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Continuation of geriatric discharge medication in primary care and its association with rehospitalizations – a cohort study

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Transition of care in geriatric patients is a complex and high risk process, particularly the continuation of discharge medication in primary care. We aimed to determine how general practitioners' management of geriatric patients' discharge medication is associated with rehospitalizations. A prospective monocentric cohort study was done in an acute geriatric inpatient clinic with six-months follow-up. Acutely hospitalized patients ≥ 70 years old with functional impairment and frailty currently taking medications were followed up after hospital discharge and continuation (n=27) or change (n=44) of discharge medication by the General Practitioner was determined. Outcomes were rehospitalizations, days spent at home and time until recurrent rehospitalizations. 71 patients (mean age 82 years, 46 women [65 %]) were followed up for six months after hospital discharge. In a negative binomial regression model, the rehospitalization rate after three months was 3.8 times higher in participants whose discharge medication was changed ($p = 0.023$). The effect did not persist over six months. Patients who were continued on their discharge medication were rehospitalized significantly later and/or less often during the six months observation period, statistically measured by a recurrent events survival model (HR 0.267, $p = 0.003$). In conclusion, continuation of discharge medication after an acute hospitalization in a specialized geriatric clinic could prevent early rehospitalizations.

1. Introduction

Transition from hospital to primary care is a high-risk process. The World Health Organization, as part of its Global Patient Safety Challenge 'Medication Without Harm', identified medication safety during transitions of care as a priority (World Health Organization 2017). One of the key risks associated with the transition from hospital to primary care is the transmission of incomplete information (Kattel et al. 2020; Kripalani et al. 2007), which may lead to inappropriate prescribing, medication errors, non-adherence, adverse drug reactions (ADRs) and ultimately to patient harm (Alqenae et al. 2020; Boockvar et al. 2006; Coleman and Berenson 2004; Forster et al. 2003; Forster et al. 2004; Moore et al. 2003; Redmond et al. 2018). Studies particularly found that one in ten hospital admissions in older patients was caused directly by ADRs (Oscanoa et al. 2017) and that drug-related problems in general were responsible for up to 30 % of hospital admissions in geriatric patients, with more than half considered avoidable (Chan et al. 2001; El Morabet et al. 2018). Put in the context of hospital discharges, older patients appear to be especially prone to a post-discharge medication-related harm (PDMRH) (Alqenae et al. 2020; Parekh et al. 2018).

Therefore, successful communication of changes to drug therapy regimens between care settings is of high importance to avoid PDMRH. Discharge letters are widely accepted in this context, but have proved to be inferior to verbal communication due to incomplete information and delayed arrival at general practitioners' (GP) offices (Baxter et al. 2020; Kattel et al. 2020; Unnewehr et al. 2015). A small observational study linked 38 % of rehospitalizations to insufficient communication of medication changes at discharge (Witherington et al. 2008). Simultaneously, GPs have high interest in rationales for changing medication during hospitalization and quick availability of discharge letters. However, research has shown that this is often not the case (Adam et al. 2015; Munday et al. 1997; Strehlau et al. 2018).

Most important in the context of transition of care is how GPs assess discharge letters and specifically their medication recommendations: A Dutch study showed that hospital medication recommendations were continued in 53 % of discharges when justified by the inpatient geriatric consultant team in the discharge letter (Deschodt et al. 2021), a French study in an acute geriatric setting found an 83 % continuation rate including distinctive pharmacist-written explanations (Rouch et al. 2018). Two studies which evaluated drug regimen changes at discharge without explanation of medication changes during hospitalization showed a 56 % (Weir et al. 2019) (Canada) or 21 % (Krause et al. 2019) continuation rate (Germany).

After receiving a discharge letter, a patient's GP has two choices: To either continue the discharging hospital's medication recommendation or to change it (back) based on their knowledge and experience with individual patients. To our knowledge, there are only two geriatric studies which examine the impact of patients' (rather than GPs') nonadherence in terms of medication on rehospitalization (Coleman et al. 2005) and mortality after acute myocardial infarction (Jackevicius et al. 2008). Therefore, our objective was to analyze the association of particularly the GPs' decision (GPD) to continue or change geriatric discharge medication with rehospitalizations, days spent at home (DSAH) and time until rehospitalization (TUR), while considering geriatric patients' impaired functionality, disease burden and frailty.

2. Investigations and results

We screened 470 patients between January and September 2018 for eligibility in a consecutive cohort and recruited 85 patients.

In total, 71 participants (64.8 % female) were included and either allocated to GPD "changed" (n=44; 62 %) or GPD "continued" (n = 27; 38 %) based on GPs' decision after discharge (Fig. 1). Their baseline characteristics and features of their geriatric phenotype are displayed in Table 1.

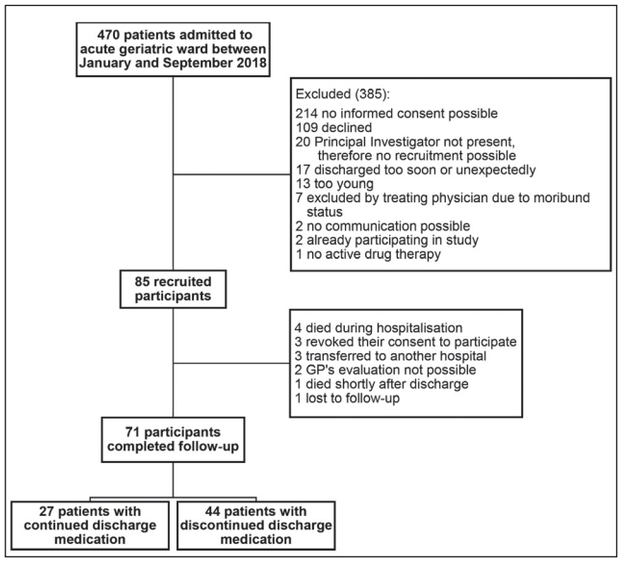

Fig. 1: Recruitment flow diagram and number of patients with "continued" or "changed" discharge medication.

2.1. Differences in frequency, immediacy and recurrence of rehospitalizations in favor of GPD "continued"

Primary end point of the study was the rehospitalization rate after one, three and six months. All p-values are derived from the multivariable analysis if not otherwise stated. Eligible covariates for the models were patient age (*p = 0.136*), Hospital Frailty Risk Score (*p = 0.076*), Charlson Comorbidity Index (*p = 0.218*), number of drugs prescribed by GP (*p = 0.048*) and Timed "Up&Go" Test (*p = 0.691*) for rehospitalizations at three months and patient age (*p = 0.084*), Hospital Frailty Risk Score (*p = 0.055*), Charlson Comorbidity Index (*p = 0.613*), number of drugs prescribed by GP (*p = 0.194*), BMI (*p = 0.133*) and Frailty classified (*p = 0.709*) for rehospitalizations at six months. As these differences obviously came about by chance and did not have any causal association with the subsequent GPs' decision on the discharge medication they were considered as covariates in our following multivariable analyses (Appendix Tables 1, 2 and 3). Due to the low number of rehospitalizations after one month (GPD "continued" group: 3 events; GPD "changed": 8 events), an in-depth multivariable analysis could not be performed methodically. However, after three months with 5 events in the GPD "continued" and 18 events in the GPD "changed" group, a changed discharge medication by univariable means was associated with a predicted mean value of 0.73 hospital stays compared to 0.2 in the "continued" group – a 3.6 fold difference. After adjustment for the above-mentioned covariates, the odds even resulted in a 3.8-fold difference with predicted mean values per participant of 0.6 [95 % CI 0.38-0.97] and 0.16 [95 % CI 0.05-0.52] hospital stays, respectively *(p = 0.023)*. At six months, we observed 23 rehospitalizations in the GPD "changed" and 8 rehospitalizations in the GPD "continued"

Table 1: Baseline demographic and clinical characteristics of enrolled patients (SD: Standard deviation, IQR: Interquartile range)

	GPD[a] "changed"	GPD[a] "continued"
Number of patients (%)	44 (62)	27 (38)
Age, mean (SD)	80.6 (6.1)	84 (5.4)
Sex female (%)	31 (70.5)	15 (55.6)
Body mass index, mean (SD)	27.8 (5.1)	25 (5.4)
Smoking status (%)	--	--
Current	1 (2.3)	3 (11.1)
Past	3 (6.8)	6 (22.2)
Never	40 (90.9)	18 (66.7)
Having a customer account at their local pharmacy (%)	--	--
Yes	40 (90.9)	23 (85.2)
No	4 (9.1)	4 (14.8)
Who is preparing the medication? (%)	--	--
Patient	26 (59.1)	16 (59.3)
Spouse	6 (13.6)	1 (3.7)
Other family members	4 (9.1)	6 (22.2)
Nursing service	2 (4.5)	2 (7.4)
Nursing home	3 (6.8)	0 (0)
Directly from package without preparing	3 (6.8)	2 (7.4)
Fried's Frailty, number of criteria met (%)	--	--
1 criterium met	2 (4.5)	1 (3.7)
2 criteria met	3 (6.8)	5 (18.5)
3 criteria met	12 (27.3)	5 (18.5)
4 criteria met	21 (47.7)	14 (51.9)
5 criteria met	6 (13.6)	2 (7.4)
Frailty classified, median [IQR]	3 [3; 3]	3 [3; 3]
Mini Mental State Examination, mean (SD)	25.5 (3.9)	25.7 (3.7)
Charlson Comorbidity Index, median [IQR]	2 [1;3]	1 [1;2]

Timed "Up&Go" test at admission, median [IQR], sec	21.5 [18.75; 29.75]	26 [21.5; 39.5]
Timed "Up&Go" test at discharge, median [IQR], sec	21 [14.5; 28]	20.5 [16.25;31.75]
Number of drugs prescribed at discharge, mean (SD)	8.8 (4.1)	7.7 (3.1)
Number of drugs prescribed by GP, mean (SD)	8.6 (4)	7.5 (2.9)
Barthel Index at admission, median [IQR]	35 [30; 40]	35 [20; 35]
Barthel Index at discharge, median [IQR]	70 [61.25; 75]	70 [60; 75]
Geriatric Depression Scale, median [IQR]	2 [1; 5]	2 [0;5]
Hospital Frailty Risk Score, mean (SD)	8.7 (5.3)	8.1 (4.5)
Short FES-I, median [IQR]	7 [7; 16]	8 [7; 22.75]
Grip strength, mean (SD), kg	16 (7.6)	15.4 (10)
Gait speed, mean (SD), sec/15 feet	10.4 (3.7)	12.3 (4.3)
Nutritional Risk Screening, median [IQR]	2 [1; 4]	1 [1; 3]
[a]GPD: General practitioner's decision regarding discharge medication	--	

group. Since the difference was not statistically significant in the multivariate analysis ($p = 0.081$), no predicted mean values were calculated.

Regarding the immediacy of rehospitalizations, 25 of the 44 patients in the GPD "changed" group experienced the event rehospitalization over the total course of six months, whereas 19 did not. Eleven of the 27 patients in the GPD "continued" group were rehospitalized and 15 completed the follow-up without an event. Three patients died and were censored, two of them having experienced an event and one not. Mean time until the first rehospitalization was 106.6 days (95 % CI 87.6-125.6) for GPD "changed" and 132.6 days (95 % CI 112.1-153.1) for the decision "continued"; $p = 0.067$, shown in Fig. 2.

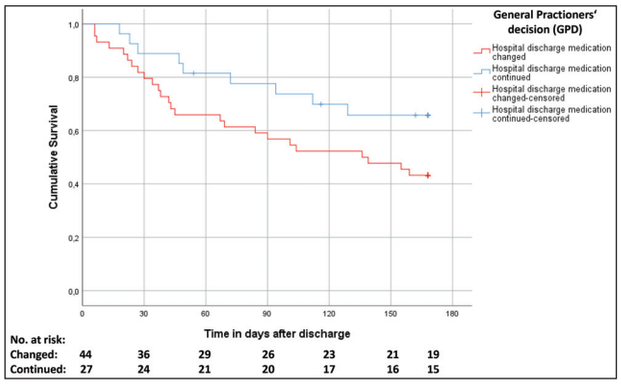

Fig. 2: Log rank test survival plot for time until first rehospitalization after discharge depending on the general practitioners' decision (GPD).

To address the topic of recurrence in rehospitalizations of one individual with the Andersen Gill model, eligible covariates for the multivariable analysis were the Charlson Comorbidity Index ($p = 0.061$), number of drugs prescribed by the GP ($p = 0.092$), patient age ($p = 0.049$) and classified TUG ($p = 0.025$) (Appendix Table 3). Patients with the GPD "continued" had a hazard ratio for recurrent rehospitalizations of 0.27 (95 % CI 0.11-0.65, $p = 0.003$). Hazard ratios for the covariates, referring to increasing values in both categorical and metric values, were as follows: Charlson Comorbidity Index 1.03 (95 % CI 0.93-1.16, $p = 0.525$), number of drugs prescribed by the GP 1.05 (95 % CI 0.98-1.11, $p = 0.153$), patient age 0.93 (95 % CI 0.87-1.00, $p = 0.063$) and classified TUG 2.13 (95 % CI 1.27-3.57, $p = 0.004$). We visualized the predicted time until the recurrent events in the AG model while holding the covariates at their means or using the lowest value for categorical covariates (classified TUG), respectively, in Fig. 3.

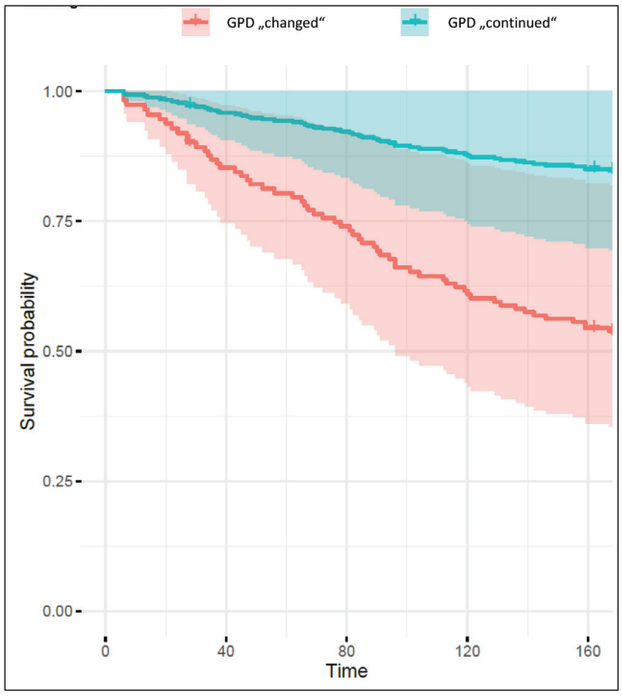

Fig. 3: Andersen Gill recurrent events model survival plot for being hospitalized more, earlier or both depending on the GPD regarding discharge medication

In Fig. 4, we visualized the six possible constellations of the GPD and classified TUG values using a conventional Cox model due to the statistically significant "protective" association of the GPD "continued" and low classified TUG values in the AG model.

2.2. Number of drugs as predictor for rehospitalization

After three months, the number of drugs prescribed by the GP showed a significant association with the rate of rehospitalization: Predicted mean values for four prescribed drugs were 0.21 (95 % CI 0.1-0.46) compared to 0.31 rehospitalizations per participant (95 % CI 0.16-0.57) at the cohort`s median of eight drugs within three months after discharge; p = 0.048.

2.3. Days spent at home

By univariable means, study participants with continued discharge medication spent a predicted mean of 19.1 (63.7 %) days of the first month after discharge, 67.8 (56.5 %) days after three months and 149.8 (83.2 %) days after six months at home. In the GPD

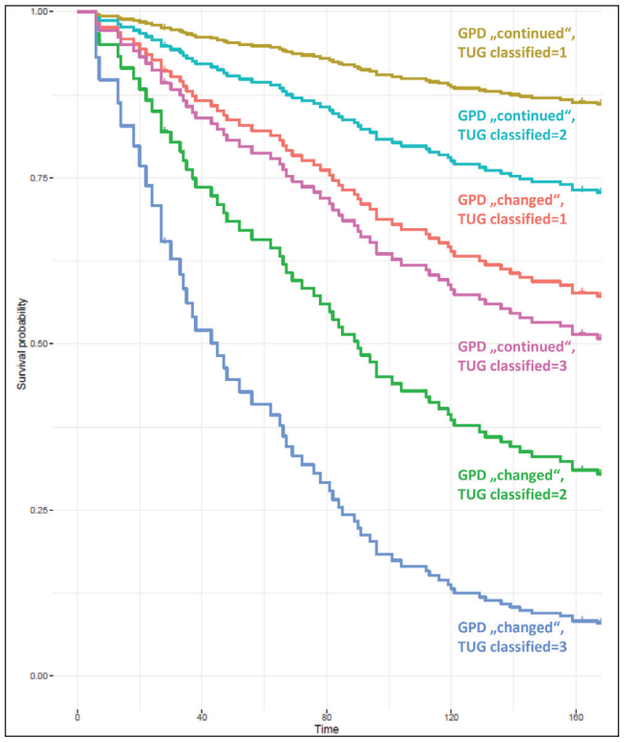

Fig. 4: Cox regression survival plot for rehospitalizations depending on GPD regarding discharge medication and classified Timed "Up&Go" Test for all six possible constellations due to the statistically significant "protective" association of the GPD "continued" and low classified TUG with the outcome of the AG model.

"changed" group the respective numbers were 16.2 (54 %) for the first month, 61.8 (51.5 %) for three months and 137.5 (76.4 %) for six months. We found no significant interaction with the GPD (*p=0.484*; *p=0.301*; *p=0.125*). However, in the multivariate analysis the discharge type had a statistically significant association after one month (*p<0.0001*) resulting in the following predicted mean values: Home 26 days (95% CI 23.2-29.2), rehabilitation facility 5.3 days (95% CI 4.2-6.7) short-term care 5.2 days (95% CI 3.8-7.1) and nursing home 28 days (95% CI 17-46.1). The discharge type also showed a significant association in the multivariate analysis after three months (*p=0.0017*) with the included covariates patient age (*p=0.346*), BMI (*p=0.518*) and TUG classified (*p=0.247*). Predicted mean values are reported in Table 2 depending on the discharge type and classified TUG values. After six months, the multivariable analysis did not show any association of the GPD with DSAH (*p=0.346*) with the included covariates patient age (*p=0.251*), Hospital Frailty Risk Score (*p=0.246*) and BMI (*p=0.349*).

3. Discussion

3.1. Changing the discharge medication might result in more and earlier rehospitalizations (main findings)

In our specialized clinic, every patient underwent an evaluation of their medication by a geriatrician upon hospitalization which is often changed in the hospital after discussion in a multiprofessional team. While we observed the effect of these changes during the inpatient setting, we were interested in 1) the rate of acceptance of our changes by the GP after discharge and 2) the effect of our medication changes on potential readmissions. We found that patients whose GP changed our discharge medication were at risk to be hospitalized more often, earlier or both after their index hospitalization. This suggests that geriatric patients might benefit from the initial multiprofessional re-evaluation of and changes to their medication as well as from continuation of this regimen after discharge. This would especially hold true for hospitalizations that were initially caused by adverse drug reactions, incorrect dosing of drugs or unrecognized drug interactions in the setting of polypharmacy (Chan et al. 2001; El Morabet et al. 2018; Parekh et al. 2018). The patients in our cohort were well characterized regarding functional and cognitive status and the covariates chosen all account for a potential imbalance due to the post hoc allocation and disease burden, impaired functionality, frailty, malnutrition and obesity.

3.2. Ambulatory medication regimens are often changed during hospitalizations

A change of the ambulatory medication during hospitalizations in older people is very common, especially when an acute illness occurs or symptoms of an existing condition has substantially worsened (Rouch et al. 2018) which was true for nearly all of our patients. Medication reconciliation, the complete and comprehensive collection of all drugs used in the ambulatory setting and their correct adaption in the hospital setting during admission as well as the structured and concise presentation of the recommended drug therapy at the time of discharge while providing reasons for the changes made during hospitalization can greatly improve continuation of discharge medication in primary care: In a French study, medication reconciliation at discharge resulted in a significantly higher rate of geriatric discharge medications' continuation in primary care (Montaleytang et al. 2021). Additionally, an RCT with medication reconciliation at admission, discharge and further on in primary care as well as medication reviews and attempts to optimize pharmacotherapy during the index hospitalization by a pharmacist led to a significant reduction of errors in primary care, which was to be expected due to the collaboration with GPs and community pharmacists (Marinović et al. 2021). These results can be explained by an improved communication at discharge: When GPs are provided with reasons for changing drug therapy during hospitalization, they are more likely to continue them in primary care. However, medication reconciliation by a clinical pharmacist in our study was only provided at admission, patients were discharged within the framework of standard care using exclusively the discharge letters written by the treating hospital physician.

Table 2: Days spent at home after three months depending on discharge type and Timed "Up&Go" Test (TUG)

	Classified TUG[a] Test 1 (≤ 10 s), s	Classified TUG[a] Test 2 (11-29 s), s	Classified TUG[a] Test 3 (≥ 30 s), s
Discharge type	--	--	--
Home	79.2 (95 % CI 62.2-100.9)	76.9 (95 % CI 69.4-85.3)	65.7 (95 % CI 55-78.5)
Rehabilitation facility	58 (95 % CI 42.7-78.7)	56.3 (95 % CI 48.2-65.8)	48.1 (9 5% CI 38.5-59.9)
Short-term care	52.3 (95 % CI 36.5-74.9)	50.8 (95 % CI 39.5-65.3)	43.3 (95 % CI 33.8-55.6)
Nursing home	82.7 (95 % CI 44.1-154.9)	80.3 (95 % CI 44.9-143.5)	68.5 (95 % CI 39.7-118.3)
[a]Timed "Up&Go"	--	--	--

On the other hand, GPs often know their patients for a long period and recommended medication regimens might have already been tried in primary care, were ineffective or resulted in adverse drug reactions. Interviewing GPs for their reasons to change discharge medication was not possible in our setting because we as a university clinic did not intend to put GPs into the position of having to justify themselves for their drug regimen choices while simultaneously monitoring their patients for negative effects of these decisions. Studies show a variety of reasons, mostly miscommunication and delayed discharge letters rather than deliberatively changing medications (Gröber-Grätz et al. 2014; Strehlau et al. 2018). However, this was addressed in our cohort by providing discharge letters to GPs directly at the time of discharge and confirming their consideration with a follow-up call one week later. Another factor that requires considering is that fewer rehospitalizations could also be due to patients' clinical stability after the index hospitalization. This could be the result of efforts initiated by the GP that were not connected to the medication, i.e. regular physio- or ergotherapy as well as high quality institutional care or specific programs for community-dwelling patients.

3.3. Communicating reasons for medication change in the hospital after discharge and interventions to continue that drug regimen in primary care are crucial

In literature, the effect of this medication continuation on clinical outcomes like rehospitalization is rarely specified: In a small RCT investigating emergency department visits and rehospitalization after 30 days, usual care was compared to a combination of medication reconciliation and review, condition specific patient education, enhanced discharge planning and phone follow-up. Emergency department visits and rehospitalizations were significantly lower in the intervention group within one month after discharge (Koehler et al. 2009). Although we did not implement such complex medication reconciliation, we provided discharge letters generated during usual care and confirmed their receipt and consideration by the GP in generating a post-discharge medication treatment. Delayed or missing discharge letters were often criticized as a problem in transition of care which we hereby eliminated. Since patients in our cohort with continued discharge medication experienced fewer rehospitalizations, especially medication reconciliation at discharge (e. g. enhanced discharge planning in the aforementioned study) might be an important component.

In general, interventions regarding transition of care and medication reconciliation might be a suitable task for pharmacists due to their clinical knowledge and ability to explain medication regimens to patients (Capiau et al. 2020; Redmond et al. 2018; Snyder et al. 2020).

Especially hospital-initiated interventions connecting primary to secondary care and accompanying this transition appear to be beneficial: A meta-analysis including such interventions found an overall lower likelihood of readmissions (odds ratio 0.8 [95% CI 0.7–0.9]). In particular, patients receiving two or more post-discharge home visits or follow-up calls had a substantially lower likelihood of readmissions (OR 0.5 [95% CI 0.4–0.8]) (Branowicki et al. 2017).

However, it is also important to emphasize that the effects of in-hospital medication reviews or changes in the hospital setting in general have a short half-life in the transition from secondary to primary care: Two reviews state that the impact on rehospitalizations in older patients was mostly seen after one month and decreased after that (Dautzenberg et al. 2021; Renaudin et al. 2016). Therefore, it is possible that the effect in our cohort was also present after one month, although the model was not calculable. This decreasing effect also fits our results after six months: Persistence of GPD's effect would have been implausible, especially in older patients with many rehospitalizations and medication changes; it will eventually be overridden by subsequent rehospitalizations and their discharge medication recommendations.

As stated above, we found literature about how GPs assess discharge medication, if they continue it in primary care and how to improve communication by medication reconciliation. However, the effect of this "medication adherence by the GP" to hospital medication recommendations on hard clinical outcomes like rehospitalizations has not been specifically investigated yet.

3.4. The time until recurrent rehospitalization included how often and how frequent patients were hospitalized and worsened when discharge medication was changed

The number of rehospitalizations and days spent at home are an attempt to represent the loss of qualitative lifetime and the problems that occur during transitions of care. However, they do not sufficiently reflect if patients were either frequently hospitalized for a short duration of time or had one hospital stay that lasted for a longer period. Therefore, we decided to use the Andersen Gill model which summarizes the number of rehospitalizations, the time until the first rehospitalization and the intervals between hospital stays, plots them for each patient and estimates a risk to be either hospitalized earlier, more often or both. In addition to the effect of the GPD on rehospitalizations alone, this model illustrates in a rather holistic approach that patients with a GPD "changed" are subjected to more frequent transitions of care with shorter gaps between them and the stress linked to them.

3.5. Days spent at home as an indicator for quality of life was difficult to interpret due to the different discharge types

Regarding days spent at home, a concluding assessment is very difficult to make due to the different discharge types and the big difference between the settings (i.e. rehabilitation facility and home). However, an interesting observation was the tendency towards more days spent at home after three months with lower TUG values.

3.6. Recent studies regarding discharge medication, its evaluation by General Practitioners and the association with rehospitalizations

We conducted a broad search for recent publications between 2018 and 2023 to update our initial literature review. We did not find studies that evaluated the effect of GPs' evaluation of discharge medication on rehospitalization or other use of healthcare facilities. A greater portion of the publications were interviews or quality improvement studies with GPs' or other healthcare workers to gain their opinion on how to improve discharge letters. Almost always the participants highlighted information on discharge medication and reasons for drug changes (Nguyen et al. 2021; Weetman et al. 2021).

However, some studies with geriatric patients were in the vicinity of our research question: A British study undertook a retrospective record review to determine which recommendations in discharge letters were followed by the GPs and how non-compliance was associated with harm. Changes made by the GP that were comprehensibly documented and explained were not taken into account. In 46 % of all discharges, recommendations by the hospital in general (e. g. tests or procedures) were not followed. In 17 % of the cases, the recommended discharge medication was not continued by the GPs and the risk of change was highest with newly started drugs during hospitalization. The overall estimated patient harm after discharge was 8 % and of moderate severity according to the authors who used three different and validated rating scales but not severe clinical incidents like rehospitalizations. (Spencer et al. 2018). A small Irish study implemented a post-discharge, pharmacist-led medicines optimization clinic and investigated the effect on readmission parameters. Significant results in 180-day readmissions, ED visits and unplanned GP consultations were observed (Odeh et al. 2020). However, in both publications of Spencer et al. and Odeh et al. the evaluation of their recommendations by the GP was not documented or taken into account.

A new municipality-based, nurse-led and GP-supported transition of care intervention was inferior to the already existing hospital-based geriatric team intervention in preventing 30-day readmission among frail, geriatric patients (Hansen et al. 2021). This result is relevant since the discharge model in our study was similar to the geriatric team.

A Swiss study investigated the effect of trained junior and senior physicians to provide medication reviews with enhanced information transfer to the GP vs. usual care in geriatric patients. Primary outcome was time to first rehospitalization and a plethora of secondary outcomes including 30-day readmissions. However, no difference was found between the groups and acceptance of discharge medication by the GP was not evaluated (Grischott et al. 2023). Another implementation program with patient-centered discharge medicine review services, provided by a clinical pharmacist, did not submit the recommendations directly to the GP but rather to the patients: They were asked to discuss those important to them with the GP. Of 368 recommendations made, 351 (95%) were actioned by patients, resulting in 284 (77% of those actioned) being implemented, and 206 regularly taken medicines (19.7 % of all regular medicines) deprescribed after discharge (Basger et al. 2023).

Another study identified the optimal timing of making discharge letters available to the GP to reduce rehospitalizations the most by using insurance billing data from Canadian elderly or chronically ill patients: The period of largest contribution to readmission reduction was seen in the first 10 days, while physician visits occurring later than 21 days after discharge did not further contribute to reducing hospital readmissions (Riverin et al. 2018). A similar study examined the risk of rehospitalization within 30 days depending on the availability of discharge summaries to GPs within 7 days after discharge. Discharge summary availability was associated with a lower risk of 30-day readmission (adjusted odds ratio [95% CI] = 0.25 [0.07-0.91]) (Hurtaud et al. 2019). These results fit into our methods since we provided GPs with discharge letters immediately after discharge.

A small French study provided the results of medication reconciliation carried out in the hospital to the GP. Although many discrepancies could be corrected during hospitalization, in only 24 % of the cases the GP was aware of medication reconciliation at discharge and discharge letters arrived at GPs' offices after a mean of 36 days. Therefore, the results of medication reconciliation were often not taken into account (Montaleytang et al. 2021). We avoided this problem of GPs not being aware of medication reconciliation by confirming the reception and processing of our discharge recommendations using a half-structured interview.

A study already discussed in the introduction should be emphasized: Rouch et al. (2018) provided explanations on why medications were changed in the discharge letter and managed to transit their discharge medication into primary care in 83 % of the cases. As already stated in the interview studies, this could be a viable aspect: When GPs are not explained why their medication was suddenly changed or discontinued in-hospital, they cannot recreate the thought process during hospitalization and are left with a medication plan that is often not comprehensible and are almost forced to modify it to the best of their knowledge.

To summarize our results and findings in the literature, continuing geriatric support in primary care, providing reasons for medication changes to GPs, and advising patients and caretakers about the medication lead to fewer critical events in the weeks after discharge. Our study adds a small piece to the complex process of transitions of care by trying to answer the question whether discontinuing the recommendations of a specialized geriatric clinic might have a negative effect in primary care in this specific cohort.

To the best of our knowledge, this is the first study to examine the clinical consequences of this important decision made by the GP during the transition of care in geriatric patients.

Limitations of our study are the monocentric design, the small sample size and the partial information about reasons for rehospitalizations that were obtained by discharge letters as well as patients' and GPs' reports which did not exclusively identify the handling of our discharge medication as the reason for a hospital stay after the index hospitalization. Also, the post-hoc allocation of patients led to a data-driven analysis of time until rehospitalization since all information was available at the time of the analysis. Therefore, results of the Andersen Gill model with its very explicit result and high significance should be interpreted carefully and confirmed in future studies. Additionally, medication reconciliation and releasing discharge letters by a pharmacist might have prevented medication errors, though this effect would have occurred in both groups. Strengths of this study were its novel approach, good characterization of patients in terms of functional status, frailty and disease burden, the well-functioning acquisition of information to determine rehospitalizations and DSAH and the comprehensive evaluation methods.

Our findings cannot definitively confirm that any hospitalization in geriatric patients has to be seen as a disruptive event that requires profound adjustments especially in pharmacotherapy. Deriving that conclusion from our data would be inaccurate since geriatric patients with many comorbidities and therefore medications are very complex and there are a plethora of factors that contribute to a patient's well-being or the need to be hospitalized in the community setting that we were not able to completely monitor. Nonetheless, our explorative results emphasize that the discharge process especially in older people is not finished with leaving the hospital: It needs to be accompanied by extensive communication between discharging geriatrician and GP. At the very least, reasons for medication changes during the hospital stay have to be clearly stated.

4. Experimental

We collected data during the prospective monocentric cohort study "The pharmacist in the acute geriatric inpatient treatment team – Impact on rehospitalizations and transsectoral communication" between January 2018 and September 2018 (AGITATE; ClinicalTrials Identifier NCT03412903, RWTH Aachen University Hospital ethics committee approval 230/17). The eligibility, exclusion reasons and recruitment course are displayed in Fig. 1. Inclusion criteria were: 70 years or older, an expected inpatient stay of seven days or longer, current drug therapy and participation in a multiprofessional, acute geriatric treatment. Exclusion criteria were moribund status defined by the treating physician and inability to give informed consent.

During this index hospitalization, patients had a comprehensive review of their medication also reconciling their functional and cognitive status. The only deviation from standard care in this study was medication reconciliation at admission by a pharmacist to ensure consideration of all drugs taken in the ambulatory setting.

For proper multivariate adjustments, all study participants underwent a comprehensive geriatric assessment during this stay which comprised potential covariates such as Fried's Frailty score (Fried et al. 2001), Hospital Frailty Risk Score (Gilbert et al. 2018), Charlson Comorbidity Index (Charlson et al. 1987) and Timed "Up&Go" Test (TUG) (Podsiadlo and Richardson 1991).

Upon completion, patients were discharged to either home, rehabilitation facilities or nursing homes. This process included comprehensive verification and forwarding of discharge letters to patients and GPs to definitively ensure that the information was available to them (Strehlau et al. 2018). Additionally, GPs' offices were contacted one week after discharge using a structured interview to verify that [i.] they had received the discharge letter, [ii.] patients had had a post-discharge appointment and [iii.] medication plans had been updated. This new medication plan was compared with the last geriatric expert's recommendation, either by our clinic or – in case of a directly consecutive geriatric rehabilitation – by the discharging rehabilitation physician. Based on this information it was dichotomously determined whether the GP went in favor of continuing or changing the geriatrician's hospital discharge medication: General Practitioner's decision (GPD) "continued" or "changed". Notably, we categorized any *de novo* starting or the omission of drugs as an expression of change. Only small dose adjustments in clearly specified drug classes (antihypertensives, diuretics, analgesics, insulin and laxatives) were tolerated within GPD "continued" as this could be plausible due to changed living conditions at home (Rouch et al. 2018; Viktil et al. 2012).

4.1. Outcomes and follow-up

Primary outcome of the study was the number of nonelective rehospitalizations at one, three and six months after discharge. Secondary outcomes included days spent at home (DSAH) (Groff et al. 2016) at one, three and six months, time until the first rehospitalization and time until recurrent rehospitalizations after discharge. For that, we contacted patients and GPs at one, three and six months to obtain information about rehospitalizations, discharge letters and current medication plans. We then counted the number of rehospitalizations for each observation time. The DSAH were inversely derived from the number of days patients spent in a medical facility with at least one overnight stay.

We next tested our research question whether GPD "changed" was associated with more and earlier rehospitalizations and fewer DSAH, respectively.

4.2. Statistics

We used a negative binomial regression model to individually analyze the number of rehospitalizations and DSAH after one, three and six months which also accounted for over-dispersion. We identified covariates with clinical relevance that described the patients' morbidity and functional status, univariably tested their association with GPD and hereby assessed their eligibility for multivariable analyses: Fried's Frailty (absolute and classified values [0 points = robust, 1 or 2 points = pre-frail, ≥ 3 points = frail]), Hospital Frailty Risk Score, Charlson Comorbidity Index, Timed "Up&Go" Test (absolute and classified values [≤ 10 s = 1, 11-29 s = 2, ≥ 30 s = 3]), grip strength, number of drugs prescribed by the GP, patient age, body mass index (BMI) and discharge type. Cutoff *p*-value for inclusion in the multivariable model was < 0.2. The univariable analyses are available as tables S1, S2 and S3.

Time until the first rehospitalization was analyzed with a log rank test that tested the association of the GPD "changed" or "continued" with an earlier rehospitalization. Since that model only accounts for one event and discards all subsequent rehospitalizations and their immediacy after the preceding event, thereby ignoring a large proportion of data, we used a recurrent events survival analysis – the Andersen Gill model (Andersen and Gill 1982). It is a time-to-event approach based on the Cox proportional hazard model and is suitable when correlations among events for each patient are influenced by the covariates which is true for the covariates we test for this model. The resulting hazard ratio expresses the risk that patients experience rehospitalizations earlier and then more frequent after the first rehospitalization with smaller gap times between each individual event. We univariably tested the same covariates as in the negative binomial regression to identify these with eligibility for a multivariable analysis. Contrasts for the AG model were calculated while holding all other covariates at their means to assess the impact of one covariate on the predicted mean (see Table 1). Cutoff *p*-values for inclusion in the multivariable model was < 0.1.

Regarding the number of prescribed drugs, the predicted mean values are juxtaposed with four drugs, which is one less than the common definition of polypharmacy, and the median of the cohort (Table 1), respectively. Descriptive data is reported with means and standard deviations (normally distributed) or medians and interquartile ranges (not normally distributed). We used R version 4.0.4, SAS 9.4, IBM SPSS Statistics Version 25 and Microsoft Excel 2016 for the analyses.

4.3. Ethical considerations

This study complied with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Subjects have given their written informed consent to participate in the study as well as publication of their pseudonymized data in the course of this publication. The study protocol was reviewed and approved by University Hopital Aachen's committee on human research, approval number 230/17. Cognitively impaired patients were not eligible for this study and therefore not approached to participate. The cognitive status of possible probands was determined beforehand by a resident physician, an attending physician and a clinical psychologist.

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Conflicts of interest: Mathias Freitag received payments for lectures for pharmacy students, pharmacists in specialty training and physicians by the Apothekerkammer Nordrhein (Pharmacy Association Nordrhein) and Ärztekammer Nordrhein (Medical Association Nordrhein). He also received financial support by the Deutsche Gesellschaft für Geriatrie (German Society of Geriatrics) for attending the congress of the European Geriatric Medicine Society in 2018. Albrecht Eisert received payments for lectures for pharmacy students and pharmacists in specialty training by the Apothekerkammer Nordrhein (Pharmacy Association Nordrhein). Tanja Bülow received funding from the European Union's Horizon 2020 research and innovation program under grant agreement number 825575.The societies and associations no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The authors have no relevant financial or non-financial interests or competing interests to disclose.

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Supplementary Material

Supplementary Table S1: Negative Binomial Regression model for rehospitalizations and its p-values

	p-values overall		
Rehospitalizations after one month	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)	MULTIVARIAT (with p<0.2 from univ. incl. discharge type)
General Practitioners' decision (GPD)	0.3380		
Hospital Frailty Risk Score	0.7207		
Charlson Comorbidity Index including age	0.8666		
Charlson Comorbidity Index	0.6655		
Fried's Frailty	0.9403		
Fried's Frailty classified	0.9106		
Number of drugs prescribed by GP	0.7008		
Grip strength	0.3905		
Timed "Up&Go" Test	0.2788		
Timed "Up&Go" Test classified			
Age	0.0478		
Discharge type	0.3035		
Body Mass Index	0.2425		
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.4230		
	Could not be performed since the outcome's variability was too low to fit a model		

Rehospitalizations after three months	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)	MULTIVARIAT (with p<0.2 from univ.)
General Practitioners' decision (GPD)	0.0118	0.0340	0.0228
Hospital Frailty Risk Score	0.1078	0.0722	0.0762
Charlson Comorbidity Index including age	0.1686		
Charlson Comorbidity Index	0.0867	0.2108	0.2184
Fried's Frailty	0.5795		
Fried's Frailty classified	0.7520		
Number of drugs prescribed by GP	0.0676	0.0189	0.0479
Grip strength	0.4410		
Timed "Up&Go" Test	0.4798		
Timed "Up&Go" Test classified	0.0772	1 vs. 3=0.9818; 2 vs. 3=0.6913	
Age	0.0082	0.0802	0.1358
Discharge type	0.7282		
Body Mass Index	0.3166		
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.2141		
Rehospitalizations after six months	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)	MULTIVARIAT (with p<0.2 from univ.)
General Practitioners' decision (GPD)	0.0126	0.0807	0.1184
Hospital Frailty Risk Score	0.1027	0.0511	0.0551
Charlson Comorbidity Index including age	0.4281		
Charlson Comorbidity Index	0.1897	0.4958	0.6131
Fried's Frailty	0.3148		
Fried's Frailty classified	0.1879	0.6479	0.7093
Number of drugs prescribed by GP	0.1327	0.2360	0.1938
Grip strength	0.3814		
Timed "Up&Go" Test	0.8366		
Timed "Up&Go" Test classified	0.3970		
Age	0.0225	0.1050	0.0836
Discharge type	0.7301		
Body Mass Index	0.1848	0.1808	
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.1876		0.1329
		AIC=145.6561	AIC= 145.4103

Supplementary Table S2: Negative Binomial Regression model for days spent at home and its p-values

	p-values overall	
Days spent at home after one month	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)
General Practitioners' decision	0.4844	
Hospital Frailty Risk Score	0.9318	
Charlson Comorbidity Index including age	0.7003	
Charlson Comorbidity Index	0.5922	
Fried's Frailty	0.4784	
Fried's Frailty classified	0.3529	
Number of drugs prescribed by GP	0.8629	
Grip strength	0.8670	
Timed "Up&Go" Test	0.7244	
Timed "Up&Go" Test classified	0.5215	
Age	0.5382	
Discharge type	<0.0001	
Body Mass Index	0.3496	
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.8958	
	AIC=491.9378	

Days spent at home after three months	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)
General Practitioners' decision	0.3010	
Hospital Frailty Risk Score	0.3567	
Charlson Comorbidity Index with age	0.5375	
Charlson Comorbidity Index	0.4648	
Fried's Frailty	0.3729	
Fried's Frailty classified	0.8083	
Number of drugs prescribed by GP	0.5828	
Grip strength	0.5859	
Timed "Up&Go" Test	0.4145	
Timed "Up&Go" Test classified	0.1101	0.2467
Age	0.1800	0.3457
Discharge type	<0.0001	0.0017
Body Mass Index	0.1852	0.5183
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.2653	
		AIC=506.5005

Days spent at home after six months	UNIVARIAT	MULTIVARIAT (with p<0.2 from univ.)	MULTIVARIAT (with p<0.2 from univ.)
General Practitioners' decision	0.1253	0.3460	0.4237
Hospital Frailty Risk Score	0.1996	0.2457	0.2847
Charlson Comorbidity Index with age	0.4945		
Charlson Comorbidity Index	0.4051		
Fried's Frailty	0.3501		
Fried's Frailty classified	0.8493		
Number of drugs prescribed by GP	0.5464		
Grip strength	0.5642		
Timed "Up&Go" Test	0.8057		
Timed "Up&Go" Test classified	0.4186		
Age	0.0734	0.2511	0.2486
Discharge type	0.2280		
Body Mass Index	0.1659	0.3487	
Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	0.1163		0.2640
		AIC=636.5591	AIC=636.7737

Supplementary Table S3: Variable selection for the Andersen Gill model

Univariable	Hazard Ratio	95%-CI	p-value
General Practitioners' decision (GPD)	0.3119	[0.1499, 0.6489]	0.00183
Likelihood ratio test= 14.44 on 1 df, p=1e-04			

GPD + one variable	Associations	Hazard Ratio	p-value
1	GPD	0.3275	0.00202
	Hospital Frailty Risk Score	1.0593	0.10145
2	GPD	0.2988	0.00231
	Charlson Comorbidity Index including age	1.1322	0.18132
3	GPD	0.3058	0.00247
	Charlson Comorbidity Index	1.1507	0.06105
4	GPD	0.3238	0.00217
	Fried's Frailty	1.2213	0.18927
5	GPD	0.3296	0.00257
	Fried's Frailty classified	1.8404	0.11433
6	GPD	0.3292	0.00289
	Number of drugs prescribed by GP	1.0515	0.09226
7	GPD	0.3053	0.00367
	Grip strength	1.0319	0.31823
8	GPD	0.2464	0.00122
	Timed "Up&Go" Test	1.0103	0.12047
9	GPD	0.2381	0.000854
	Timed "Up&Go" Test classified	2.0170	0.02521
10	GPD	0.3828	0.00997
	Age	0.9355	0.04858
11	GPD	0.3068	0.00181
	Discharge type	0.8463	0.45881
12	GPD	0.3237	0.00305
	Body Mass Index	1.0127	0.65102
13	GPD	0.5785	0.201
	Body Mass Index classified (<20 kg/m², 20-29.9 kg/m², ≥30 kg/m²)	1.3899	0.388

GPD + variables with p<0.1	Variables	Hazard Ratio	95%-CI	p-value
	GPD	0.2670	0.1105; 0.6456	0.00337
	Charlson Comorbidity Index	1.0371	0.9270; 1.1602	0.52451
	Number of drugs prescribed by GP	1.0462	0.9833; 1.1132	0.15316
	Timed “Up&Go“ Test classified	2.1280	1.2696; 3.5665	0.00416
	Age	0.9318	0.8650; 1.0037	0.06259
Likelihood ratio test= 38.43 on 5 df, p=3e-07				

GPD + variables with p<0.2	Variables	Hazard Ratio	95%-CI	p-value
	GPD	0.3274	0.1400; 0.7656	0.00999
	Hospital Frailty Risk Score	1.0435	0.9619; 1.1320	0.30581
	Charlson Comorbidity Index	1.0413	0.9283; 1.1680	0.49016
	Fried’s Frailty classified	1.4556	0.5598; 3.7845	0.44127
	Number of drugs prescribed by GP	1.0525	0.9760; 1.1350	0.18345
	Timed “Up&Go“ Test classified	1.6559	0.9107; 3.0109	0.09829
	Age	0.9348	0.8717; 1.0026	0.05916
Likelihood ratio test= 41.36 on 7 df, p=7e-07				

GPD + all variables	Variables	Hazard Ratio	95%-CI	p-value
	GPD	0.2600	0.09535; 0.7092	0.00851
	Hospital Frailty Risk Score	1.0303	0.95794; 1.1082	0.42156
	Charlson Comorbidity Index	1.0094	0.88600; 1.1499	0.88860
	Fried’s Frailty classified	1.4208	0.52999; 3.8088	0.48514
	Number of drugs prescribed by GP	1.0675	0.98306; 1.1592	0.12029
	Grip strength	1.0270	0.98289; 1.0732	0.23399
	Timed “Up&Go“ Test classified	2.3401	1.13603; 4.8202	0.02112
	Age	0.9362	0.87876; 0.9975	0.04155
	Discharge type	0.7340	0.51503; 1.0460	0.08701
Likelihood ratio test= 46.86 on 9 df, p=4e-07				