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Iatrogenic risk factors associated with hospital readmission of elderly patients: A matched case-control study using a clinical data warehouse

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Summary

What is known: Hospital readmission within 30 days of patient discharge has become a standard to judge the quality of hospitalizations. It is estimated that 14% of the elderly, people over 75 years old or those over 65 with comorbidities, are at risk of readmission, of which 23% are avoidable. It may be possible to identify elderly patients at risk of readmission and implement steps to reduce avoidable readmissions.

Objective: The aim of this study was to identify iatrogenic risk factors for readmission. The secondary objective was to evaluate the rate of drug-related readmissions (DRRs) among all readmissions and compare it to the rate of readmissions for other reasons.

Methods: We conducted a retrospective, matched, case-control study to identify non-demographic risk factors for avoidable readmission, specifically DRRs. The study included patients hospitalized between 1 September 2014 and 31 October 2015 in an 800-bed university hospital. We included patients aged 75 and over. Cases consisted of patients readmitted to the emergency department within 30 days of initial discharge. Controls did not return to the emergency department within 30 days. Cases and controls were matched on sex and age because they are known as readmissions risk factors. After comparison of the mean or percentage between cases and controls for each variable, we conducted a conditional logistic regression.

Results: The risk factors identified were an emergency admission at the index hospitalization, returning home after discharge, a history of unplanned readmissions and prescription of nervous system drugs. Otherwise, 11.4% of the readmissions were DRRs, of which 30% were caused by an overdose of antihypertensive. The number of drugs at readmission was higher, and potentially inappropriate medications were more widely prescribed for DRRs than for readmissions for other reasons.

What is new and conclusion: In this matched case-control retrospective study, after controlling for gender and age, we identified the typical profile of elderly patients at risk of readmission. These patients had an unplanned admission at the index hospitalization and prescribed nervous system drugs at discharge from the index admission; they have a history of unplanned readmission within 30 days and return home after discharge.

KEYWORDS
aged, data warehouse, patient readmission, risk factors

1 | WHAT IS KNOWN

Hospital readmission within 30 days of patient discharge has become a standard to judge the quality of hospitalizations. Among these readmissions, unscheduled hospitalizations directly related to the index hospital stay are considered to be avoidable.[1]

The elderly are defined as people over 75 years of age or those over 65 with comorbidities.[2] They show a progressive loss of reserve and adaptive capacity and an overall deterioration in health that can result in disability or loss of independence.[3] Hospitalizations may be particularly deleterious for these patients, making them even more dependent.[4] It has been estimated that 14% of elderly are at risk of readmission, of which 23% are avoidable.[1]

Readmission results from decompensated comorbidities, resulting in overcrowded emergency departments (EDs) and increased hospital expenses.[5] Since 2013, the French Ministry of Health has warned health professionals about the high risk of readmission for the elderly and has made the reduction in readmissions a priority.[1] Various interventions have been tested to reduce readmission rates: discharge planning protocols, comprehensive geriatric assessments, discharge support arrangements and education.[6] However, the "Haute Autorité de Santé" (HAS) advocates identifying frail patients who need these interventions. Indeed, the identification of such patients is essential, as it is not "necessary nor efficient to intervene for every patient".[1]

Prescribed drug-related readmissions (DRRs) represent between 4.2%[7] and 24.3%[8] of readmissions. They may be due to adverse reactions of drugs prescribed at discharge, suboptimal therapy or medication nonadherence.[9] Some drugs are known to be generally associated with poor health outcomes and are listed as potentially inappropriate medications (PIMs).[10,11] The American Geriatrics Society has assembled the latest PIM list: The American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[12] However, the results of studies on PIMs and readmissions are conflicting. Hagstrom et al[13] showed that the prescription of PIMS had no effect on the readmission rate, whereas Pavon et al[14] showed that the prescription of benzodiazepines, which are listed as PIMs, was associated with a higher readmission risk (OR = 1.23).

The DRRs should be mostly avoidable, with appropriate intervention on the management of the elderly at risk of readmission. It may be possible to identify elderly patients at risk of readmission, particularly DRRs, and implement to reduce avoidable readmissions.

We identified patients at risk of readmission using a clinical data warehouse (CDW). The CDW allows the performance of complex queries while achieving reliable and high-quality results.

2 | OBJECTIVE

The aim of this study was to identify iatrogenic risk factors for readmission.

The secondary objective was to evaluate the rate of DRR among all readmissions and compare it to the rate of readmissions for other reasons.

3 | METHODS

We conducted a retrospective, matched, case-control study to identify non-demographic risk factors for avoidable readmission, specifically DRR.

3.1 | Data source

The hospital is a teaching hospital of 795 beds with 24 clinical departments (15 medical wards and nine surgical units). The clinical information system has been associated with a CDW since 2009, making it possible to reuse healthcare data and clinical research.

All medical records and prescriptions are computerized. The data needed for the study were stored in the CDW and extracted using Oracle® software, or manually by reading the electronic medical record.

An ethics committee approved the study protocol (CERHUPO, CDW_2015_0023).

3.2 | Study participants

Patients were at least 75 years old and admitted to the university hospital from 1 October 2014 to 30 September 2015.

Cases consisted of elderly patients who experienced an unscheduled readmission within 30 days after the index admission. Readmissions had to originate at the ED to be considered unscheduled. All patients who were readmitted without a prior ED visit were excluded. Readmission included simple ED visits.

Controls consisted of elderly patients who had not had any unscheduled readmissions during the 30 days after the index admission. All controls who died during the index hospitalization were excluded.

Cases and controls were randomly matched.

3.3 | Study variables

We identified readmission risk factors by the literature review (Table 1). For each risk factor, we listed the category, the odds ratio (or hazard ratio or relative risk), the reference and the variables to be used in our study. Many readmission risk factors appeared to be already known in

TABLE 1 Risk Factors described in the literature

Risk factors		OR (*or HR or RR*) [95% CI]	References	Variables selected for our study
Patient characteristics				
Sex	Women	OR = −1.539	Fethke et al[18]	Matching for sex and age
Age	Age > 80 years	OR = 1.8 [1.02-3.2]	Marcantonio et al[19]	
Marital status	Widow	OR = 1.745	Fethke et al[18]	Single = divorced, single or widow Married = married or living together
	Single	OR = 2.195 [0.979-4.919]	Morrissey et al[20]	
Residence	Living in a home for the elderly	HR = 1.617 [1.176-2.224]	Alassaad et al[21]	Private home or home for the elderly
	Living in a convalescent home	RR = 1.9 [1.1-3.3]	Zanocchi et al[22]	
Social support	Poor familial support according to patient	RR = 2.7 [1.2-6.1]	Kwok et al[23]	Living alone or not
Education level	Medium-High education level	RR = 1.8 [1.1-3.6]	Zanocchi et al[22]	Socio-professional category
Comorbidities	Pulmonary disease	HR = 1.834 [1.296-2.595]	Alassaad et al[21]	Charlson index, depression, prescription of antidepressant drugs
	Cancer	HR = 1.659 [1.198-2.297]		
	CIRS Score	OR = 2.24 [1.25-4.03]	Franchi et al[24]	
	Liver disease	OR = 2.32 [1.42-3.77]		
	Cardiovascular disease	OR = 1.48 [1.0-2.17]		
	Charlson index > 2	RR = 1.8 [1.1-3.6]	Zanocchi et al[22]	
	Antidepressant prescription	HR = 0.573 [0.410-0.799]	Alassaad et al[21]	
Activity of daily living	Becoming dependent for feeding (ADL-Katz scale)	OR = 1.9 [1.2-2.9]	Lanièce et al[5]	Dependence for feeding, continence, mobility and hygiene
Risk factors		**OR (*or HR or RR*) [95%CI]**	**Reference**	**Variables of our study**
Admission characteristics				
Type of admission	78.4% of medical readmitted patients *vs* 65.8% medical non-readmitted patients (P < .0001)		Davis et al[25]	Planned admission or emergency, medical or surgical admission
Length of stay (LOS)	LOS (days)	RR = 3.2 [1.5-7.3]	Zanocchi et al[22]	LOS (days)
Primary diagnosis	*See comorbidities*			Primary diagnosis
Discharge	Elderly adults discharged to nursing homes after a hospitalization had a 41% higher chance of 30-day hospital readmission than those discharged to the community.		Bogaisky et al[26]	Return home or transfer
History of readmission	Previous hospital admission (6 months before index admission)	2.09 [1.44-3.03]	Franchi et al[24]	30-day readmission history
Therapeutic characteristics				
Polymedication	>4 drugs at discharge	OR = 1.757 [0.999-3.090]	Morrissey et al[20]	Number of prescribed drugs at discharge
Potentially Inappropriate Medication (PIM)	Benzodiazepine prescriptions	OR = 1.23 [1.04-1.44]	Pavon et al[14]	Number of PIMs
	Antacid prescriptions	HR = 1.436 [1.101-1.872]	Alassaad et al[21]	
	Opioid prescriptions	HR = 2.063 [1.517-2.806]		

OR, Odds ratio; HR, hazard ratio; RR, relative risk.

the literature, but few were related to the medications prescribed at discharge of the index hospitalization. Age and sex are known to be re-admission risk factors.[15-17] Thus, controls were matched to cases (1:1), based on their sex and index age (within 5 years), to control for these two risk factors, to have similar populations between cases and controls and to keep patient characteristics, admission characteristics and therapeutic characteristics in the multivariate analysis.

The study variables were as follows:

- Patient characteristics: Marital status, level of social support (living alone or accompanied, nursing home residents or elderly living at home), socio-professional category, comorbidity (Charlson index), the presence of depression, dependence in activities of daily living and malnutrition.
- Admission characteristics: Programmed admission or emergency admission, medical or surgical pattern, primary diagnosis and history of readmission (any hospitalizations followed by an emergency readmission within 30 days described in the medical record) and length of stay.
- Therapeutic characteristics: Each drug listed on the discharge prescriptions was classified according to the ATC (Anatomical Therapeutic Chemical) Classification, whether it was a PIM, and the number of drugs.[5,14,18-26]

3.4 | Study outcomes

The primary outcome of the study was to identify iatrogenic risk factors for readmission for elderly patients to identify those who require interventions.

The secondary outcomes were to evaluate the rate of DRR among all readmissions and to describe the drug-related problems.

3.5 | Statistical analysis

All statistical analyses were conducted using R software (R Version 3.3.3; 2017-03-06).

3.5.1 | Univariate analysis

We compared the mean (quantitative variables) or percentage (qualitative variables) between cases and controls for each variable to select those for the logistic regression. We used t tests for the quantitative variables and chi-squared tests to compare the percentages of qualitative variables.

The selected variables for the multivariate analysis were those that were significant following comparison ($P < .05$) or those with a *P-value* < .10 for risk factors largely described in the literature.

3.5.2 | Multivariate analysis

After generating a diagram of eigenvalues and performing a factor analysis, we conducted a principal component analysis to determine the correlations between selected variables. Knowledge of the correlations allowed removing variables from the logistic regression. We retained the variable with the smallest *P-value* when two were correlated. The variables were removed from the logistic regression until most had a significant *P-value* (<.05) and a low Akaike information criterion (AIC).

3.5.3 | Secondary objective

The secondary outcome was to compare DRR with readmissions for other reasons. We used *t* tests and chi-squared tests for quantitative and qualitative variables, respectively.

4 | RESULTS

From 1 September 2014 to 31 October 2015, 6,574 elderly patients meeting our criteria were admitted to the hospital. Within 30 days after discharge of the index hospitalization, 422 patients (6.4%) were readmitted, whereas 6,096 were not. These 422 patients were randomly matched with 422 controls among the 6,096 patients, creating 422 case-control pairs. Among the 422 unplanned readmissions, 137 (32.5%) were ED visits, without hospital admission.

4.1 | Bivariate analysis

Bivariate analysis allowed the comparison of cases and controls to select the variables used for multivariate analysis (Table 2).

The patient characteristics of cases significantly differed from controls for the Charlson index and depression, as indicated in the medical record ($P = .00681$ and.0281, respectively). The place of residence had a *P-value* < .1 ($P = .053$). There were no statistical differences between the case and control groups for all other variables (marital status, residence, social support, depression, feeding, continence, hygiene and mobility). The socio-professional category and nutritional status were removed from statistical analysis because of too much missing data (41% and 59%, respectively).

We then compared the index admission characteristics between cases and controls. By univariate analysis, an unplanned index admission, a medical index admission, a return to home at discharge and a history of avoidable readmissions were significantly higher for the case than control group ($P = 7.43 \times 10^{-5}$, 0.00313, 0.00346 and 6.79×10^{-5}, respectively). There were no statistical differences between the case and control groups for all other variables (length of stay and primary diagnosis).

Finally, we compared the treatment characteristics at discharge of the index hospitalization. Cases significantly differed from controls for the number of drugs ($P = .00230$), polypharmacy ($P = .0131$), PIM ($P = .00637$), systemic hormonal preparations ($P = .0377$) and nervous system drugs ($P = .000556$) (ATC classes H and N). The prescription of drugs of the alimentary tract and metabolism had *P-value* < .1 ($P = .0672$). There was no statistical difference between the case and control groups for the other ATC classes.

4.2 | Multivariate analysis

Selected variables for the multivariate logistic regression analysis were social support (living alone or not), the residence (private home or retirement home), the presence of depression or dementia, Charlson index, type of index admission (planned or emergency vs medical or surgical), history of readmission, number of prescribed drugs at discharge of the index hospitalization and polypharmacy, number of PIMs, number of drugs in classes A, H and N (metabolism, hormonal preparations and nervous system drugs) and type of discharge (return home or transfer to another health institution). These variables were statistically significant by univariate analysis or highly described in the literature. Following factor analysis and principal component analysis, we observed that planned or

TABLE 2 Univariate analysis

Variables	Cases N = 422	Controls N = 422	*P*-value
Patient Characteristics			
Marital status: n (%)			.534
Single	230 (56.1%)	210 (53.7%)	
Residence: n (%)			.053•
Private home	382 (90.5%)	397 (94.1%)	
Home for elderly	40 (9.5%)	25 (5.9%)	
Social support: n (%)			.174
Living alone	159 (39.2%)	164 (44%)	
Living with someone	247 (60.8%)	25 (5.9%)	
Comorbidities: n (%)			
History of myocardial infarction: n (%)	39 (9.2%)	35 (8.3%)	.626
Congestive heart failure: n (%)	240 (56.9%)	22 (52.6%)	.213
Chronic arterial occlusive disease of the lower extremities: n (%)	49 (11.6%)	43 (10.2%)	.508
History of stroke: n (%)	36 (8.5%)	40 (9.5%)	.631
Dementia: n (%)	103 (24.4%)	77 (18.2%)	.029
Chronic pulmonary disease: n (%)	67 (15.9%)	69 (16.4%)	.852
Connective tissue diseases: n (%)	27 (6.4%)	26 (6.2%)	.887
Gastroduodenal ulcer: n (%)	42 (10%)	38 (9.0%)	.638
Diabetes: n (%)	72 (17.1%)	66 (15.6%)	.577
Kidney disease: n (%)	72 (17.1%)	58 (13.7%)	.182
Malignant disease: n (%)	160 (37.9%)	146 (34.6%)	.316
Charlson index: m (sd)	6.82 (1.94)	6.45 (1.99)	.00681**
Depression (notified in medical record): n (%)	51 (12.1%)	32 (7.6%)	.0281*
Feeding: n (%)			.818
Dependent	23 (5.5%)	27 (6.4%)	
Partial dependence	92 (21.8%)	94 (22.3%)	
Independent	307 (72.7%)	301 (71.3%)	
Continence: n (%)	302 (71.6%)	311 (73.7%)	.487
Hygiene			.571
Dependent	63 (14.9%)	61 (14.5%)	
Partial dependence	178 (42.2%)	165 (39.1%)	
Independent	181 (49.9%)	196 (46.4%)	
Mobility: n (%)			.568
Bedridden	57 (13.5%)	60 (14.2%)	
Partial dependence	168 (39.8%)	153 (36.3%)	
Independent	197 (46.7%)	209 (49.5%)	
Index Admission Characteristics			
Admission planned or emergency: n (%)			7.43×10^{-5}***
Emergency	311 (73.7%)	257 (60.9%)	
Medical or surgical admission: n (%)			.00313**
Medical	294 (69.7%)	253 (60%)	
Length of stay (≥ 5 days): n (%)	216 (51.2%)	195 (46.2%)	.148
Discharge: n (%)			.00346**
Return home	314 (74.4%)	275 (65.2%)	
Transfer	108 (25.6%)	147 (34.8%)	

(Continues)

TABLE 2 (Continued)

Variables	Cases N = 422	Controls N = 422	*P*-value
History of avoidable readmission: n (%)	106 (25.1%)	60 (14.2%)	6.79×10^{-5}***
Treatment Characteristics at Discharge of the Index Hospitalisation			
Number of drugs: m (sd)	7.51 (3.59)	6.75 (3.66)	.00230**
Polypharmacy (> 5 drugs): n (%)	298 (70.6%)	264 (62.6%)	.0131*
Potentially inappropriate medication (>1): n (%)	268 (63.5%)	229 (54.3%)	.00637**
Drugs according to Anatomical Therapeutic Chemical (*ATC*) Classification			
Class A drugs (>1): n (%)	327 (77.5%)	303 (71.8%)	.0576•
Class B drugs (>1): n (%)	299 (70.9%)	315 (74.6%)	.216
Class C drugs: (>1): n (%)	343 (81.3%)	335 (79.4%)	.489
Class G drugs (>1): n (%)	57 (13.5%)	49 (11.6%)	.406
Class H drugs (>1): n (%)	95 (22.5%)	71 (16.8%)	.0377*
Class J drugs (>1): n (%)	65 (15.4%)	57 (13.5%)	.434
Class L drugs (>1): n (%)	28 (6.6%)	19 (4.5%)	.177
Class M drugs (>1): n (%)	46 (10.9%)	49 (11.6%)	.744
Class N drugs: (>1): n (%)	318 (75.4%)	272 (64.5%)	.000556***
Class R drugs (>1): n (%)	57 (13.5%)	63 (14.9%)	.554

Primary diagnosis according to ICD-10: A&B, certain infectious and parasitic disease; C&D, neoplasms, diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; E, endocrine, nutritional and metabolic disease; F, mental and behavioural disorders; G, diseases of the nervous system; H, diseases of the eye and adnexa, diseases of the ear and mastoid process; I, diseases of the circulatory system; J, diseases of respiratory system; K, diseases of digestive system; L, diseases of the musculoskeletal system and connective tissue; M, diseases of the musculoskeletal system and connective tissue; N, diseases of the genitourinary system; R, symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified; S&T, injury, poisoning and certain other consequences of external causes; Z, factors influencing health status and contact with health services. ATC Classification: class A, alimentary tract and metabolism; class B, blood and blood-forming organs; class C, cardiovascular system; class G, genitourinary system and sex hormones; class H, system hormonal preparations, excluding sex hormones and insulin; class J, anti-infectives for systemic use; class L, antineoplastic and immunomodulating agents; class M, musculoskeletal system; class N, nervous system; class R, respiratory system.
***.001, **.01, *.05, •.1.

TABLE 3 Conditional logistic regression

Variable	Coefficient	Exp (coef) = OR	95% CI	*P*-value
Charlson index	0.069	1.07	0.99-1.16	.09*
Emergency admission	0.67	1.96	1.41-2.71	5.22×10^{-5}***
Return home at discharge	0.61	1.84	1.32-2.59	.00038***
History of readmissions	0.51	1.66	1.14-2.43	.0086**
Prescription of nervous system drugs	0.59	1.81	1.30-2.52	.00049***

****.001, **.01, *.05.*

unplanned admission and medical or surgical admission were correlated, as well as the number of prescribed drugs and polypharmacy. These correlations helped to construct the logistic regression model (Table 3).

The starting logistic regression model (with all selected variables) had an AIC of 547 813. The conditional logistic regression (Table 3) had an AIC of 537 916. In this model, an index admission in emergency, a return home at discharge, a history of readmissions and the prescription of nervous system drugs were still significantly associated with the risk of readmission after adjustment for the Charlson index. Thus, an emergency admission at the index hospitalization increased the readmission risk (OR = 1.96, 95% CI = 1.41-2.71). Returning at home after discharge and having history of unplanned readmissions also increased the risk of readmission (OR = 1.84 and 1.66, respectively), as well as the prescription of nervous system drugs (OR = 1.81, 95% IC: 1.30-2.52). Among all the 844 subjects, 43 (5.1%) who had an index admission in emergency, a return to home at discharge, a history of readmissions and the prescription of nervous system drugs were readmitted. On the contrary, 8 (0.95%) patients had none of these characteristics.

4.3 | Secondary objective

In this study, 11.4% of the readmissions were DRRs, of which 30% were caused by an overdose of antihypertensive drugs, leading to falls and hypotension (6.4% and 8.5% of the reasons for DRR, respectively).

The number of drugs at readmission was higher, and PIMs were more widely prescribed for DRRs than for readmissions for other reasons ($P = 6.688 \times 10^{-5}$ and 0.00837, respectively).

5 | WHAT IS NEW AND DISCUSSION

In our study, after controlling for gender and age, patients at risk of readmission had an unplanned admission at the index hospitalization and prescribed nervous system drugs at discharge from the index admission. Furthermore, they had a history of unplanned readmission at 30 days and returned home after discharge.

Unplanned admissions were mostly related to a medical pattern. This correlation can be explained by comorbidities that lead to decompensation of a chronic condition and thus unplanned admission. Moreover, comorbidities[16,24] and medical admissions[25] are known factors of readmission. Thus, these two readmission risk factors show that an unplanned admission is also a risk factor for readmission. Indeed, in 2012, Van Walraven et al[27] had already found that unplanned admission was a readmission risk factor, as it is one of the variables of the clinical LACE index.

We also found that the prescription of nervous system drugs at discharge, including antidepressants, increases readmission risk. Although patient and admission characteristics are well-known readmission risk factors, therapeutic risk factors have only recently been studied. The link between psychotropic drugs and readmission has been previously shown,[14] especially for DRR.[28] Indeed, psychotropic drugs (class ATC N) are highly responsible for adverse drug reactions.[29]

A history of admissions or ED visits is known to be a risk factor for readmissions. Indeed, in a systematic review, Garcia-Perez et al[30] found that patients admitted in the previous three or 6 months had an increased risk of readmission.[16] Furthermore, these variables are part of two existing clinical scores for predicting readmission risk: previous hospital admission for the HOSPITAL score and ED use in the previous 30 days or hospitalization in the previous 90 days for the Triage Risk Screening Tool (TRST).[31] However, we demonstrate here that patients with a history of unplanned readmission within 30 days, that is any hospitalization followed by an unplanned readmission within 30 days, were more likely to be readmitted. This may be because readmitted patients have chronic comorbidities at high risk of decompensation: a comorbidity that decompensates once can certainly decompensate again.

The secondary outcome of this study was to describe DRRs in cases. Patients with a DRR had more PIMs prescribed than those readmitted for reasons other than an adverse drug reaction. To our knowledge, no previous study has investigated the impact of PIMs on DRRs. However, JM. Pavon et al.[14] and H. Chayé et al[28] showed a link between psychotropic and cardiological drugs and readmission (including DRR).

This study had several limitations and strengths. The main limitation was that we did not consider readmission to another facility as the electronic health records were limited to readmissions in the same hospital. There was also a misclassification bias: we did not consider unscheduled readmissions which did not originate from an ED visit, because the distinction from scheduled admissions was not possible using the CDW. Thus, we may have underestimated the readmission rate, as controls might have been readmitted to another health institution or died after the index hospitalization. A matched case-control study design prevents this limitation. Finally, only readmissions annotated as iatrogenic were considered for be DRRs, which may have led to an underestimation of the DRR rate. The strength of this study is its focus on iatrogenic risk factors. These risk factors are modifiable by actions taken at discharge, unlike patient and admissions characteristics.

In conclusion, this study identified several readmission risk factors: emergency admission at the index hospitalization, the prescription of nervous system drugs and a history of unplanned readmissions. We will be able to use these factors to identify patients at risk of readmission during their hospitalization, and offer them a programme at discharge to reduce this risk, such as a comprehensive chronic treatment review with education on the self-management of the disease and transition-of-care communication. Indeed, thanks to the computerized medical records, patients presenting at least one of the identified risk factors will be selected to have the discharge programme. A clinical score including the identifying risk factors will also be researched. Multimodal geriatric discharge planning intervention has already shown its efficacity.[32] Identifying patients at risk will help to select those for whom such planning intervention would be efficient.

CONFLICT OF INTEREST

No conflict of interests has been declared.

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