))
1, exposure to at least one drug-related problem with low potentiality of harm	142 (26.5)	167 (30.2)
2, exposure to at least one drug-related problem with significant potentiality of harm	28 (5.2)	45 (8.1)
3, exposure to at least one drug-related problem with global impact potentially life-threatening	0 (0)	3 (0.5)
Patients not exposed to a drug-related problem	300 (56.0)	273 (49.4)
Total	536	553

Table 6: Potential exposure to iatrogenic events by NCC MERP classification scale scores [20] in the intervention and control groups.

	Control/intervention sequence		Intervention/control sequence	
	Period 1: Control	**Period 2: Intervention**	**Period 1: Intervention**	**Period 2: Control**
	24 units, n=307	24 units, n=258	24 units, n=278	24 units, n=246
0, exposure to at least one drug-related problem with no potential harm	37 (23.1)	27 (23.5)	39 (32.2)	28 (23.3)
1, exposure to at least one drug-related problem with low potentiality of harm	96 (60.0)	71 (61.7)	71 (58.7)	71 (59.2)
2, exposure to at least one drug-related problem with significant potentiality of harm	26 (16.3)	17 (14.8)	11 (9.1)	19 (15.8)
3, exposure to at least one drug-related problem with global impact potentially life-threatening	1 (0.6)	0 (0.0)	0 (0.0)	2 (1.7)
Patients not exposed to a drug-related problem	160 (52.1)	115 (44.6)	121 (43.5)	120 (48.8)

Figures legends

Figure 1: Timeline cluster diagram

Figure 2: Flow chart of the intervention

Figure 3: the pharmacist intervention (French Society of Clinical Pharmacy)

Figure 4: Flow-chart of the study.

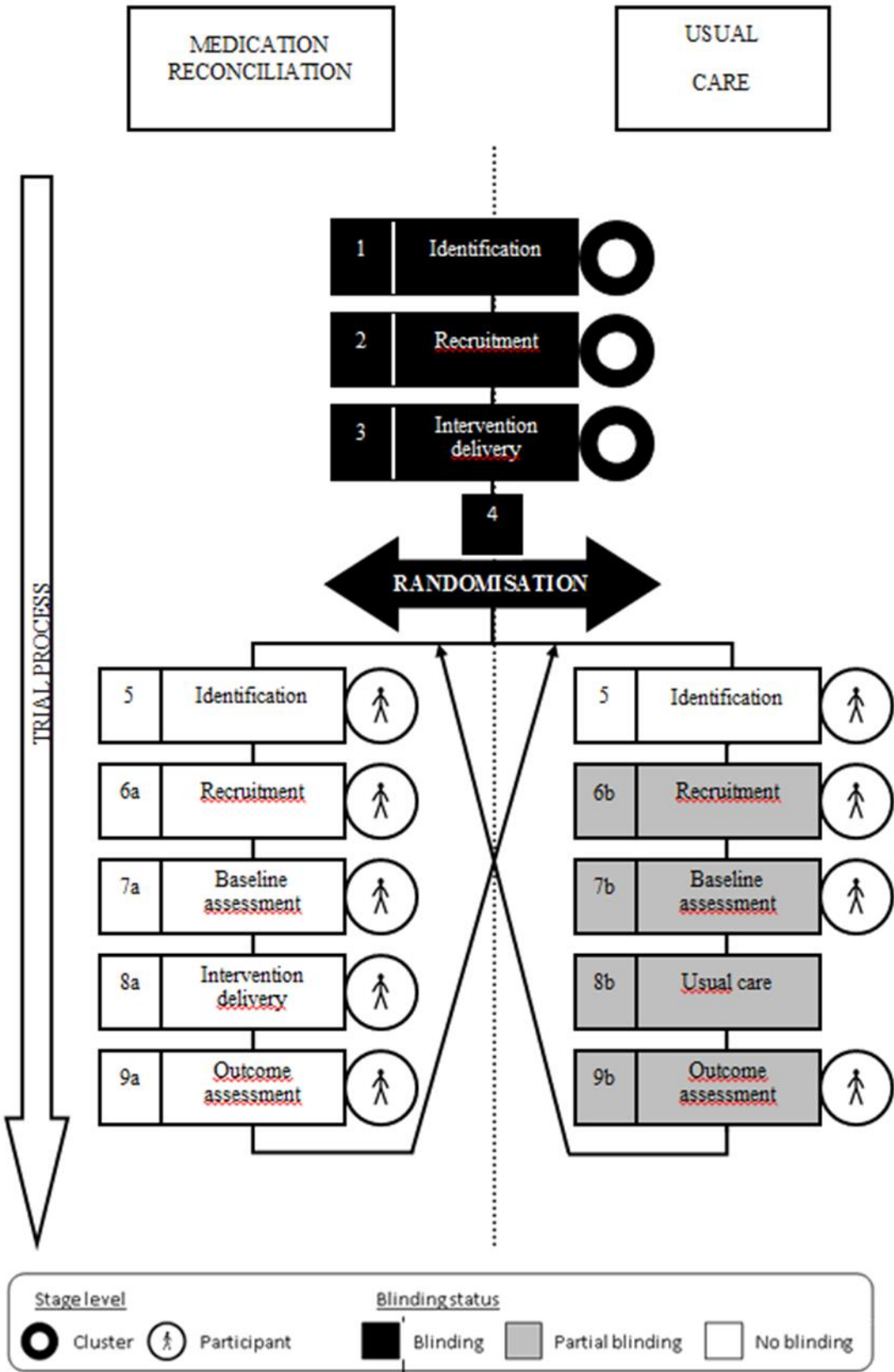**Figure 5: sub-groups analyses**

Appendices

Ethical approval: The protocol was approved by the local ethics committee (CPP TOURS - Region Centre - Ouest 1) for all centers.

This article respects the CONSORT checklist of information to include when reporting a cluster randomised trial; Bruno Giraudeau is garant of it.

Protocol

The initial protocol was in French, and is available from Xavier Pourrat on request. It was published in Trials (2014 Jun 30;15:260) and the corresponding article is linked to this paper.

Figure 1: Timeline cluster diagram

|	
1	**Cluster identification** French hospital pharmacists are approached by the study team. Each hospital pharmacist who agrees to participate in the trial identifies 2 units from their hospital, one surgical and one medical unit.
2	**Cluster recruitment** Medical heads from hospital units receive information and provide written consent to take part to the study.
3	**Intervention delivery at cluster level** Hospital pharmacists are trained in medication reconciliation. Community pharmacists working in nearby participating hospital units are informed of the study in 3 ways: an article in a professional journal supported by the pharmacist unions, in a professional journal supported by the national council of the order of pharmacists, and a letter from the study scientific committee distributed by wholesale drug distributors.
4	**Randomisation: cross-over design** Randomisation is performed in a 1:1 ratio by an independent statistician with stratification on the hospital. Each hospital unit is randomised to perform medication reconciliation or usual care for a first 14-day period and is crossed over to the other group for a second 14-day period.
5	**Participant identification** In each hospital unit, unblinded hospital pharmacists identify eligible patients.
6a	**Participant recruitment in the medication reconciliation group** Participants are recruited by unblinded hospital pharmacists. They receive complete information and provide oral consent for intervention and for data collection.
6b	**Participant recruitment in the usual care group** Participants are recruited by unblinded hospital pharmacists. They receive partial information because they are not aware of the existence of the medication reconciliation group and provide oral consent for data collection.
7a	**Participant baseline data collection in the medication reconciliation group** Baseline data are collected by the unblinded hospital pharmacists. There is no blinding for patients. Contact details for the patient's community pharmacist are collected.
7b	**Participant baseline data collection in the usual care group** Baseline data are collected by the unblinded hospital pharmacists. Patients are not aware of the existence of the medication reconciliation group. Contact details for the patient's community pharmacist are collected.
8a	**Intervention delivery** Medication reconciliation at patient discharge is performed by a hospital pharmacist, followed by phone transmission of treatment modification to the patient's community pharmacist. No blinding for hospital pharmacists, community pharmacists and patients.
8b	**Usual care** No blinding for community pharmacists, but they are not aware that the patient is involved in a trial. No blinding for patients, but they are not aware of the existence of the medication reconciliation group.
9a	**Participant outcome assessment in the medication reconciliation group** Drug-related problem within 7 days after discharge assessed by a research pharmacist recruited for the study, using a standardized evaluation form. Assessment is centralised and performed by a phone call to both the participant and community pharmacist. No blinding for the research pharmacist, community pharmacists and patients.
9b	**Participant outcome assessment in the usual care group** Drug-related problem within 7 days after discharge assessed by a research pharmacist recruited for the study, using a standardized evaluation form. Assessment is centralised and performed by a phone call to both the participant and the community pharmacist. No blinding for the research pharmacist, community pharmacists are not aware that the patient is involved in a trial and patients are not aware of the existence of the medication reconciliation group.

Figure 2: Flow chart of the intervention
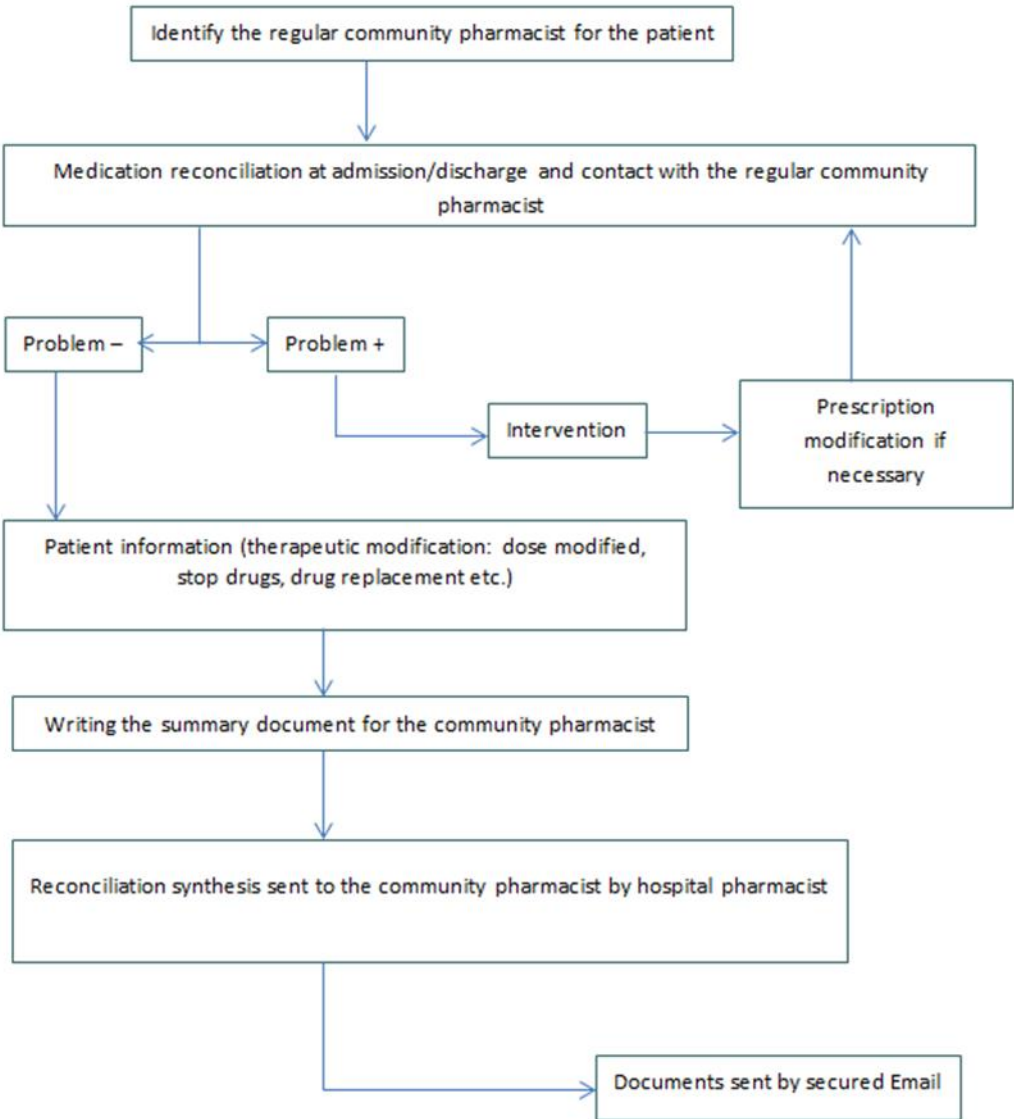
Figure 3: the pharmacist intervention (French Society of Clinical Pharmacy)

PHARMACIST INTERVENTION FORM

⧖ DATE: / /   ☐ INTERVENTION N°:   ▭ CENTER N°:

PATIENT:

Last name:
First name:

Age: years / Weight: Kg
Sex: ☐ M   ☐ F

1- DRUG RELATED PROBLEM (1 choice):

1 ☐ Non conformity to guidelines or contra-indication
2 ☐ Untreated indication
3 ☐ Subtherapeutic dosage
4 ☐ Supratherapeutic dosage
5 ☐ Drug without indication
6 ☐ Drug interaction
    ○ To be taken into account
    ○ Use with caution
    ○ Combination to be avoided
    ○ Combination contra-indicated
    ○ Documented but not in VIDAL®
7 ☐ Adverse drug reaction
8 ☐ Improper administration
9 ☐ Failure to receive drug
10 ☐ Drug monitoring

2- INTERVENTION (1 choice):

1 ☐ Addition of a new drug
2 ☐ Drug discontinuation
3 ☐ Drug switch
4 ☐ Change of administration route
5 ☐ Drug monitoring
6 ☐ Administration modalities optimisation
7 ☐ Dose adjustment

Hospital ward:
☐ Psychiatry
☐ Acute care
☐ Long term care
☐ Rehabilitation ward

DRUG NAME (INN):

3- DRUG CLASSIFICATION (ATC):
☐ A Alimentary tract & metabolism
☐ B Blood & blood forming organs
☐ C Cardiovascular system
☐ D Dermatological
☐ G Genito urinary system & sex hormones
☐ H Systemic hormonal preparations
☐ J Anti-infective for systemic use
☐ L Anti-neoplastic & immunomodulating agents
☐ M Musculo-skeletal system
☐ N Nervous system
☐ P Antiparasitic products
☐ R Respiratory system
☐ S Sensory organs
☐ V Various

4- INTERVENTION FOLLOW-UP:
☐ Accepted
☐ Non accepted
☐ Non assessable

DETAILS ⇒ If necessary, give details on any aspects of the detected DRP and describe the intervention. precisely
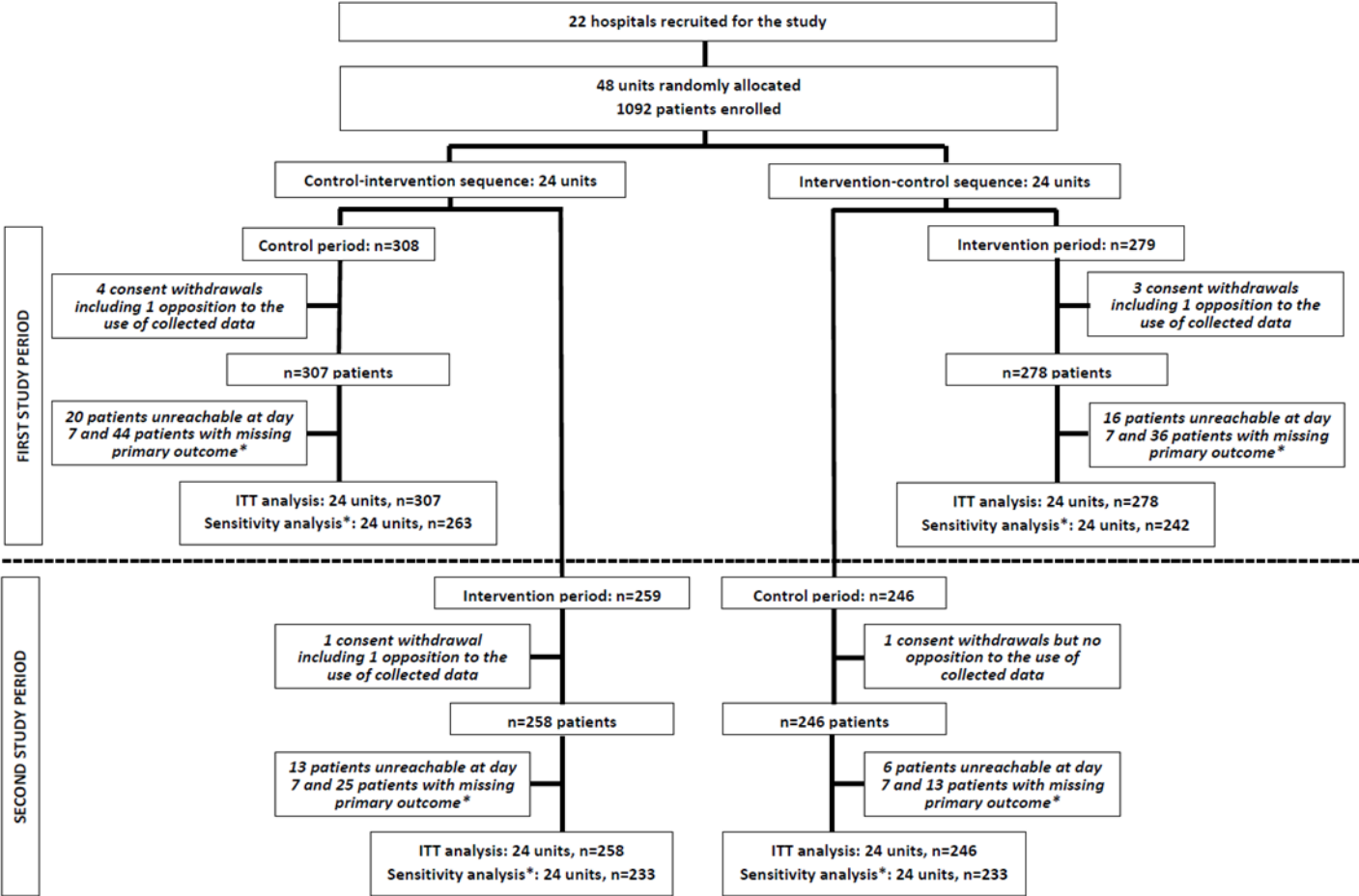
Context

Problem

Intervention

Figure 4: Flow-chart of the study

Figure 5: sub-groups analyses

Subgroup	n/N Intervention	n/N Control		Interaction p-Value	OR [95% CI]
Unit type					
Surgery	82/213	108/218			0.64 [0.43; 0.94]
Medical	154/323	172/355		0.2331	0.86 [0.64; 1.17]
Age					
≥ 75 years old	78/152	80/150			0.90 [0.57; 1.42]
< 75 years old	15/384	200/403		0.3452	0.71 [0.53; 0.94]
Number of drugs prescribed					
≥ 5	149/298	163/277			0.76 [0.55; 1.07]
< 5	87/249	117/276		0.8821	0.73 [0.51; 1.04]
Total	236/536	280/553			0.77 [0.61; 0.98]

Favour intervention   0.4   0.5   0.77   1   1.5   Favour control

OR= Odds-ratio

CI= confidence Interval