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Are quality of life, functional capacity, and urinary incontinence associated with fecal incontinence? The Fibra-BR Study

Cuidados de saúde, capacidade funcional e incontinência urinária estão associados à incontinência fecal? Estudo Fibra-BR

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Abstract

Objective: To assess the prevalence of fecal incontinence and its association with clinical, functional, and cognitive-behavioral variables, medication use, frailty, falls, and quality of life in community-dwelling older adults (aged 65 years or older).

Methods: Cross-sectional, multicenter study carried out across 16 Brazilian cities. The question “In the last 12 months, did you experience fecal incontinence or involuntary passage of stool?” was defined as the indicator variable for fecal incontinence. Bivariate analyses were carried out to assess the prevalence of fecal incontinence and sociodemographic characteristics, comorbidities, cognition, functional capacity, depression, frailty, quality of life, and falls. Logistic regression analysis was also performed, with fecal incontinence as the dependent variable.

Results: Overall, 6855 subjects were evaluated; 66.56% were female, 52.93% white, and the mean age was 73.51 years. The prevalence of fecal incontinence was 5.93%. It was associated with worse self-care (OR 1.78 [1.08–2.96]), dependence for basic activities of daily living (OR 1.29 [1.01–1.95]), and urinary incontinence (OR 4.22 [3.28–5.41]). Furthermore, the absence of polypharmacy was identified as a protective factor (OR 0.61 [0.44–0.85]).

Conclusion: The overall prevalence of fecal incontinence was 5.93%. On logistic regression, one quality of life variable, dependence for basic activities of daily living, and polypharmacy were significantly associated with fecal incontinence.

Key words: fecal incontinence; older adult; quality of life; frailty; prevalence.

Resumo

Objetivo: Avaliar a prevalência de incontinência fecal e sua associação com variáveis clínicas, funcionais, cognitivo-comportamentais, uso de fármacos, fragilidade, quedas e qualidade de vida em indivíduos com 65 anos ou mais que vivem na comunidade.

Metodologia: Estudo transversal e multicêntrico, realizado em 16 cidades brasileiras. A pergunta “Nos últimos 12 meses o(a) senhor(a) apresentou incontinência fecal ou perda de fezes de forma involuntária?” foi a variável indicadora de incontinência fecal. Análises bivariadas avaliaram a prevalência de incontinência fecal e suas características sociodemográficas, comorbidades, cognição, funcionalidade, depressão, fragilidade, qualidade de vida e quedas. Também realizou-se análise de regressão logística tendo a incontinência fecal como variável dependente.

Resultados: No total, 6855 indivíduos foram avaliados; 66,56% eram do sexo feminino, 52,93% brancos e a média de idade de 73,51 anos. A prevalência de incontinência fecal foi de 5,93% e estava associada com pior cuidado com a própria saúde [OR 1,78 (1,08–2,96)], dependência para as atividades básicas de vida diária [OR 1,29 (1,01–1,95)] e incontinência urinária [OR 4,22 (3,28–5,41)]. Além disso, observou-se que a ausência de polifarmácia [OR 0,61 (0,44–0,85)] foi identificada como associação de proteção.

Conclusão: A prevalência de incontinência fecal foi de 5,93%. Na regressão logística, uma variável de qualidade de vida, dependência para atividades básicas de vida diária e polifarmácia mostrou-se significativamente associada à incontinência fecal.

Palavras-chave: incontinência fecal; idoso; qualidade de vida; fragilidade; prevalência.



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INTRODUCTION

As chronic noncommunicable diseases (NCDs) become more prevalent as a result of population aging, so too are cognitive and functional limitations becoming more common among older adults.¹⁻³ Among these chronic conditions, fecal incontinence (FI) has been the subject of little research, despite its enormous impact on the lives of those affected.⁴ A major consequence of FI is social isolation, which leads to a drastic reduction in quality of life. Early recognition of FI improves the prognosis, as it allows implementation of effective therapeutic interventions to address functional, clinical, and psychosocial aspects.⁴ FI is defined as the involuntary passage of stool or inability to control one's bowels.⁵ Many patients find it difficult to admit they have this condition, and when they do seek medical care, FI is rarely the complaint.⁶

Among older adults, FI represents a major cause of institutionalization, and costs with adult diapers alone exceed US\$ 400 million per year.⁷ In the United States, expenses associated with FI in long-term care facilities (LTCFs) may reach US\$ 1.7 billion annually.⁷

Far beyond its financial cost, FI is associated with poor quality of life (QoL) among those affected.⁸⁻¹² In 2006, Yusuf et al.⁸ evaluated the impact of FI on four QoL domains: lifestyle, behavior, depression, and embarrassment. Patients developed depression, suicidal ideation, and felt embarrassed in social situations after the onset of FI. Likewise, FI was associated with limitations in functional capacity (FC). The authors found that the quality of life was impaired in all assessed domains. These findings were corroborated by Bedard et al.,¹⁰ who also found a major impact of FI on QoL. According to Tamanini et al.,¹³ the greater one's functional dependence, the greater the prevalence of FI. Finally, Deb et al.¹⁴ argue whether FI per se should not be considered a marker of frailty in older adults.

Internationally, the prevalence of FI in the community ranges from 2.2 to 36.2%.^{7,15} In LTCFs, its prevalence can exceed 50%,^{16,17} and is even higher (up to 80%) among hospitalized patients with dementia.¹⁸ In Brazil, those few studies on the topic have reported a prevalence ranging from 3.6% to 11.7% among community-dwelling samples. However, these estimates are difficult to compare due to the different methodologies used and specific characteristics of the studied populations; furthermore, few of these studies were limited to older adults.^{13,19,20}

In light of this knowledge gap, the present study was designed to assess the prevalence of FI among

older adults living in the community in a sample of Brazilian cities and analyze the association of FI with falls, comorbidities, quality of life, FC, polypharmacy, frailty, and depression.

METHODS

The baseline database of the *Fragilidade em Idosos Brasileiros* [Frailty in Brazilian Older Adults] network, Fibra-BR, was used. Information for this database was collected between December 2009 and January 2010. A detailed description of the study methods has been published elsewhere.²¹

Fibra-BR is a cross-sectional, observational, multi-center study conceived by a consortium of four Brazilian universities (Universidade do Estado do Rio de Janeiro, Universidade de São Paulo – Ribeirão Preto, Universidade Federal de Minas Gerais, Universidade Estadual de Campinas). The main objective of the study was to estimate the prevalence of and factors associated with frailty in a sample of 7,242 community-dwelling individuals aged 65 or older. Bedbound older adults or those requiring a wheelchair to ambulate were excluded, as were those who were unable to perform physical or cognitive performance tests; those with advanced Parkinson's disease, limiting sequelae of stroke, terminal cancer, or cognitive impairment, the latter defined by a Mini Mental State Examination (MMSE) score of 17 or less.

Participants were residents of 16 municipalities chosen at the convenience of the principal investigators. In each municipality (representing states in the Southeast, South, North, Midwest and Northeast regions), individuals were selected probabilistically by sex and age group.^{21,22}

The present study included all individuals aged 65 or older enrolled in the baseline Fibra-BR database, except those who did not answer the question regarding the presence of FI. Once the exclusion criteria had been applied, the final sample consisted of 6,855 individuals.

For the purposes of this study, FI was identified by self-reporting, through inclusion of the following question in the research questionnaire: "In the last 12 months, did you experience fecal incontinence or involuntary passage of stool?". This was defined as the dependent variable.

Data were collected through a structured questionnaire consisting of items designed to assess sociodemographic characteristics (sex, age, educational attainment in years of schooling, income as a function of the national minimum wage), health habits, self-reported comorbidities (hypertension, stroke, diabetes mellitus, depression, etc.),

self-perceived health, and activities of daily living; all of these were defined as independent variables.^{23,24} Cognitive assessment was performed using the MMSE.²⁵ In the present study, FC was defined on the basis of two criteria. To characterize dependence for basic activities of daily living (BADL), the Katz scale was used, after exclusion of the question regarding presence of urinary and fecal incontinence.²³ Instrumental activities of daily living (IADL) were scored according to the Lawton and Brody scale.²⁴ Individuals who needed help to perform or were unable to perform at least one activity were considered dependent. Anthropometric measurements (weight and height) were obtained, the body mass index (BMI) was calculated, and the Cardiovascular Health Study criteria for the diagnosis of frailty were applied.²² Polypharmacy was defined by the recorded use of five or more medications. Presence of urinary incontinence (UI) was also self-reported.

Five questions were used to assess quality of life, which made up the subjective health assessment part of the questionnaire. These were as follows: “In general, would you say your health is: excellent, very good, good, fair/poor, very poor”; “When you compare your health with that of other people your age, how do you rate your health at the present time? Better/the same/worse”; “Compared to 1 year ago, do you consider your health today: better/the same/worse”; “Regarding your care for your health, would you say it is generally: excellent, very good, good, fair/poor, very poor”; and “Compared to 1 year ago, how do you rate your level of activity at the present time? Better/the same/worse”. This model was based on the suggestion of Yusuf et al.,⁸ i.e., use of the domains available for this analysis.

Following a theoretical model proposed by the authors, the variables were divided into three groups. In the first group, known risk factors for FI were included (number of comorbidities, history of stroke, diabetes mellitus, cognitive decline, age, and sex); in the second, factors of undetermined direction (UI, FC, frailty syndrome, and polypharmacy); and in the third group, adverse health outcomes (falls, worse quality of life, and depression).

Description of the sample and comparison of the prevalence of FI were carried out using contingency tables with the absolute and relative frequencies of the dependent variable (fecal incontinence), considering, for descriptive purposes, all the independent variables included in the model, following the hypotheses of directionality explained above. The chi-square test was performed to verify the statistical significance of associations.

To test the proposed associations, a logistic regression model was used with FI as the dependent variable. The model was adjusted for the variables age, sex, stroke, diabetes mellitus, cognitive decline (measured by the MMSE), and high number of comorbidities, all of which are known risk factors for FI. Variables of unknown direction and adverse health outcomes made up two other blocks of the logistic regression model. All findings with $p < 0.05$ were considered statistically significant. Statistical analyses were carried out in SPSS Version 23 (IBM Corp, Armonk, NY, USA).

The study received financial support from the Brazilian National Council for Scientific and Technological Development (CNPq) (filing no. 555087/2006-9) and from the Rio de Janeiro State Research Foundation (FAPERJ) (filing no. E-26/171.489/2006). All participants provided written informed consent, and the study protocol was approved by the Research Ethics Committee of Hospital Universitário Pedro Ernesto.

RESULTS

Of the 6855 individuals in the analyzed sample, 407 (5.93%) answered “yes” to the question regarding presence of FI in the 12 months preceding the interview: 4563 (66.56%) were female, 3607 (52.93%) white, 4228 (61.67%) under the age of 75 (mean age, 73.51 years), 4194 (61.20%) had up to 4 years of formal schooling, and 3065 (46.46%) earned minimum wage or less (Table 1).

Bivariate analysis showed an association between FI and the following conditions: falls, worse self-perception of health, worse perception of health when compared to that of others, worse perception of health when compared to one’s own health a year ago, perception of poor care for one’s own health, worse activity level when compared to a year ago, and self-reported diagnosis of depression. Among the variables of unknown directionality, associations were observed between FI and UI, functional dependence (IADL and BADL), polypharmacy, and the frailty syndrome (Table 1).

The final logistic regression model adjusted for the control variables already explained in the theoretical model showed that the presence of FI is associated with worse care for one’s own health (OR 1.78 [1.08–2.96]), dependence for BADL (OR 1.29 [1.01–1.65]), and presence of UI (OR 4.21 [3.28–5.40]). In addition, intake of few medications was inversely associated with FI, i.e., absence of polypharmacy was a protective factor against FI (OR 0.61 [0.44–0.85]) (Table 2).

TABLE 1. Sociodemographic characteristics, comorbidities, cognition, functional capacity, depression, frailty, quality of life, and falls (stratified by presence of fecal incontinence). Fibra-BR sample (n = 6855).

	Fecal incontinence				Total	
	No		Yes			
	n	%	n	%	n	%
Sex*						
Male	2187	95.41	105	4.58	2292	33.44
Female	4261	93.38	302	6.61	4563	66.56
Age (years)						
65 to 74	3990	94.37	238	5.62	4228	61.67
75 to 84	2081	93.82	137	6.17	2218	32.36
85 y or older	377	92.21	32	7.82	409	5.97
Race						
White	3377	93.62	230	6.37	3607	52.93
Other	3033	94.54	175	5.45	3208	47.07
Educational attainment [†] (years)						
0 years	1202	94.12	75	5.87	1277	18.63
1 to 4 years	2741	93.96	176	6.03	2917	42.57
5 to 8 years	1141	93.60	78	6.39	1219	17.79
8+ years	1363	94.65	77	5.34	1440	21.01
Income (× minimum wage) [†]						
0 to 1	2875	93.80	190	6.19	3065	46.46
1+ to 2	1254	94.07	79	5.92	1333	20.21
2+ to 5	1346	94.25	82	5.74	1428	21.65
5+ to 10	468	93.78	31	6.21	499	7.56
10+	258	94.85	14	5.14	272	4.12
Stroke ^{*,†}						
No	6075	94.36	363	5.63	6438	93.99
Yes	368	89.32	44	10.67	412	6.01
Diabetes mellitus ^{*,†}						
No	5184	94.59	296	5.40	5480	80.05
Yes	1256	91.94	110	8.05	1366	19.95
MMSE						
< 18	350	91.62	32	8.37	382	5.57
19 to 24	2667	94.17	165	5.82	2832	41.31
25 to 30 years	3431	94.23	210	5.76	3641	53.12
Comorbidities ^{*,†}						
0	1190	96.43	44	3.56	1234	18.01
1–2	3363	95.18	170	4.81	3533	51.56
3–4	1603	91.60	147	8.40	1750	25.54
> 5	289	86.26	46	13.73	335	4.89
Urinary incontinence ^{*,†}						
No	5029	96.93	159	3.06	5188	75.72
Yes	1416	85.09	248	14.90	1664	24.28

Continue...

TABLE 1. Continuation.

	Fecal incontinence				Total	
	No		Yes			
	n	%	n	%	n	%
Frailty* [†]						
Nonfrail/Robust	2701	96.08	110	3.91	2811	41.47
Prefrail	3144	93.12	232	6.87	3376	49.80
Frail	533	90.03	59	9.96	592	8.73
IADL dependence* [†]						
Dependent	2635	91.90	231	8.05	2867	44.46
Independent	3424	95.61	157	4.38	3581	55.54
BADL dependence*						
Dependent	114	84.44	21	15.55	135	1.97
Independent	6334	94.25	386	5.74	6720	98.03
Polypharmacy*						
Absent	4724	93.78	313	6.21	5037	80.02
Present	1199	95.31	59	4.68	1258	19.98
Self-perception* [†]						
Excellent/Very good/Good	3393	96.01	141	3.98	3534	51.68
Fair	2604	92.50	211	7.49	2815	41.17
Poor/Very poor	434	88.75	55	11.24	489	7.15
Health compared to others* [†]						
Better	4261	94.41	252	5.58	4513	67.07
Same	1575	94.65	89	5.34	1664	24.73
Worse	491	88.94	61	11.05	552	8.20
Health compared to 1 year ago* [†]						
Better	1169	93.52	81	6.48	1250	18.29
Same	3548	95.27	176	4.72	3724	54.49
Worse	1712	92.04	148	7.95	1860	27.22
Health care* [†]						
Excellent/Very good/Good	4441	94.95	236	5.04	4677	68.36
Fair	1756	92.66	139	7.33	1895	27.70
Poor/Very poor	237	88.10	32	11.89	269	3.94
Activity level compared to 1 year ago* [†]						
Better	983	94.51	57	5.48	1040	15.25
Same	3662	95.04	191	4.95	3,853	56.52
Worse	1768	91.89	156	8.10	1924	28.23
Self-reported depression*						
Absent	5413	94.71	302	5.28	5715	83.49
Present	1026	90.79	104	9.20	1130	16.51
Falls in the past year* ^S						
Absent	4077	94.99	215	5.00	4292	68.15
Present	1841	91.82	164	8.17	2005	31.85

*p < 0.05; [†]Missing values; MMSE: Mini-Mental State Examination; IADL: instrumental activities of daily living; BADL: basic activities of daily living.

TABLE 2. Logistic regression between fecal incontinence, outcome variables, and variables of unknown direction. Fibra-BR sample (n = 5143).

Variable	Unadjusted		Adjusted*	
	OR (95%CI)	p-value	OR (95%CI)	p-value
Urinary incontinence	4.43 (3.47–5.67)	< 0.001	4.22 (3.28–5.41)	< 0.001
Self-perceived health status				
Very good/Good				
Fair	1.36 (1.04–1.79)	0.027	1.31 (0.99–1.73)	0.059
Poor/Very poor	1.48 (0.94–2.35)	0.094	1.3 (0.81–2.09)	0.28
Health compared to others				
Better				
Same	0.78 (0.58–1.05)	0.1	0.79 (0.58–1.06)	0.11
Worse	0.94 (0.62–1.43)	0.78	0.96 (0.63–1.46)	0.85
Health compared to 1 year ago				
Better				
Same	0.8 (0.57–1.12)	0.2	0.8 (0.57–1.12)	0.20
Worse	0.85 (0.59–1.23)	0.39	0.84 (0.58–1.22)	0.20
Health care				
Very good/Good				
Same	1.31 (1.01–1.72)	0.045	1.34 (1.02–1.75)	0.033
Worse	1.60 (0.97–2.63)	0.063	1.78 (1.08–2.96)	0.024
Activity level compared to 1 year ago				
Better				
Same	0.95 (0.65–1.38)	0.78	0.98 (0.67–1.43)	0.90
Worse	1.04 (0.69–1.56)	0.86	1.03 (0.68–1.56)	0.87
Depression	1.46 (1.11–1.93)	0.006	1.15 (0.83–1.58)	0.41
Falls	1.27 (0.99–1.62)	0.056	1.22 (0.95–1.56)	0.12
Polypharmacy	0.61 (0.44–0.85)	0.003	0.61 (0.44–0.85)	0.004
Frailty syndrome				
Robust				
Prefrail	1.33 (1.01–1.76)	0.044	1.32 (0.99–1.75)	0.055
Frail	1.52 (0.99–2.35)	0.056	1.51 (0.97–2.34)	0.068
BADLs	1.27 (0.99–1.62)	0.056	1.29 (1.01–1.65)	0.039
IADLs	0.95 (0.91–1.01)	0.087	0.96 (0.9–1.01)	0.14

*Logistic regression adjusted for age, sex, stroke, diabetes mellitus, MMSE, and high number of comorbidities. Reference: presence of fecal incontinence. BADL: basic activities of daily living; IADL: instrumental activities of daily living.

DISCUSSION

In the present study, we calculated the prevalence of FI as 5.93% (95% CI 5.3–6.5) and tested the hypothesis that, in the Brazilian population, FI would be associated with adverse health outcomes common among older adults: falls, depression, and poorer quality of life. However, only one proxy QoL variable – worse self-care – was significantly associated with

FI. Other factors of recognized causal bidirectionality also showed a significant association: two as risk factors (BADL dependence and UI) and one as a protective factor (intake of few medications as opposed to polypharmacy). Regarding the significant association between presence of UI and presence of FI in our study, some authors suggest that double incontinence is perhaps the most frequent finding in population-based studies.⁸

As this was a cross-sectional study, we were unable to establish a valid causal association between risk factors or exposure factors and the outcome of interest. As described in the Methods section, we analyzed data from the Fibra-BR network, an extensive, multicenter survey, the primary objective of which was not that of the present study. Therefore, our analyses were limited to the available variables. To ensure optimal use of the database, we designed a model based on evidence from the existing literature which allowed us to convert our conceptual hypotheses into an appropriate operational framework. In this model, some conditions – which are very well established as causal factors – were treated operationally as control variables.^{5,7,26}

For other variables, however, there is not enough evidence that the exposure did not change as a result of the presence of FI; therefore, reverse causality cannot be ruled out as an explanatory element for certain findings. Significant risk (BADL dependence, the frailty syndrome, UI) and protective (number of medications, independence for IADL) factors found in the present study fit into this category of variables.^{7,13}

The Fibra-BR study was carried out with older adults (aged 65 years or older) and excluded from its sample both institutionalized individuals and those who, despite living in the community, had significant physical and/or cognitive limitations. This exclusion probably removed from the examined sample individuals with more precarious functional capacity, a population which usually exhibits a higher prevalence of FI (such as older adults with limiting sequelae of stroke and those with an MMSE below 17). Therefore, we believe the prevalence found herein is similar to that observed in studies carried out with younger samples.^{6,15,19,20,27} In previous studies in Brazil, the prevalence of FI ranged from 3% to 43%.^{17-19,28} However, of these four studies, one was carried out with institutionalized older adults,²⁸ two in samples that included individuals under 60 years of age,^{19,20} and only one with a sample similar to that of the present study.¹³ Another factor that may contribute to these differences – and to the extreme range of variation in prevalence observed in these studies – is the absence of a standardized operational definition of FI.

Some studies have associated FI with changes in mobility; however, few directly addressed its association with falls.^{13,15,18} Although we found no such association, falls remain an important variable with substantial clinical plausibility, considering that the urge to avoid involuntary passage of stool in incontinent older adults, often with mobility restrictions, tends to increase their risk of falling. This hypothesis should be further investigated in future studies.

Depression in our sample was assessed through self-reporting. The biases introduced by this type of information

in epidemiological research may explain the lack of a significant association with the dependent variable. Hypothetically, the social isolation generated by FI should be associated with greater odds of developing depression in this population. An association of FI with depression and worse QoL – directly evaluated – has already been described in previous studies.^{10-13,29,30}

The Fibra-BR study did not include a specific questionnaire to assess QoL; for this reason, we used five proxy questions instead. Of these, only worse self-care was positively associated with FI. Once again, the fact that individuals with extreme functional impairment were excluded from the sample (given the exclusion criteria of the original study) may explain this finding. It bears stressing that previous studies identified a worse perception of health by patients with FI.^{9,26,28-30}

Other factors with potential reverse causality could indirectly contribute to worse QoL. BADL dependence and presence of UI are among these factors; both contribute to social isolation and, consequently, worse QoL.⁸ These conditions were also positively associated with FI in this study. Although an association between FI and the frailty syndrome is biologically plausible, we did not identify previous studies in the literature that suggest such an association. In our model, the inclusion of this variable among those with undetermined causal directionality aimed to respect the current state of knowledge regarding this potential association.

Some limitations of the present study must be noted. These include not having been designed for the specific purpose of assessing FI, which certainly excluded individuals who, due to the nature of their underlying conditions, would otherwise have been included in the sample. This may have underestimated the prevalence of the dependent variable. However, the identification of a prevalence of FI of approximately 6% among individuals with relatively good functional status is surprising and highlights the importance of better awareness of this condition by health care providers.

Another limitation is the absence of a specific, validated QoL questionnaire, which forced us to use proxies to assess this condition. This may have compromised the associations of interest and may even explain the absence of significant associations between FI and four of the five proxy QoL variables adopted for analysis.

Strengths of the study include the number of individuals interviewed (a sample of approximately 7000 participants) and the fact that different states and cities across all five regions of Brazil were included, which ensures good representativeness of the older Brazilian population. Another strength of the present study worth stressing is the inclusion of variables

that have been rarely explored in other studies on FI, such as frailty, polypharmacy, and QoL.

The present study collected data between the years 2009 and 2010. Nevertheless, we do not believe that substantial changes would have occurred in prevalence or in the tested associations, since the risk factors for FI included in our study model did not change significantly in frequency.

For the evaluation of risk factors, causes, and consequences of FI, prospective longitudinal studies would be most appropriate. However, to generate hypotheses (e.g., a relationship between FI and frailty) and confirm already established data (the relationship between FI, UI, and functional dependence), the present study proved adequate.

Finally, the present study is justified by the issue – reiterated in several previous investigations – of the importance of raising awareness among health care providers of FI and its complexity, especially concerning symptoms and associated factors, with the aim of informing optimal management and prevention strategies. In 2012, Nyrop et al.⁴ evaluated the perceptions of health care professionals on the topic of FI. Although most (89.7%) recognized that FI has major repercussions for patients' lives, just over half of physicians (54.1%) screened for FI, only 32.9% believed that LTCFs would be capable of providing good care for this condition, and 27.1% believed that FI could be exacerbated in a setting of institutionalization.

CONCLUSION

In the present study, the calculated prevalence of FI was 5.93% (95%CI 5.3–6.5). Worse care for one's health, dependence for basic activities of daily living, and urinary incontinence were significantly associated with FI as risk factors, while the absence of polypharmacy was associated with protection against FI.

Conflict of interest

The authors report no conflicts of interest.

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Author contributions

EMC: project administration, formal analysis, conceptualization, data curation, writing – original draft, writing – review & editing, investigation, methodology, funding acquisition, resources, software, supervision, validation, visualization. VGM: project administration, formal analysis, conceptualization, data curation, writing – original draft, writing – review & editing, investigation, methodology, funding acquisition, resources, software, supervision, validation, visualization. ALN: writing – review & editing, investigation, methodology, funding acquisition, resources, validation, visualization. EF: writing – review & editing, investigation, methodology, funding acquisition, resources, validation, visualization. LSP: writing – review & editing, investigation, methodology, funding acquisition, resources, validation, visualization. FMD: writing – review & editing, investigation, methodology, funding acquisition, resources, validation, visualization. MP: project administration, formal analysis, conceptualization, data curation, writing – original draft, writing – review & editing, investigation, methodology, funding acquisition, resources, software, supervision, validation, visualization. RAL: project administration, formal analysis, conceptualization, data curation, writing – original draft, writing – review & editing, investigation, methodology, funding acquisition, resources, software, supervision, validation, visualization.

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