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Received 7 April 2015; accepted in revised form 23 September 2015

Age and Ageing 2016; **45:** 115–120
doi: 10.1093/ageing/afv166

Use of a frailty index to identify potentially inappropriate prescribing and adverse drug reaction risks in older patients

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Abstract

Background: potentially inappropriate prescribing (PIP) is a significant problem in health care today. We hypothesise that if doctors were given a single indicator of PIP and adverse drug reaction (ADR) risk on a patient's prescription, it might stimulate them to review the medicines. We suggest that a frailty index (FI) score may be such a suitable indicator.

Objectives: to determine whether a positive relationship exists between a patient's frailty status, the appropriateness of their medications and their propensity to develop ADRs. Compare this to just using the number of medications a patient takes as an indicator of PIP/ADR risk.
Setting and method: a frailty index was constructed and applied to a patient database. The associations between a patient's FI score, the number of instances of PIP on their prescription and their likelihood of developing an ADR were determined using Pearson correlation tests and χ^2 tests.
Results: significant correlation between FI score instances of PIP was shown ($R = 0.92$). The mean FI score above which patients experienced at least one instance of PIP was 0.16. Patients above this threshold were twice as likely to experience PIP (OR = 2.6, $P < 0.0001$) and twice as likely to develop an ADR (OR = 2.1, $P < 0.0001$). Patients taking more than six medications were 3 times more likely to experience PIP.
Conclusion: an FI score is a potentially relevant clinical indicator for doctors to critically assess a patient's prescription for the presence of PIP and ultimately prevent ADRs, especially when used in tandem with the number of medications a patient takes.

Keywords: *frailty, inappropriate prescribing, older people, adverse drug reactions*

Introduction

Potentially inappropriate prescribing (PIP) among older patients has been identified as a significant problem in health care today. PIP rates of 20–40% have been reported in primary care [1, 2], with rates of 33–58% and 44–70% in secondary and tertiary care, respectively [3–5]. Common consequences of high levels of sub-optimal prescribing are adverse drug events (ADEs), adverse drug reactions (ADRs), excess hospitalisations and increased costs [6, 7].

Much quantitative research has taken place in recent times to identify the prevalence and severity of PIP. Interest is currently focused on identifying the causal factors surrounding this phenomenon in an effort to minimise and prevent PIP and its effects. Recent qualitative research in the field has identified several areas for such intervention [8, 9]. It has been shown that doctors often possess an inherent fear of changing a patient's prescription, even when they know it may not be appropriate for that patient [8]. For other prescribers, checking for appropriateness of medications is a low priority [8]. Doctors are quite aware that PIP is a significant problem, but busy working environments, lack of time for prescription surveillance and lack of specific geriatric pharmacotherapy training all serve as barriers to optimal prescribing for older patients in their minds [9]. Considering these issues, one can hypothesise that, if doctors were given a single indicator of PIP and consequent ADR risk on a patient's prescription, it might stimulate them to review the medicines on that prescription, with a view to minimising PIP. We suggest that a frailty index (FI) score may be such a suitable indicator.

Frailty is a common syndrome among the older population, and identification of frailty within these patients has become a real priority of those involved in geriatric medicine [10–12]. To date, several tools for measuring frailty have been developed [13–15], but two in particular have dominated the literature. Firstly, Fried *et al.* [16] developed the frailty phenotype, which was later validated in the Cardiovascular Health Study. Secondly, Rockwood *et al.* [17] developed the frailty index (FI). Recently, Cesari *et al.* [18] showed that although these are often thought of as alternatives to each other, they are different instruments, with different purposes, and should therefore be seen as complementary to one another.

There has been much debate recently as to how best to operationalise frailty assessment scales and utilise them effectively in everyday practise [19, 20]. The majority of studies exploring frailty and its significance focus on the correlation between it and mortality or adverse outcomes such as hospitalisation, self-reported quality of life, intensity of treatment, nursing home admission, after-hours GP visit or social vulnerability [21]. However, a link between an individual patient's frailty status and the appropriateness of their medications has never been explored.

If a positive relationship between these entities exists, then an FI score above a certain threshold could be used as an indicator to prescribers that a patient's medications should be reviewed for instances of PIP/potential ADRs. Whether this approach is superior to, for example, just using the number of medications a patient takes to identify risk of PIP/ADRs is unknown.

The aim of this paper is to determine whether such a relationship between a patient's frailty, the appropriateness of their medications and their propensity to develop ADRs exists, and whether this is a more useful tactic than just using the number of medications alone to identify patients for review.

Methods

For methods and references included in this section (Supplementary data, Appendices S1 and S4, available in *Age and Ageing* online).

Results

From all the variables in the database, 34 were deemed suitable for inclusion in the frailty index as per the methods proposed by Searle *et al.* [22]. Seven hundred and eleven patients in the database had the information required for inclusion. Of the 34

variables, 32 were binary and 2 were continuous (number of medications and abbreviated mental test score (AMTS)). The variables and their cut-off points (for the continuous variables) are displayed in Supplementary data, Table S1, available in *Age and Ageing* online. These were determined by correlating the continuous variables with the interim index consisting only of binary variables and identifying the values corresponding to a frailty score of 0.2 on the interim index.

FI scores among the 711 patients ranged from 0 to 0.51, with a mean of 0.15.

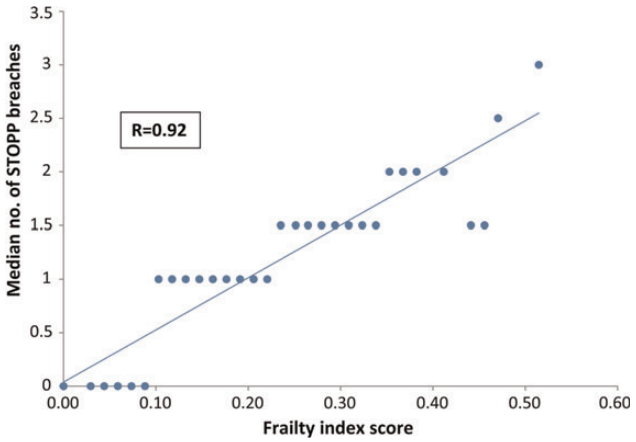

Figure 1. Frailty index score plotted against median number of breaches of the STOPP criteria.

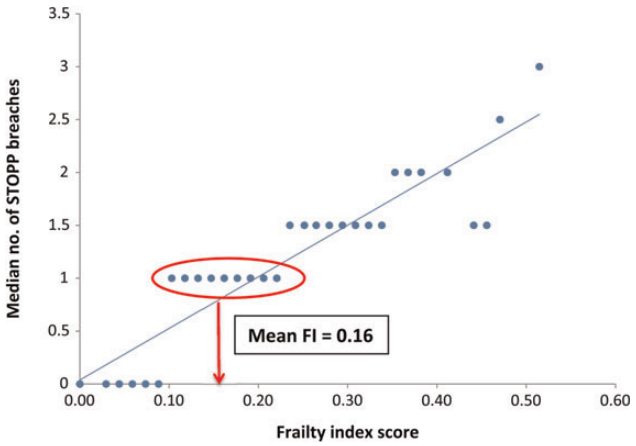

Figure 2. The mean FI score, above which patients had at least one instance of PIP present on their prescription, is 0.16.

Four hundred and three patients experienced at least one instance of PIP, defined by a breach of the STOPP guidelines, within 7 days of their hospital stay. In these 403 patients, there were a total of 733 instances of PIP.

A significant correlation between FI score and median number of STOPP breaches was observed ($R = 0.92$). Figure 1 shows the frailty scores plotted against the median number of breaches of the STOPP criteria for each observed point on the FI scale.

To determine the threshold above which a patient should be brought to the attention of the prescriber, we calculated the mean FI score at which the median number of STOPP breaches was equal to 1, i.e. the FI score at which patients had at least one instance of PIP on their prescription. This was shown to be 0.16. Figure 2 shows how this threshold was determined.

As the 'number of medications' is a continuous variable in the frailty index, the threshold for this was determined as described above, by identifying the mean number of medications taken by patients with an FI score of 0.2 on the interim index. This was found to be 6.

To determine whether adverse outcomes such as PIP and ADRs are actually dependent on frailty status/number of medications, χ^2 tests were performed using the following cross-tabulations (Supplementary data, Tables S2 and S3, available in *Age and Ageing* online). The results are summarised in Table 1.

Supplementary data, Table S2, available in *Age and Ageing* online show the number of patients who experienced at least 1 instance of PIP, as well as the number of patients who experienced no PIP, both above and below the frailty index threshold of 0.16. 68.1% of patients with a frailty index score of ≥0.16 experienced at least one instance of PIP compared with just 44.7% of patients with score of <0.16. Also displayed in Supplementary data, Table S2, available in *Age and Ageing* online is the number of patients who experienced at least 1 ADR, as well as the number of patients who experienced no ADRs, both above and below the frailty index threshold. 29.4% of patients with a frailty index score ≥0.16 experienced at least on ADR compared with just 16.4% of patients with score of <0.16.

Supplementary data, Table S3, available in *Age and Ageing* online show number of patients who experienced at least one instance of PIP, as well as the number of patients who experienced no PIP, both above and below the 'number of medications' threshold of 6. 64.4% of patients taking six or more

Table 1. Association between frailty index score, number of medication, PIP occurrence and ADR occurrence

Patients with FI score ≥0.16	% Experiencing at least one ADR	Odds ratio and 95% CI	χ^2	*P* value
	29.4% (Compared with 16.7% of patients with FI <0.16)	2.1 (1.474, 3.044)	16.030	<0.0001
	% Experiencing at least one instance of PIP	Odds ratio and 95% CIC	χ^2	*P* value
	68.1% (Compared with 44.7% of patients with FI <0.16)	2.6 (2.0, 3.6)	39.831	<0.0001
Patients taking more than six medications	% Experiencing at least one ADR	Odds ratio and 95% CI	χ^2	*P* value
	21.5% (Compared with 26.8% of patients with less than six meds)	0.75 (0.515, 1.089)	2.299	0.129
	% Experiencing at least one instance of PIP	Odds ratio and 95% CIC	χ^2	*P* value
	64.4% (Compared with 37.6% of patients with less than six meds)	3.01 (2.15, 4.21)	42.887	<0.0001

medications experienced at least one instance of PIP compared with just 37.6% of patients with <6 medications.

Also displayed in Supplementary data, Table S3, available in *Age and Ageing* online is the number of patients who experienced at least one ADR, as well as the number of patients who experienced no ADRs, both above and below the 'number of medications' threshold. 21.5% of patients with six or more medications experienced at least one ADR compared with just 26.8% of patients with <6 medications.

Table 1 compares the frailty index with just using 'number of medications' by way of association with PIP and ADR occurrence.

Patients with an FI score ≥0.16 were twice likely to experience at least one instance of PIP and twice as likely to experience at least one ADR during the index hospitalisation.

Instances of PIP and instances of ADRS were found to be significantly dependent on frailty scores ($P < 0.0001$ for both).

Patients taking more than six medications were not statistically more likely to experience an ADR, however, were 3 times more likely to experience at least one instance of PIP.

PIP was found to be highly dependent on number of medications taken ($P < 0.0001$). ADR occurrence was not significantly dependent on number of medications ($P = 0.129$).

Discussion

Implications for clinical practice

The principal novel findings in this study are as follows: (i) a significant positive relationship between a patient's frailty status and the appropriateness of their medications exists. This is a clinically relevant finding as frailty is relatively easily quantified using a frailty index, compared with medication appropriateness, which is not as easily determined, and, as has been shown, is often not acted upon when PIP is identified [8]. These findings show that an FI score >0.16 would be a suitable prompt for prescribers to review a patient's medications, with a view to minimising PIP.

(ii) As mentioned, an FI score of 0.2 has traditionally been accepted as 'approaching frailty' [16, 23, 24]. It appears logical therefore to use this as the threshold, above which a patient's prescription would be highlighted to a prescriber for review. However, the present study shows that at a frailty score of 0.16 and above, most patients will have at least one instance of PIP on their prescription list. This difference of 0.04 in the FI score equates to 1 less deficit a patient would need to be considered 'at risk' (using a 34 variable frailty index such as the one presented here). This becomes significant when we consider that 95% of the patients in the database had <10 of the deficits in the frailty index.

(iii) The results of the statistical analysis strengthen the argument for using an FI score as a means of identifying patients at risk of PIP and associated ADRs. Highly significant P values and odds ratios >2.0, all indicate that patients with an FI score ≥0.16 are at significantly increased risk of PIP and ADRs. Furthermore, when the frailty index is compared with just using 'number of medications', we see that while both ADR and PIP occurrences are significantly dependent on FI scores, only PIP is significantly dependent on 'number of medications'. In fact, patients taking more than six meds were 3 times more likely to experience PIP. Therefore, while this suggests that a frailty index is superior in terms of identifying patients at risk of both ADRs and PIP, utilisation of both a frailty index threshold and a 'number of medications' threshold would seem to be the optimum, i.e. patients with FI score ≥0.16 and taking more than six medications are at high risk for PIP and ADRs.

FI scores and PIP criteria may not secure the attention of some prescribers. However, most physicians are aware of ADRs and accept that they are an area of concern in frailer older patients [25]. Therefore, if a patient is highlighted to a doctor on the basis of a frailty score above a threshold that indicates a heightened risk of that patient experiencing an ADR, it is likely to carry more significance to the doctor than simply indicating that the patient is taking a potentially inappropriate medication (PIM).

Implications for future research

Implementation of this initiative to determine whether it successfully reduces PIP rates and ADR rates in a clinical setting is the next logical step in terms of research. This idea of intervention based on the concept of enablement has recently been suggested as an area that should be targeted to reduce PIP [9]. Historically, the quality of interventions aimed at reducing PIP has been questionable [26]. However, it is only in recent times that qualitative research methodologies have been utilised to inform such interventions. If these methodologies are implemented correctly, the result could be more targeted interventions with quantifiably better clinical outcomes.

It should also be considered, that while older patients are often under the care of multiple doctors, their primary care physician is in the best position to oversee the management of their care. Previous studies have shown that an FI can be operationalised in primary care using routinely gathered data [27, 28]. Future research in primary care settings, identifying cut-off points for continuous variables and implementing systems to identify frailty could potentially lead to improved care for these patients.

While we have shown that an intervention based upon highlighting patients with an FI score above a certain threshold to prescribers for careful medication review would be justified; nevertheless, educational interventions focused on specific aspects of geriatric pharmacotherapy are still required to enable doctors make clinically sound decisions in frailer, older, multi-morbid patients with polypharmacy. This need for tailored training has been raised in several studies to date and has also been shown to be effective in preventing PIP [4, 9].

Strengths of the study

This study has for the first time shown a significant correlation between a patient's frailty status and the appropriateness of their medications as well as their propensity to

develop ADRs. The methodologies used are valid and well published. The richness of data available from the original database compounds the strength of this study, as do the statistical comparisons performed exploring the added benefits of using a frailty index compared with just using the number of medications a patient takes to determine their risk of PIP and ADRs.

Limitations of the study

The dataset used for this study was limited to 711 patients.

A prospective study to validate the frailty index would be of benefit.

The health economic impact of the tool and its implications would be warranted.

While much of the patient data used to create the FI is routinely available, collecting all the data required may be somewhat complex in secondary care and may negatively impact the feasibility of such an initiative being implemented.

The dataset used for this study utilised STOPP/START version 1. The STOPP/START guidelines have since been updated and now contain 22 new STOPP rules and 12 new START rules as well as new categories in each [29]. Given that this study used breaches of STOPP/START criteria to determine appropriateness of patients' medications, the methodologies should be repeated using the updated guidelines.

The max FI score in this study was 0.51. This is considerably lower than the commonly reported 99% limit to deficit accumulation seen in secondary care (0.69) [30]. This limits the generalisability of these results and warrants further research.

Conclusion

A significant positive relationship exists between a patient's frailty status, the appropriateness of their medications and their likelihood of developing an ADR. At an FI score of 0.16 and higher, patients are twice as likely to have at least one PIM prescribed. Also, patients above this threshold are twice as likely to experience an ADR compared with those below the threshold. While ADR occurrence is not significantly dependent on the number of medications a patient takes, PIP is. Therefore, the use of both a frailty index as well as 'number of medications' seems the best approach to identify patients at risk.

Key points

- Significant correlation exists between a patient's frailty status and the appropriateness of their medications.
- Patients with a frailty score of 0.16 or greater are twice as likely to experience PIP and ADRs.
- A frailty index score is a potentially relevant clinical indicator of PIP and ADRs.

Conflicts of interest

None declared.

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Received 7 April 2015; accepted in revised form 23 September 2015

Age and Ageing 2016; **45:** 120–127
doi: 10.1093/ageing/afv173

Race and fall risk: data from the National Health and Aging Trends Study (NHATS)

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Abstract

Objectives: the objective of this study was to explore whether race-based difference in fall risk may be mediated by environmental and physical performance risk factors.
Methods: using data from a nationally representative longitudinal survey of 7,609 community-dwelling participants in the National Health and Aging Trends Study (NHATS), we evaluated whether racial differences in fall risk may be explained by physical performance level (measured by the Short Physical Performance Battery), mobility disability, physical activity level and likelihood of living alone. Multivariate Poisson regression and mediation models were used in analyses.
Results: in whites and blacks, the annual incidence of 'any fall' was 33.8 and 27.1%, respectively, and the annual incidence of 'recurrent falls' was 15.5 and 12.3%, respectively. Compared with whites, blacks had relative risks of 0.7 (95% confidence interval 0.6–0.8) and 0.6 (0.5–0.8) for sustaining any fall and recurrent falls, respectively, in adjusted analyses. Blacks had poorer