Modelling the Progression of Frailty in Elderly People using Process Mining and the Electronic Frailty Index (eFI)

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Abstract. Frailty is a common condition experienced by elderly people and the progression of frailty is seldom reversible. Frailty adversely affects quality of life, resilience to both disease and treatment, and ultimately mortality. One measure of frailty is the Electronic Frailty Index (eFI) which uses 36 "deficits" that can be identified within primary care electronic healthcare records. Process mining of electronic healthcare records is an emerging field typically aimed at understanding healthcare processes and care pathways. In this study we demonstrate how process mining approaches can be combined with eFI events marking frailty deterioration to track the progression of frailty in elderly people. The study combines process block analysis and statistical approaches to understand the patterns of progression including frailty triggers such as polypharmacy, hypertension and falls and how these occur in different frailty categories. Our results show that polypharmacy is usually first seen in the transition from clinically fit to mild frailty. Process mining within frailty categories provides a fresh data-driven perspective on the progression of frailty that may help to develop early warning indicators and determine preventive measures that can help combat frailty and its impact on patients. To our knowledge, this is the first attempt to apply process mining techniques to frailty.

Keywords: Process Mining, eFI Score, Frailty, Electronic Health Record

1 Introduction

Frailty is a geriatric condition common in the elderly, affecting 4% of people aged between 65 and 69 years, and 26% aged 85 years and above within the UK population [1]. Any minor distressing event, such as an acute infection, or a change to drug regimes, may dramatically accelerate the failure of functional, physical and mental health in the frail older person. This results in increased risk of hospital admissions, institutionalisation and adverse health outcomes [2]. The frailty syndrome constitutes a decline across several physiological systems, with different people having a varying

rate of progression. The progression can be viewed as the transition of several states in sequence from healthy ageing, to pre-frail, to frail and finally to severely frail [3].

Early identification and stratification of frailty during routine assessments is essential, to support proactive targeting of the most vulnerable for healthcare interventions, with a view to reducing risks of adverse outcomes [4]. A variety of frailty identification tools are available including the Tilburg Frailty Indicator, PRISMA-7 and SHARE-FI [5] which require guidance, time, specific equipment and resources that can be challenging to perform in a hectic clinical setting. Therefore, the Electronic Frailty Index (eFI) has been developed and validated [6] to calculate a frailty score using routinely collected health records, and is now routinely adopted within UK primary care settings [7]. The eFI very efficiently and quickly stratifies older patients by their calculated frailty score [8]. Two earlier studies have examined the use of frailty index score development in frailty progression without using the electronic health records (EHR) [9] and with EHR being used [10]. However, both studies did not use a frailty model to depict the frailty pathway. This paper explores the potential to use process mining as an approach to modelling frailty pathways using the eFI.

Process mining is an evolving approach for inferring and analysing real process models which started attracting attention around the year 2006 [11] by combining the analysis of business processes with data mining and machine learning disciplines. In healthcare process models are created from event logs extracted from time-stamped activities recorded in EHR systems. Insights about the effectiveness of real care processes and pathways can be obtained by automatic process model extraction, conformance checking and performance analysis [12]. A growing number of studies have employed process mining in healthcare domains including oncology [13] and cardiovascular disease [14]. In earlier work we summarized the limited literature on process mining in care of the frail elderly [15].

One approach to portray the typical progression that chronic disease has taken over time is known as disease trajectories [16]. This progression can be modelled as a process using longitudinal data from events recording disease or a patient scoring system [17]. The progression is typically modelled as a directed acyclic graph where nodes represent disease, and directed edges represent the direction of progression from one disease to another [18]. Current work on disease trajectories based on diagnosis information have not employed process mining techniques, despite the similarity in representation of the model produced, but this is an active research area for our group. Recently a study in [19] demonstrated the capability of process mining approach to study disease trajectories following the work in [18] with simulated data and [20] using Spanish public healthcare data. Regarding frailty progression, some works have studied the variance in the progression within different age groups [21] through EHR, with progression plotted over time using the Rockwood frailty index, and exploring the transition between frailty states using the Fried frailty model [22]. However, to date these studies have only applied statistical approaches rather than utilising process mining techniques or a combination of both.

While the studies reviewed above reveal the pattern of disease trajectories by representing it as disease network, they still do not sufficiently suggest performance indicators such as the time between disease occurrences. Analysis of the time intervals between frailty events could help evaluate the relationship between common frailty deficits and leverage business process perspectives such as time, cost, quality and variance [23].

2 Methodology

There are a variety of methodologies developed specially for process mining projects. In this case study we follow PM^2 [24] methodology as it provides a well-established approach and flexibility for combining multiple types of analysis approach and refinement through iterative repetition.

The PM^2 methodology comprises of six stages where: (1) planning stage involves defining the focus of the process for analysis with the specific research questions for investigation; (2) extraction stage identifying the level of detail and attributes of data and data exploration; (3) data processing stages encompasses refined steps to prepare data and to create the event log for analysis; (4) mining and analysis use the output in the previous stage as input for mining using several process mining techniques to answer research questions; (5) evaluation stage to diagnose, verify and validate the result of analysis; and (6) process improvement and support where any useful insight gathered from the previous stage used for process improvement.

3 Case Study

The case study for this work follows the first five stages of PM^2; planning, extraction, data processing, mining and analysis, and lastly the evaluation stage. The final stage of PM^2, which includes process improvement and support is beyond the scope of this work. The main activities conducted at each stage are explained in detail below.

3.1 Phase 1: Planning

The research questions for this work derived from literature and were confirmed during the discussion with a domain expert. These questions will be our starting point in understanding the frailty progression between three widely recognized clinical issues with frailty progression - falls, hypertension and polypharmacy (the prescription of five or more different medications). The questions adopted for this work as follows; (RQ1): Can process mining identify the significant progression of frailty within frailty category? (RQ2): Can process mining reveal whether polypharmacy contributes to worsening frailty for patients with different frailty status?

3.2 Phase 2: Extraction

Our case study used data extracted from the SystmOne EHR used by two GP practices in Bradford, England. The data included details of when patient visiting their GP for regular consultation, checkup, clinical testing or medical prescriptions from the year 2003 until 2018. The dataset contains 13,017 patients who were at least 64 years old at the initial point of extraction from the EHR. Events, patient procedures and findings had been coded using Read Code version 3 clinical coding scheme classification before it was replaced by SNOMED-CT on 1 April 2018.

A total of 2,096 Read Code entries had been mapped to frailty deficits by domain experts when the eFI score was first developed in [6] and this approach using these same codes was replicated in this study. Note that a patient may have duplicate deficits recorded over time and, for these, just the first occurrence was used. The initial data extract was produced with 86,903 rows. Polypharmacy was not initially included as part of the frailty deficit due to reasons that will be discussed below.

3.3 Phase 3: Data Processing

Data processing and data preparation was performed in several steps to create an event log. It included three separate steps of log enriching, aggregating event and log filtering as based from [24] to create final event log for mining and analysis.

Log Enriching. The first step involves deriving additional events for the event log. Polypharmacy is a frailty deficit that must be determined by assessing the prescription records. From the full prescription records, we identified 4,762 unique medication prescriptions using the first-six characters of British National Formulary (BNF) code used within the EHR. Polypharmacy can be identified by determining the date of prescribing of at least five unique medications at a particular time point, using chapters 1-15 of the BNF. This is consistent with how the polypharmacy deficit is characterized within the eFI, and using this method identified 5,292 patients with the polypharmacy deficit. The frailty progression based on the eFI [6] starts from the clinically fit stage, moves to the mild and moderate stages before reaching the final frailty stage of severe. The frailty category for each patient was determined according to their latest frailty score found in the record, where the score referred to the accumulation of the unique frailty deficit. The additional events consisting of frailty stages were added into the event log for each patient. The time-stamp of frailty stage events was created similar to the time-stamp of the minimum accumulated deficits in each category; clinically fit (1 deficit), mild (5 deficits), moderate (9 deficits) and severe (13 or more deficits).

Aggregating Events. There are a high number of similar deficits recorded with the same time-stamp which needed to be aggregated to obtain the right order of event in the log. Furthermore, to reduce the clutter and complexity of the discovered process model, only the first recorded event of each deficit was included.

Log filtering and Converging. The primary filtering was to select patients within the study period between the year 2003 until 2018 and next to remove those patients with a clinically fit status. Frailty index score-based filtering was applied where the final score was identified as the point of slicing of the event log. The whole dataset was partitioned based on the frailty categories; mild, moderate and severe. The event log was further reduced to have only cases with duration of more than six years. This was to eliminate the long tail of cases which could skew the analysis results. The difference in case duration was approximately four years between mild and severe categories while the minimum case duration for mild frailty was less than a year and for severe frailty was five years.

3.4 Phase 4: Mining and Analysis

In this phase, process mining and analytics techniques are performed to gain insight from the dataset. The summary of each event log is shown in Table 1. The activity for the process model consists of two types; the deficit activity (falls and the commonly seen comorbidities, e.g. hypertension) and the frailty stage activity (clinically fit, mild, moderate and severe). The highest number of activities comes from the severe group as it covered all deficit activity and frailty stage activity with seven activities and as a result, it also recorded the highest number of variants but with the lowest quantity of events among the three frailty categories due to the small number of cases (patients).

Table 1. Summary of an extracted event log from each category

Category	# Case	# Events	# Activities	# Variants	Mean Case Duration	Median Case Duration
Mild	1,077	3,955	5	55	10.6 years	10.6 years
Moderate	587	2,924	6	86	12.3 years	12.6 years
Severe	313	2,031	7	114	13.0 years	13.6 years

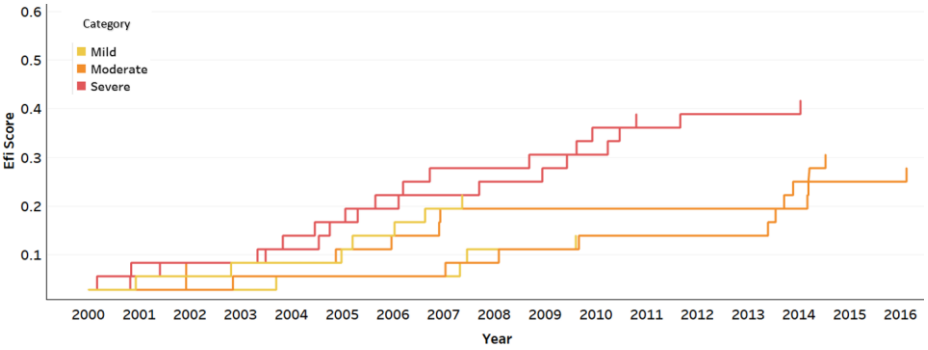

Fig. 1. Frailty step graph illustrating six cases of frailty progression based on the electronic frailty index (eFI). Two patients in each of mild, moderate and severe categories are shown.

Figure 1 shows two cases randomly selected from each of the three frailty categories with the start date of the first event baselined to the first day in the year 2000 with the rest of the events following according to the real duration between events. Given the same start point of events and within the comparable range of case duration, the severe group can be seen to have a sharper increase in score representing a rapid decline into frailty. The cases in the mild group show a shorter case duration compared with other cases. This illustration is useful to illustrate the differences present within different frailty categories. However, the full dataset is required to understand whether these examples are typical for the population.

The next assessment of the process model used the Inductive Visual Miner (IvM) plug-in [25] within ProM to answer RQ1. The inductive miner plug-in considers the semantic executions of the model and is useful when dealing with infrequent behaviour in the log which confirm the soundness of the process model produced as a Petri net or process tree. The blue box indicates the activity present in each process model with the intensity of colour reflecting the different frequencies of events. The process model for (a) mild, (b) moderate and (c) severe is shown in Fig. 4 using the default noise filtering 0.8 and include only 60% of the most occurring traces in the event log. The 60% was chosen as the minimum threshold to depict the typical behaviour in the event log.

The behaviour of the representative traces of each process block was inspected visually. Generally, the similarity between these process models is the presence of hypertension, and polypharmacy deficits are always present at the early stage of the process. The primary distinctness behaviour observed is 1) fall deficit only occurring in the moderate Fig. 2(b) and severe Fig. 2(c) categories after a polypharmacy event. A fall may occur at any time but it's impact on frailty can be more severe in already frail patients. 2) Polypharmacy is more common towards the end of mild frailty and more frail patients with polypharmacy appears to happen before other important events such as falls.

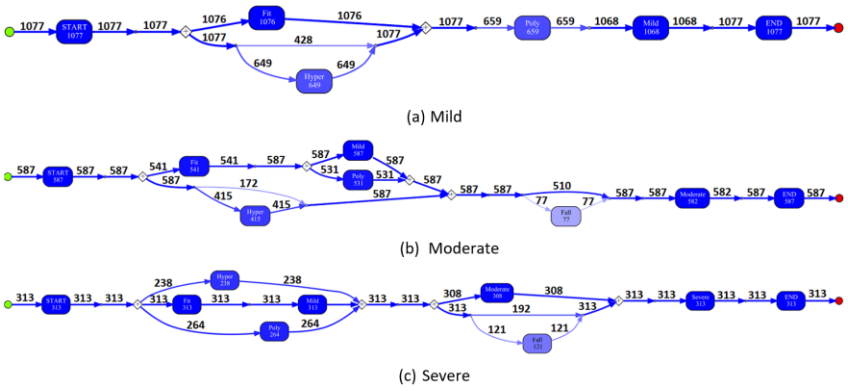

Fig. 2. The process trees using IvM plug-in. The short activity name in the box represent as followed: Fit = Clinically Fit, Hyper = Hypertension and Poly = Polypharmacy.

Conformance checking was conducted to determine the similarities or differences between each process model to assess comparability. The quality measurement of fitness and precision were calculated as the first evaluation between each event logs and process models. The fitness computes the ability of process model to reproduce traces in the event log whereas, precision demonstrates the portion of behaviour allowed by the model. Both measurement will have the maximum value of 1.00 indicating the highest fitness or precision measurement and 0.00 as lowest. The results in Table 2 show that the severe category model has the lowest fitness value compared with other models, and this concludes by having the most distinct model. The main explanation is because of the additional two stages present in the severe model as they transition to a more advance stage of frailty, and most cases from mild and moderate could not complete the model.

Table 2. Summary of an extracted event log from each category, F = Fitness, P = Precision

			Model		
	Category	Metrics	Mild	Moderate	Severe
Event Log	Mild	F	0.968	0.826	0.698
		P	0.771	0.747	0.819
	Moderate	F	0.988	0.990	0.839
		P	0.771	0.747	0.819
	Severe	F	0.763	0.882	0.980
		P	0.771	0.747	0.812

In order to answer RQ 2, we focus on the polypharmacy deficit. As illustrated in Fig. 3, each frailty category comprises of different transition stages suggest the incomparability of the process model. Frailty stage transition is the change in frailty category experienced by patients from clinically fit to other advance frailty categories. Thus, process block focus analysis [26] is performed to investigate each transition. The transition determined by the start and end of each frailty stage, and event data falls within each transition was split as an individual process block. The horizontal arrow in Fig. 3 shows the frailty stage transition from clinically fit to mild (S1), mild to moderate (S2) and moderate to severe (S3), where the vertical arrow, case type shows the final frailty category where each case belongs.

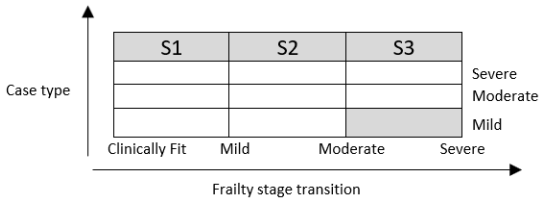

Fig. 3 The process block focuses analysis using the different case type and the frailty stage transition. The block partitioned depending on the similar start and endpoint of transition.

Statistical significance approaches have been incorporated within process mining studies [27][28] focused on measuring the *p*-value [29] as a way to find the statistical significance difference where the default threshold *p*-value of 0.05 is considered to show significant difference. It is useful to apply the statistical significance to the interval to verify process mining algorithms. We implemented the one-way analysis of variance [30] (ANOVA) to find the significant difference between groups of three or more and t-test for groups of two. As for the ANOVA test, the post-hoc test conducted if there is a significant difference found in order to identify which groups differ significantly.

We examined the interquartile (IQ) range and the percentage of polypharmacy present in each block shown in Table 3. Generally, the figure shows that the trends of polypharmacy are decreasing towards the end of the frailty stage transition for all frailty category. More than 60% of polypharmacy deficit presents in the block S1 for all categories, hence contributing to the transition of frailty from clinically fit stage to the mild frailty stage. An ANOVA was conducted to evaluate the relationship between interval and the different frailty category for block S1 and t-test for block S2. There was a significant difference between different frailty categories for the interval in the block S1 and S2. However, the Tukey post-hoc test revealed that for the S1 in the interblock interval mild (3.86 ±3.94) category had significantly longer intervals than the moderate (2.74 ±2.89) and severe (2.23 ±2.24) categories, but no significant difference was found between the moderate and severe categories. It suggests that in block S1, both the moderate and severe categories deteriorate statistically significantly faster than the mild category after polypharmacy.

Table 3. Summary of the descriptive analysis of cases in each block, where the highlighted columns are the result of the post-hoc Tukey test that have significant difference among them. Block interval = the IQ range interval within the start and endpoint of block S1 (year), Inter-block interval = the IQ interval between deficit activity (polypharmacy) and frailty stage activity (year). P % = Percentage of case with polypharmacy

	S1			S2			S3		
Category	P %	Block interval	Inter-block interval	P %	Block interval	Inter-block interval	P %	Block interval	Inter-block interval
Mild	81	**9.94 (7.98, 12.19)**	2.76 (0.00, 6.68)						
Moderate	65	**6.02 (3.77, 8.62)**	1.96 (0.13, 4.43)	32	**5.28 (3.04, 7.69)**	**1.85 (0.20, 4.50)**			
Severe	61	**3.69 (2.34, 5.89)**	1.80 (0.49, 3.13)	26	**3.29 (2.26, 4.88)**	**1.62 (0.33, 3.09)**	1	4.20 (2.58, 5.66)	1.60 (0.29, 3.10)
p-value		0.00	0.00		0.00	0.006			

We further analyse the S1 block by creating process models using another plug-in in ProM 6.9, an interactive Data-Aware Heuristics Miner (iDHM) [31]. This plug-in allows a brief investigation of parameters combining several different heuristics along with generating a general model based on the frequency of activities. The directly-follows graph produced allows us to automatically obtained the most common sequences between activities depending on the frequency threshold set for the model. Three process models produced following the default frequency threshold set at 0.1 for all frailty categories as illustrated in Figure 5.

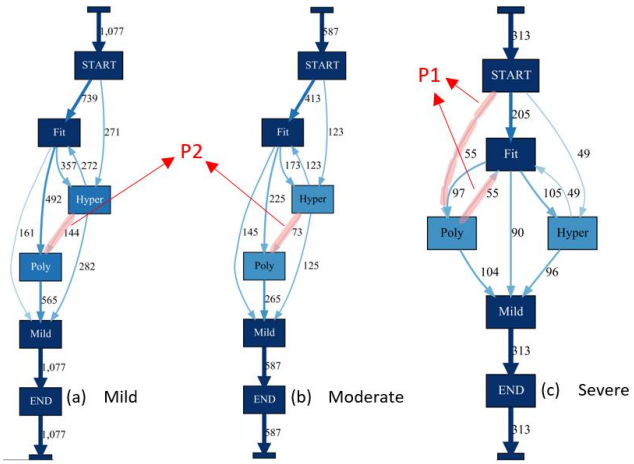

Fig. 4. The process models of the S1 process block using iDHM. The box represents the activities of the process with the intensity of the box's colour denotes the frequencies of the activities. The short activity name in the box represent as followed: Fit = Clinically Fit, Hyper = Hypertension and Poly = Polypharmacy.

The similar structure of Figure 4(a) and (b) spotted with P2 mark the path executed, which is not in the severe category. While, distinct structure observed in Figure 4(c) shows a patient can either start with either being clinically fit, hypertension or polypharmacy. There is also a path executed from polypharmacy to clinically fit, which is none in the other two process models. It indicates that polypharmacy is common as the initial activity in the flow for the severe category. Although the representation of the process models 4(a) and (b) are similar, the interblock interval to reach the mild stage is higher for the 4(a) (10 months), while taking two more months than the 4(c).

3.5 Phase 5: Evaluation

This case study investigated the frailty progression over time within different frailty categories. The process mining results produced will generate insights for domain experts on the variability of the frailty progression. The starting point of cases in the step graph (Fig. 1) allows straightforward comparability of the progression, thus sup-

porting our analysis in investigating the differences between the frailty categories. Additionally, the discussion with the domain expert at the beginning of this study, particularly in constructing the research questions (in planning phase) was crucial in directing us to focus on the critical issues in frailty progression.

From the observations of the process tree within three frailty categories, we can see that hypertension and polypharmacy are common frailty events compared to falls and this is true in all categories. Moreover, no fall events were present in the process model in the block S1 (transition from clinically fit to mild) of the block focus analysis. While further analysis may be required to explain, this could suggest that falls are only common in more advanced frailty stages. The block interval performance analysis reveals that the most prolonged duration for transition happened in the block S1 or the early frailty stage and followed by the block S2. The inter-block interval took less than 50% of the block interval in S1, could imply that polypharmacy may contribute to the quick progression to next frailty stage. A conclusion confirmed by [32].

4 Discussion and Limitation

The implementation of PM^2 for process mining in the frail elderly domain was suitable as it comprehensively supported the analysis using the healthcare data. The main challenge in this work was in the data preparation step in phase 3. The log enriching was essential as frailty progression was constructed based on the 36 frailty deficits and additional work to incorporate polypharmacy was required. Our study acknowledges some ideas on implementing the integration of various process mining techniques with statistical approach that support polypharmacy analysis using EHR data. The approach reveals the position of significant deficits within different frailty stages thus providing an evidence-based analysis to the clinicians in facilitating early preventive measure of frailty. Due to the high complexity of the EHR only the first recorded deficits are only considered in this study and that simplifies some aspects of the modelling.

In this study, the presence of polypharmacy appeared more often in the initial frailty stage suggesting that exposure to polypharmacy could potentially correlate to the early trajectory from fit to mild frailty. Associations between polypharmacy and frailty have been established in the literature [32] as well as transitions between frailty states [33], however to our knowledge this is the first study which incorporates process mining methods to identify such associations. Based on this finding, it is important not to make significant causal assumptions about the exposure to polypharmacy, as the frequent presence of the polypharmacy deficit in the early transitions could also just simply be the consequence of worsening frailty, which in turn is driving polypharmacy. In later life, the association with multi-morbidity increases, and in turn older people accumulate frailty deficits which require management with multiple medicines. Therefore, it is not appropriate to argue that polypharmacy is causing older people to become frailer in this study, but the analysis reveals that this is something to

consider further when investigating possible contributing factors in the trajectory of this condition. Furthermore, our approach in characterizing the presence of polypharmacy has limitations, as once a participant was characterized with this deficit, they were assumed to be exposed to polypharmacy for the duration of the whole study period. Although this is clinically plausible, particularly in the management of long-term conditions in older people, it is also possible that over time the number of regular prescribed medicines reduced below the threshold (5 or more medicines) that defined the polypharmacy deficit. .

5 Conclusion and Future Work

We have demonstrated how to apply a set of process mining techniques within the elderly domain in the primary care setting. The applied techniques constitute the combination of process mining, data mining and statistics. The implementation of the process block was to characterise the differences in frailty progression experienced by the different frailty categories. It reports several valuable insights to the process mining practitioners and practitioner within the domain of frail elderly.

While this work has focused on applying a data and process-driven approach to understanding the different progression of frailty categories towards polypharmacy, our future work will concentrate on to understand the interaction of a combination of frailty deficits with frailty progression. Moreover, we will further investigate the presence of polypharmacy at multiple time points along the study duration and the representation of frailty pathway using different polypharmacy definition such as "hyperpolypharmacy", prescription of at least ten different medicines. In order to achieve this, a more in-depth quantitative approach will be applied along with extensive process mining algorithms and statistical techniques.

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