Additional value of a triggerlist as selection criterion in identifying patients at high risk of medication-related hospital admission

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Research Article

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Abstract

Background 10-30% of the hospital admissions in older patients are medication-related. To increase the identification of medication-related hospital admissions in older patients a triggerlist is published in the Dutch guideline for Polypharmacy.

Aim To assess whether the triggerlist has value (added to age and polypharmacy) as selection criterion to identify patients at high risk of medication-related hospital admissions.

Method This sub-study was carried out in 100 older (≥ 60 years) patients with polypharmacy and having two triggers from the triggerlist. The admissions were assessed as either *possibly* or *unlikely* medication-related according to the Assessment Tool for identifying Hospital Admissions Related to Medications (AT-HARM10).

Results 48% of the admissions were *possibly* medication-related.

Conclusion The high prevalence of medication-related hospital admissions, suggests the triggerlist has added value as selection criterion in a cohort of older patients with polypharmacy and can be used to improve the identification of a population at high risk of medication-related hospital admissions.

Impact Of Findings On Practice Statements

- This study showed a high prevalence of medication-related hospital admissions in a cohort of older patients with polypharmacy and two triggers of the triggerlist.
- The triggerlist has added value as selection criterion to identify a population at high risk of medication-related hospital admissions.
- The triggerlist can be easily automated and may therefore contribute to a feasible and easy-to-implement approach in future research studies to identify a population at high risk of medication-related hospital admissions.

Introduction

Polypharmacy, the chronic use of five or more medications [1], increases the risk of medication-related hospital admissions (MRAs) [2]. Overall, 10–30% of the hospital admissions in older patients are medication-related [3–6]. Most of these studies define MRAs based on adverse drug reactions (ADRs) or adverse drug events (ADEs). However, MRAs may also be defined as a hospital admission where medication-related problems (MRPs) are the main cause or at least a significant contributing factor [7]. Since MRPs, besides ADRs, also encompass drug-drug interactions and medication errors, it is expected that the incidence of MRAs will significantly increase due to this broader definition [8]. To increase the identification of MRAs in older patients the Dutch multidisciplinary guideline for polypharmacy in older patients published a triggerlist that can be used to establish whether an admission is medication-related. This list contains adverse clinical events, also called triggers (such as falls, electrolyte disturbances or

bleeding) and medication (such as psychotropic medication and/or cardiac medication) that are often related to MRAs (see supplementary Table 1) [1, 9]. Nevertheless, although included in the aforementioned guideline, it has not been investigated whether the triggerlist can be used to identify a population at high risk of MRAs. Based on this hypothesis, the triggerlist is currently being used in the CHECkUP study as an additional selection criterion, next to age (≥ 60 years) and polypharmacy [10]. Especially for the purpose of selection, the use of a triggerlist is interesting in terms of feasibility, as it is convenient to complete and can be easily automated, without the need for an expert panel or other time-consuming tools or questionnaires.

Aim Of The Study

The aim of the present study was to assess whether the triggerlist has value (added to age and polypharmacy) as selection criterion to identify patients at high risk of a possible MRA.

Ethics Approval

This retrospective study is a sub-study of the CHECkUP study, which has received approval from the Medical Research Ethics Committee of Zuyderland Medical Centre (METC number: METCZ20180091). All participants gave written informed consent before any data was collected.

Method

Patients

This sub-study was carried out within the first 100 patients who were included in the CHECkUP study. The CHECkUP study is a randomised controlled trial that assesses whether an extensive weekly medication screening using a CDSS compared to usual care reduced hospital readmission within one year in older (≥ 60 years) patients with polypharmacy (defined as using ≥ 5 medications chronically) and having at least two triggers from the triggerlist. Further details are described elsewhere [10]. For this sub-study, all patients were admitted at Zuyderland MC location Sittard-Geleen.

Data Collection

On admission, demographic data (age, sex) and patient-specific characteristics (Charlson Comorbidity Index (CCI) [11], number of medications prior to admission, eGFR, number of trigger diagnoses and number of medications which causes trigger diagnoses) were collected.

Two independent reviewers, assessed whether the admission was either *possibly* or *unlikely* medication-related according to the Assessment Tool for identifying Hospital Admissions Related to Medications (AT-HARM10) [7]. Data from the admission letter, medication list upon admission, laboratory data and

discharge letter were used to complete AT-HARM10. A geriatrician and a hospital pharmacist independently assessed discrepancies and finally all discrepancies were discussed with the entire team to reach consensus.

The AT-HARM10 consists of 10 questions, comprising of MRPs, which can be answered with yes or no [7]. The first three questions are used to identify admissions that are *unlikely* to be medication-related while questions 4–10 are used to identify admissions that are *possibly* medication-related. When one of the ten questions is answered with 'yes', the assessment is finished. When all questions are answered with 'no', an expert panel is needed to assess whether an admission is medication-related. In agreement with the developers of the AT-HARM10, we will speak of *possibly* and *unlikely* medication-related admissions.

Statistical analysis

Descriptive statistics were used to present the demographics and results as means with standard deviation (SD) or medians with interquartile ranges [IQR], whichever appropriate. Statistical analyses were performed using IBM SPSS version 27.0. P-values < 0.05 were considered statistically significant.

Results

The mean age of the 100 patients included in this study was 75.2 years (SD 8.6). Forty-five were female, the median CCI was 2 (IQR 1–3) and the mean number of medicines prior to admission was 10.7 (SD 4.5). Demographic and clinical characteristics are shown in Table 1. 'Insert Table 1 here'

Table 1
Baseline characteristics of older patients with polypharmacy during index admission

Variable	All admissions (n = 100)*	MRA *possibly* (n = 48)	MRA *unlikely* *(n = 51)*	P value
Sex: n (%)	45	22 (22)	22 (22)	0.787
Female	55	26 (26)	29 (29)	0.443
Male	44	22 (45.8)	21 (41.2)	0.504
Age at admission, (years) n (%) :	52	23 (47.9)	29 (56.9)	
60–74	4	3 (6.3)	1 (2.0)	
75–89	75.2 ± 8.6	74.7 ± 9.0	75.8 ± 8.2	
≥ 90				
Mean ± SD				
Charlson Comorbidity Index Score (%) :	11	3 (6.3)	8 (15.7)	0.110
0	52	24 (50.0)	28 (54.9)	0.136
1–2	32	16 (33.3)	15 (29.4)	
3–4	4	4 (8.3)	0 (0.0)	
5–6	1	1 (2.1)	0 (0.0)	
≥7	2 (1–3)	2 (1–3)	2 (1–3)	
Median (IQR)				
Renal function, eGFR (ml/min/1.73m^2), n (%)	21	16 (33.3)	5 (9.8)	0.015
0–29	24	9 (18.8)	15 (29.4)	
30–50	55	23 (47.9)	31 (60.8)	
≥ 51				

SD: Standard Deviation, IQR = Interquartile Range

* one patient was excluded from the comparative analyses between *possibly* and unlikely MRA.

Variable	All admissions (n = 100)*	MRA *possibly* (n = 48)	MRA *unlikely* *(n = 51)*	P value
Number of medicines at index admission, n (%)	4	1 (2.1)	3 (5.9)	0.407
0–4	43	19 (39.6)	24 (47.1)	0.641
5–9	53	28 (58.3)	24 (47.1)	
≥10	10.7 ± 4.5	10.9 ± 4.3	10.5 ± 4.7	
Mean ± SD				
Trigger diagnoses	13	6 (12.5)	7 (13.7)	0.962
0–2	42	21(43.8)	21 (43.1)	0.920
3–5	45	21 (43.8)	23 (43.1)	
≥6	5.0 ± 1.9	5.0 ± 1.8	5.0 ± 2.0	
Mean ± SD				
Trigger medications	21	10 (20.8)	11 (21.6)	0.911
0–2	46	21 (43.8)	24 (47.1)	0.780
3–5	33	17 (35.4)	16 (31.4)	
≥6	4.4 ± 2.2	4.5 ± 2.2	4.4 ± 2.3	
Mean ± SD				
SD: Standard Deviation, IQR = Interquartile Range				
* one patient was excluded from the comparative analyses between *possibly* and unlikely MRA.				

The 100 admissions were scored by two independent reviewers using the AT-HARM10. Ultimately, 48 admissions were assessed as being *possibly* medication-related, 51 as *unlikely* medication-related, and on one admission no consensus could be reached. The independent reviewers agreed on 64 of the admissions, identifying 35 as *possibly* medication-related and 29 as *unlikely* medication-related, respectively. After discussing the discrepancies, another 13 admissions were assessed as *possibly* medication-related and 22 admissions as *unlikely* medication-related. These results are summarized in Fig. 1. 'Insert Fig. 1 here'.

We found no significant differences with regard to age, sex, CCI, number of medicines or triggerlist diagnoses/medications when comparing *possibly* and *unlikely* MRAs. Patients with a possible MRA were more likely to have an impaired renal function (p = 0.015, Table 1).

Discussion

This sub-study of the CHECkUP is the first to show that adding the triggerlist as selection criterion in a cohort of older patients (≥ 60 years) with polypharmacy, improves the identification of a population at high risk of MRA, as 48% of the admissions were classified as *possibly* medication-related by using the AT-HARM10.

The triggerlist was first introduced in the Dutch multidisciplinary guideline for polypharmacy in older patients and was proposed as a list to establish whether a hospital admission is medication-related. Although the triggerlist has high face validity (i.e. the individual components (adverse clinical events) in itself are indeed associated with MRPs and based on data from the HARM-, IPCI- and QUADRAT studies [1, 2, 9, 12, 13]), when it was introduced its use had not been investigated yet. To date, only one study has used the triggerlist and in this study it was used to investigate whether emergency department (ED) visits of patients that were not hospitalized, were medication-related [14]. This retrospective cohort study showed that, based on the triggerlist, half of the ED visits were *possibly* related to a MRP. Ultimately, medication was deemed as a potential cause in 23% of the respective ED visits and 15.5% was potentially preventable. As such, it was shown that the triggerlist was a good selection criterion for patients in the ED, although consequently a high percentage of false positives was found.

While due to different definitions and the lack of a gold standard the incidence of MRAs varies considerably, it is important to adequately identify the population of interest, i.e. those at high risk of MRA. This is especially important in intervention studies like CHECkUP and other studies that aim to optimize medication in (frail) older patients [10, 15] and although by including older patients with polypharmacy the a-priori risk of a hospitalization being medication-related is already high, we hypothesized that by additionally using the triggerlist as selection criterion, the posteriori probability will increase even further. Although we were, by design, unable to directly test this hypothesis, the current literature supports our assumption and the additional application of the triggerlist as selection criterion as we found 48% of the hospitalizations being medication-related. The incidence of MRAs varies between 5.6% and 30% in adult patients without any risk factors [2, 4, 5, 6, 12] and specifically focusing on older patients, a recent meta-analysis found an incidence of MRAs of 10% [6, 12]. Other studies that select patients with a higher risk for MRAs are the studies of Lea et al. [16] and Zerah et al. [17]. Both studies included older patients (mean age 79 years in both studies) with multimorbidity, defined as ≥ 4 medications of at least 2 ATC groups [16] or ≥ 3 chronic medical conditions and polypharmacy [17]. As such, these studies found a prevalence of hospitalizations being medication-related of 38% and 42%, respectively.

We did not find any significant differences with regard to age, sex, CCI, number of medicines or triggerlist diagnoses/medications when comparing *possibly* and *unlikely* MRAs. This is not surprising as in this study, by including only older patients (≥ 60 years) with polypharmacy and two trigger diagnoses, the number of patients using < 5 medicines is minimal and not sufficient to demonstrate a significant association, which is in agreement with Lea et al. [16].

This study is not without limitations. First, the study is limited by its retrospective design. All hospital admissions were evaluated based on the data in the hospital electronic information systems, which were registered by other physicians. We also had no information about compliance or over-the-counter drugs. Second, patients were recruited from a single centre limiting the generalizability of our results. Third, our sample size was relatively small. Although the sample size was deliberately limited to 100 patients (as it was a sub-study of CHECkUP), the point estimate of MRAs has a somewhat greater uncertainty. Finally, when assessing whether a hospital admission was medication-related, the two independent reviewers reached agreement in 64% of the admissions by using AT-HARM10. We believe this might be due to the difference in clinical experience between both reviewers (a pharmacy student and a general pharmacist with 40 years of working experience). Nevertheless, since all discrepancies were discussed by a multidisciplinary panel, which is considered the gold standard, we believe our final point estimate of MRAs is realistic. Despite this, the application of AT-HARM10 in another patient population in another country and also its feasibility still contribute to the further validation of this assessment tool to identify MRAs.

Conclusion

The high prevalence of MRAs, suggests the triggerlist has added value as selection criterion in a cohort of older patients (≥ 60 years) with polypharmacy and can be used to improve the identification of a population at high risk of MRA, as 48% of the admissions were classified as *possibly* medication-related by using AT-HARM10.

Declarations

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Competing Interests

The authors declare that they have no competing interests**.**

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Aimée Linkens, Myrthe Janssen, Luc Peeters, Björn Winkens, Vanja Milosevic and Hugo van der Kuy. The first draft of the manuscript was written by Aimée Linkens, Myrthe Janssen

and Bart Spaetgens and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript

Data Availability

The de-identified datasets generated and analysed during the current study may be made available from the corresponding author on reasonable request.

Conflicts of interest

All authors declare that they have no competing interests.

Ethics approval

This retrospective study is a sub-study of the CHECkUP study, which has received approval from the Medical Research Ethics Committee of Zuyderland Medical Centre (METC number: METCZ20180091).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

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Figures

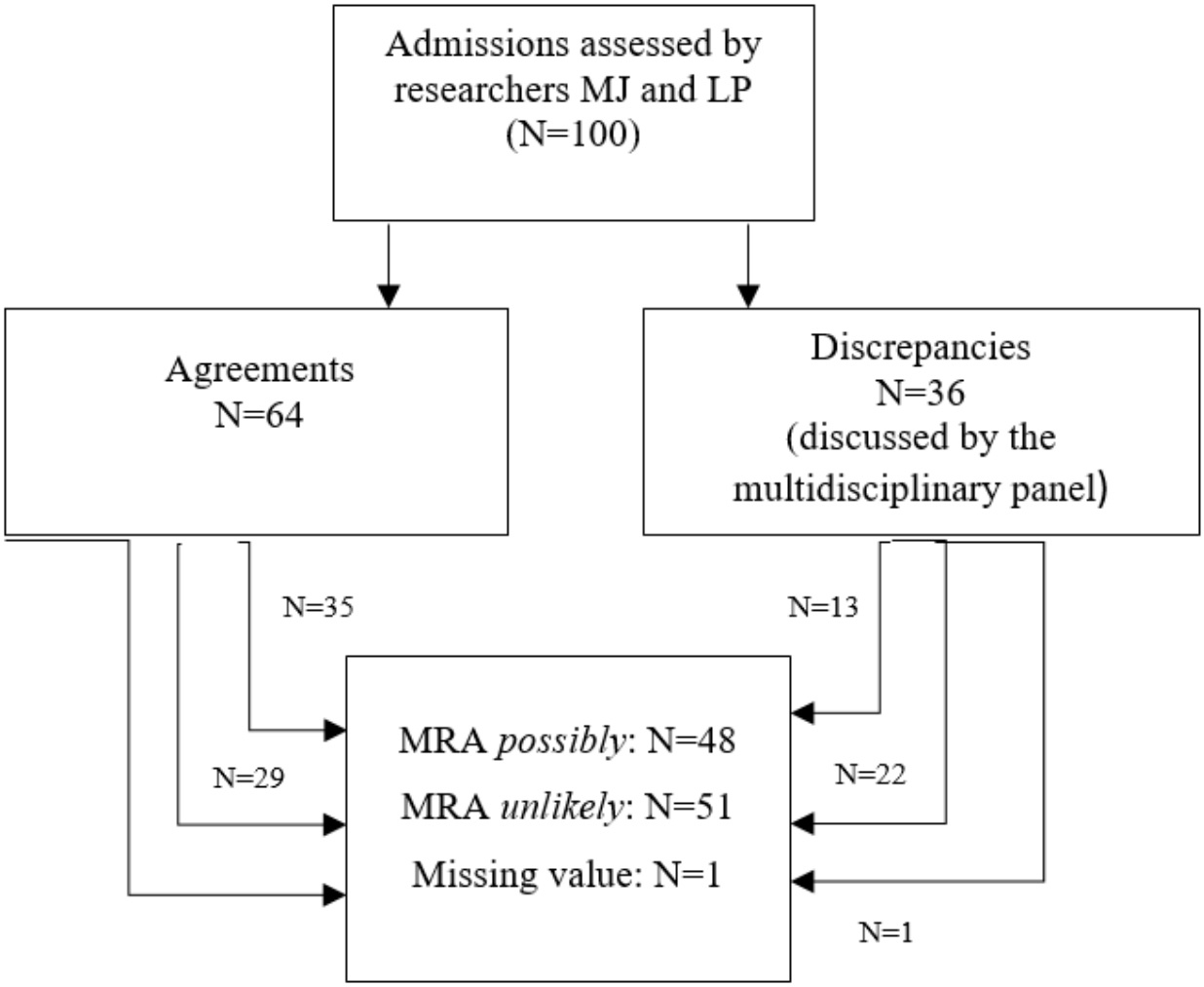

Figure 1

Number of *possibly* and *unlikely* medication-related hospital admissions according AT-HARM10

Supplementary Files

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- Supplementarytable1triggerlist.docx