The predictive value of traditional cardiovascular risk factors for mortality in the oldest old: untangling the role of frailty

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Abstract

Background

To date, there is no consensus regarding cardiovascular risk management in the very elderly (80 years and older). Studies have shown that the relationship between traditional cardiovascular risk factors (such as hypertension and hypercholesterolemia) and mortality is lost or even inverted within this age group. This relationship could be modified by the presence of frailty. In this study we further examined the effect of frailty on the association between cardiovascular risk factors and mortality in the oldest old, to identify those people who might benefit more from cardiovascular risk management.

Methods

A representative sample of 566 participants of the BELFRAIL study, a prospective, observational, population based cohort study of subjects aged 80 years and older, was included. Data on cardiovascular risk factors was recorded. Frailty was assessed by use of three models: the Fried criteria, the PUTS model, and the Groningen Frailty Indicator. Follow-up data on mortality and cause of death was gathered.

Results

Frail subjects were more likely to be older, more likely to be female, less likely to be higher educated, and more often had a history of cardiovascular disease. No cardiovascular risk factor was able to predict mortality in either primary or secondary prevention. Presence of frailty was a strong risk factor for mortality. In robust patients, a history of cardiovascular disease increased the risk for mortality. In frail patients, there was no association between any of the traditional risk factors and mortality.

Conclusion

Traditional cardiovascular risk factors were not able to predict mortality in very old subjects. Frailty showed to be a strong risk factor for mortality in this age group. However, frailty could not be used to identify further subjects who might benefit more from cardiovascular risk management.

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INTRODUCTION

The Western world is faced with an upcoming 'grey epidemic' – over the past decades, the proportion of elderly and very elderly people in our societies has been rapidly increasing, and will continue to do so in the decades to come. In Belgium, the percentage of people aged 65 and older is expected to increase from around 17% in 2010 to almost 25% in 2060. Moreover, in this period, the number of people aged 85 and older is expected to more than triple (1). In this ageing society cardiovascular disease is highly prevalent and a major cause of morbidity, disability and mortality. It is not surprising that cardiovascular disease is still the leading contributor to global burden of disease in older people (2). This is putting a heavy burden on health care systems. Therefore, cardiovascular prevention, both primary and secondary prevention, remains a priority in healthcare.

While there is an abundance of evidence for the importance of adequate cardiovascular risk management even at older age (3-4), more and more studies emerge implying that when looking at the oldest age groups (aged 80 years and older), the predictive value of classical cardiovascular risk factors, like hypertension or hypercholesterolemia, is lost or even inverted (5-6). This might be related to the fact that the oldest old are a very heterogeneous population, with the active independent community-dwelling elder at one end, and the bedridden geriatric patient at the other end of the spectrum. Possibly the predictive value of cardiovascular risk factors is lost in the presence of frailty. Indeed, several recent studies advocated categorizing individuals based on biological instead of chronological age in order to facilitate personalized cardiovascular risk management for the aging population, leading to a patient instead of a disease-based approach (7).

Markers of biological age or frailty, such as gait speed, underlying comorbidities and polypharmacy, or a combined measure such as a frailty index could be used to understand the complex relation between classic cardiovascular risk factors and risk of clinical outcomes and

to identify older individuals who are likely (not) to benefit from cardiovascular risk management (7-9).

Therefore, this study was performed in order to determine the predictive value of classic cardiovascular risk factors, according to the presence of frailty, for all-cause and cardiovascular mortality in a large prospective cohort of patients aged 80 and older.

METHODS

Study population

This study is embedded within the BELFRAIL-study, a prospective, observational, population based cohort study of subjects aged 80 years and older in Belgium. All participants in the study gave informed consent, and the Biomedical Ethics Committee of the Medical School of the Université catholique de Louvain (UCL) of Brussels approved the study. The study design, methods and characteristics of the cohort have been published in detail elsewhere (10). Briefly, 29 general practitioner (GP) centers included a total of 567 subjects between November 2, 2008 and September 15, 2009. Only three exclusion criteria were used: dementia (defined as known mini mental state examination (MMSE) score <15/30), palliative care, and medical emergency. Patients were questioned and examined by both a GP and a clinical research assistant (CRA). The GP recorded social situation, medical history and medication, and conducted a thorough clinical examination. The CRA performed an extensive examination containing performance testing, several questionnaires, and technical examinations.

Frailty

The definition of frailty used in this study was based on three different frailty models: the Fried criteria, the PUTS model, and the Groningen Frailty Indicator.

The Fried criteria were developed and validated by Fried et al. (11) and consist of 5 items: unintentional weight loss (as reported by the general practitioner), weakness (measured

grip strength (with Jamar Plus digital hand held dynamometer) in the lowest quintile), poor endurance/exhaustion (self-report of exhaustion), slowness (slowest quintile in a test of timed walking speed), and sex-adjusted low physical activity level (LAPAQ score in the lowest quintile). Individuals with three or more of these five criteria were considered frail.

The Puts model (12) is comprised of nine frailty markers, being: body weight, peak expiratory flow, cognitive functioning, vision problems, hearing problems, incontinence, sense of mastery, depressive symptoms, and physical activity. Frailty was defined as the presence of three or more frailty markers.

The Groningen Frailty Indicator (13) is a 15-item questionnaire focusing on the core domains of functioning. The items are the following: shopping, walking outdoors, dressing and undressing, going to the toilet, physical fitness, vision problems, hearing problems, unintentional weight loss, use of >3 medicines, memory complaints, experience of emptiness, missing people around, feeling abandoned, feeling sad/dejected, and feeling nervous/anxious. A person was considered frail when six or more items were present.

In our current study, participants were considered frail if they met the frailty criteria for one of the three aforementioned models. All others were classified as ‘robust’.

Cardiovascular risk factors

The GP was asked to report the smoking status of the patient (no versus current or prior) and the presence of hypertension, diabetes and cardiovascular disease. The presence of cardiovascular disease was classified as either minor (history of angina pectoris, transient ischemic attack (TIA), peripheral arterial disease or episode of decompensated heart failure) or major (history of myocardial infarction (according to the GP or positive ECG (Minnesota Code 1-1 or 1-2 (excluding 1-2-8))), stroke, percutaneous transluminal coronary angioplasty (PTCA) or stent, coronary surgery or arterial surgery). The GP measured the systolic and diastolic blood pressure in sitting position on both arms, which was repeated after two

minutes. For the current study, only the highest readings (left or right) of the second measurement were used. Three categories of systolic blood pressure (<140mmHg, 140-160mmHg and ≥160mmHg) and three categories of diastolic blood pressure were used (<70mmHg, 70-90mmHg and ≥90mmHg). The clinical research assistant calculated the Body Mass Index (BMI) based on a standardized measurement of weight and height.

A blood sample was collected in the morning after fasting, and serum samples were stored frozen at -80°C until analysis. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and the serum concentration of creatinine were measured using the UniCel® DxC 800 Synchron (Beckman-Coulter, Brea, USA). Tertiles of total cholesterol and HDL-C were made. The glomerular filtration rate was estimated (eGFR) using the MDRD formula.

Data on relevant antihypertensive medication including diuretics, B-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors (ACE-I), angiotensin II receptor blockers (ARB) and potassium sparing agents were recorded. Furthermore, the presence of lipid modifying agents was also registered.

Outcome

Three detailed follow-up questionnaires were filled in by the participating GPs after 1.4 ± 0.3 years, after 3.0 ± 0.3 years and after 5.1 ± 0.3 years. These questionnaires included questions on mortality and cause of death. The causes of death were divided into cardiovascular and non-cardiovascular causes, according to the GPs' assessment and the subsequent review by 2 independent researchers blinded to all clinical data.

Data Analysis

Continuous variables are presented as the mean and standard deviation (SD). Categorical variables are presented as numbers and frequencies. Comparisons between different categories of subjects were performed using the Chi^2 test for categorical variables or

the Student's t test for continuous variables. Survival curves were computed using the Kaplan-Meier method and compared using the log-rank Chi square test. Different strata based on the presence of frailty and tertiles of total cholesterol and HDL-C and predefined categories of systolic and diastolic blood pressure were made. Determination of the factors independently associated with outcome was performed by use of a Cox's proportional-hazards survival analysis. This analysis was performed in the total population, in subjects with and without a history of cardiovascular disease and in frail and robust subjects. All individual risk factors were adjusted for age, gender and level of education. Furthermore, all individual cardiovascular risk factors with $p < 0.10$ were proposed for inclusion into a multivariable Cox's proportional-hazards survival model. In order to avoid multicollinearity, the correlation coefficients between all covariates were calculated. In case of multicollinearity (r-value >0.80), only one of the two covariables was considered in the multivariable model. The data analysis was performed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

In total 566 patients (99.8%) were included for the present study. A history of cardiovascular disease was present in 280 subjects (49.5%): a history of minor cardiovascular disease was present in 191 subjects (68.2%) and a history of major cardiovascular disease was present in 198 subjects (70.7%). At least one of the three frailty models was assessed in 559 patients: 123 subjects (22.0%) were frail according to the GFI, 112 (20.6%) were frail according to the Puts model and 39 (7.3%) were frail according to the Fried criteria. In total 361 patients (66.7%) were robust, and 180 patients (33.3%) were frail according to one of the three models.

Table 1 gives an overview of the characteristics of the study population according to the presence of frailty. Frail subjects were more likely to be older, more likely to be female, and were less likely to be higher educated. A history of either minor or major cardiovascular

disease was more often seen in the frail subjects. There was no significant difference between both groups regarding the presence of traditional cardiovascular risk factors. Frail persons had a lower eGFR compared to robust persons. The prescription of antihypertensive medication or cholesterol lowering medication was not significantly different between frail and robust persons.

In Table 2 the association between traditional cardiovascular risk factors and all-cause and cardiovascular mortality was investigated in the total population and in patients in primary and secondary prevention separately. In general, no classic cardiovascular risk factor was able to predict mortality neither in the total population nor in patients in primary or secondary prevention. Only in the total population the level of HDL-C showed an inverse association with all-cause mortality (adjusted HR 0.89 95%CI (0.81-0.98)). A trend towards an inverse association with all-cause mortality was also observed for BMI and systolic blood pressure in patients in primary prevention and between HDL-C and cardiovascular mortality in the total population.

In Figure 1 the Kaplan-Meier curves show the survival of patients according to their measured blood pressure and level of cholesterol in combination with the presence of frailty. The presence of frailty was able to identify patients at high risk for all-cause and cardiovascular mortality (adjusted HR 2.5 95%CI (1.9 - 3.2) and adjusted HR 2.2 95%CI (1.4 - 3.4), respectively). However, within robust or frail patients different categories of blood pressure and different tertiles of cholesterol were not able to further identify patients at risk for mortality (all log-rank tests, $p>0.05$).

Table 3 shows the association of traditional cardiovascular risk factors and mortality according to the presence of frailty. In robust patients, HDL-C showed a protective effect for all-cause mortality, whereas the presence of hypertension, diabetes and cardiovascular disease increased the risk. The multivariable model only retained the history of cardiovascular disease

as a risk factor for all-cause mortality (adjusted HR 1.4 95%CI (1.1 - 1.9). Furthermore, a history of cardiovascular disease increased the risk for cardiovascular mortality in robust persons. In frail individuals, no association with any of the traditional risk factors was found.

DISCUSSION

In this large, representative cohort of very old subjects aged 80 years and older, traditional cardiovascular risk factors did not show an association with all-cause or cardiovascular mortality. This pattern was seen both in subjects in primary prevention and subjects in secondary prevention. The presence of frailty, on the other hand, was able to identify patients at high risk for mortality. However, within strata of robust and frail subjects, traditional cardiovascular risk factors were not able to further identify patients at risk of mortality. Only a history of cardiovascular disease showed a strong association with mortality in robust subjects.

The current study showed that classic cardiovascular risk factors are not able to predict mortality in the oldest old. In the Leiden 85 Plus study, de Ruijter et al. (14) showed that classic risk factors included in the Framingham risk score were not able to identify patients at risk for cardiovascular mortality. This study was performed on a subpopulation of patients without a history of cardiovascular disease. Furthermore, in subjects with a history of cardiovascular disease in the same Leiden 85 Plus cohort, van Peet et al. (15) showed that traditional risk markers had little predictive value for recurrent cardiovascular events and cardiovascular mortality. Moreover, van Peet et al. showed that the history of cardiovascular disease is of important prognostic value in the oldest old (16). The current study found this association only in robust subjects.

The current study confirmed the importance of frailty to identify patients at risk for mortality. However, the current study was not able to support the hypothesis that frailty could be used to identify patients that might benefit more from cardiovascular risk management.

This is in contrast with findings from the NHANES study where walking speed was used as a simple measure, and proxy for frailty, to identify elderly adults that were most at risk for adverse outcomes related to high blood pressure (8). On the other hand, an extension of the HYVET trial did not show a difference in effect of treatment between robust and frail individuals (17).

Although traditional cardiovascular risk factors lose their predictive value in the oldest old, new biomarkers, such as homocysteine and NT-proBNP, might be used instead to identify subjects at risk (14-15). This is still relevant because, as stated before, cardiovascular risk management is a priority in this age group, given the high burden of cardiovascular disease and high risk for cardiovascular morbidity and mortality. Therefore, the search for new strategies to identify patients at risk and to identify patients that will benefit most from interventions in this heterogeneous group will be high on the research agenda in the following years.

The current study has several strengths. The BELFRAIL study is a large prospective cohort study representative of the general Belgian population aged 80 and older. To our knowledge, this study was the first to investigate the predictive value of traditional cardiovascular risk factors in robust and frail subjects, where frailty was operationalized based on three different validated models for frailty. However a few limitations should be noted. First, this was an observational study of a real world population, which means that possible changes in medication intake after baseline might be underlying the observed associations. Second, the comorbidities may have been underdiagnosed because they were reported by the general practitioner rather than being assessed.

CONCLUSION

In a large representative sample of very old subjects, traditional cardiovascular risk factors were not able to predict mortality, in either primary or secondary prevention. Frailty

showed to be a strong risk factor for mortality in this age group. However, frailty could not be used to identify further subjects who might benefit more from cardiovascular risk management. Only a history of cardiovascular disease was predictive for mortality in robust people. Possibly, risk scores that include other risk factors, such as new biomarkers like homocysteine or NT-proBNP, are more suited to identify patients at risk in this age segment.

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Table 1. Characteristics of BELFRAIL participants, stratified by presence of frailty

	Robust (n = 361)	Frail (n = 180)	*P* value
Age, mean (SD), y	84 ± 3.4	86 ± 3.9	<0.001
Male, %	155 (43)	47 (26)	<0.001
<High school education, %	120 (33)	80 (45)	0.009
Current/prior smoking, %	116 (32)	53 (30)	0.54
BMI, mean (SD), kg/m^2	28 ± 4.2	27 ± 6.0	0.60
Total cholesterol, mean (SD), mg/dL	200 ± 45	203 ± 44	0.53
HDL-C, mean (SD), mg/dL	56 ± 15	54 ± 16	0.26
LDL-C, mean (SD), mg/dL	123 ± 37	123 ± 36	0.91
eGFR, mean (SD), $mL/min/1.73m^2$	65 ± 21	60 ± 24	0.018
History of hypertension, %	254 (71)	127 (71)	0.93
History of diabetes, %	66 (18)	35 (20)	0.73
Cardiovascular disease, %	167 (46)	101 (56)	0.026
Minor cardiovascular disease, %	107 (30)	74 (41)	0.007
Angina pectoris, %	52 (15)	37 (21)	0.069
TIA, %	31 (8.8)	24 (14)	0.085
Peripheral arterial disease, %	28 (7.8)	21 (12)	0.13
History of decompensated HF, %	34 (9.5)	24 (13)	0.17
Major cardiovascular disease, %	117 (32)	71 (40)	0.096
Myocardial infarction*, %	78 (22)	40 (22)	0.87
Stroke, %	23 (6.5)	23 (13)	0.013
PTCA or stent, %	32 (8.9)	14 (7.9)	0.70
Coronary surgery, %	27 (7.5)	8 (4.5)	0.18
Arterial surgery, %	15 (4.2)	12 (6.8)	0.20
Antihypertensive medication use, %	285 (79)	152 (85)	0.11
Cholesterol lowering medication use, %	121 (34)	50 (28)	0.18
Systolic BP, mean (SD), mmHg	142 ± 20	140 ± 21	0.25
Diastolic BP, mean (SD), mmHg	75 ± 9.5	75 ± 9.2	0.66

Abbreviations: SD, standard deviation; BMI, body mass index; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein

cholesterol; eGFR, estimated glomerular filtration rate (MDRD formula); TIA, transient ischaemic attack; HF, heart failure; PTCA, percutaneous transluminal coronary angioplasty; BP, blood pressure.
*, according to the GP or positive ECG (Minnesota Code 1-1 or 1-2 (excluding 1-2-8)).

Table 2. The association of classic cardiovascular risk factors and mortality in the total population and stratified by the presence of cardiovascular morbidity

	Total population (n = 566)		No cardiovascular disease (n = 286)		Cardiovascular disease (n = 280)	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
All-cause mortality						
Current/prior smoking	1.3 (0.94 - 1.8)	0.12	1.3 (0.76 - 2.2)	0.34	1.3 (0.84 - 1.9)	0.26
BMI, per kg/m^2	0.99 (0.96 - 1.0)	0.45	0.96 (0.92 - 1.004)	0.076	1.01 (0.97 - 1.05)	0.57
Total cholesterol, per 10mg/dL	0.99 (0.96 - 1.02)	0.48	0.999 (0.95 - 1.05)	0.95	1.001 (0.96 - 1.04)	0.96
HDL-C, per 10mg/dL	0.89 (0.81 - 0.98)	0.020	0.94 (0.82 - 1.08)	0.37	0.90 (0.79 - 1.04)	0.14
LDL-C, per 10mg/dL	1.0 (0.96 - 1.03)	0.77	0.996 (0.94 - 1.06)	0.90	1.02 (0.97 - 1.06)	0.54
History of hypertension	1.2 (0.91 - 1.6)	0.18	1.0 (0.66 - 1.7)	0.85	1.2 (0.80 - 1.7)	0.41
History of diabetes	1.1 (0.84 - 1.6)	0.40	1.2 (0.70 - 2.0)	0.54	1.1 (0.75 - 1.7)	0.59
Systolic BP, per 10mmHg higher	0.97 (0.91 - 1.03)	0.34	0.90 (0.81 - 1.01)	0.062	1.01 (0.93 - 1.1)	0.78
Diastolic BP, per 10mmHg higher	0.96 (0.84 - 1.1)	0.57	1.05 (0.85 - 1.3)	0.68	0.91 (0.77 - 1.08)	0.30
Cardiovascular mortality						
Current/prior smoking	1.2 (0.72 - 2.0)	0.47	0.61 (0.22 - 1.7)	0.34	1.5 (0.79 - 2.7)	0.23
BMI, per kg/m^2	1.0 (0.96 - 1.05)	0.90	0.99 (0.93 - 1.06)	0.71	1.01 (0.96 - 1.07)	0.69
Total cholesterol, per 10mg/dL	0.99 (0.94 - 1.03)	0.57	0.995 (0.92 - 1.07)	0.91	1.01 (0.95 - 1.07)	0.84
HDL-C, per 10mg/dL	0.87 (0.76 - 1.01)	0.067	0.96 (0.77 - 1.2)	0.70	0.87 (0.70 - 1.07)	0.17
LDL-C, per 10mg/dL	0.99 (0.94 - 1.05)	0.73	0.97 (0.89 - 1.07)	0.55	1.03 (0.96 - 1.1)	0.45
History of hypertension	1.2 (0.77 - 1.8)	0.45	0.81 (0.40 - 1.6)	0.54	1.3 (0.74 - 2.4)	0.35
History of diabetes	1.3 (0.81 - 2.1)	0.27	1.2 (0.52 - 2.7)	0.71	1.3 (0.75 - 2.4)	0.32
Systolic BP, per 10mmHg higher	0.96 (0.87 - 1.06)	0.44	0.92 (0.78 - 1.08)	0.31	1.003 (0.88 - 1.1)	0.96
Diastolic BP, per 10mmHg higher	0.95 (0.77 - 1.2)	0.59	1.1 (0.81 - 1.6)	0.47	0.87 (0.67 - 1.1)	0.26

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; BP, blood pressure.
All HR were adjusted for gender, age and level of education.

Table 3. The association of classic cardiovascular risk factors and mortality stratified by the presence of frailty

	Robust (n = 361)		Frail* (n = 180)	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
All-cause mortality				
Current/prior smoking	1.3 (0.77 - 2.1)	0.35	1.2 (0.75 - 1.8)	0.50
BMI, per kg/m^2	1.01 (0.96 - 1.05)	0.82	0.98 (0.94 - 1.01)	0.22
Total cholesterol, per 10mg/dL	0.98 (0.94 - 1.02)	0.38	0.99 (0.94 - 1.03)	0.55
HDL-C, per 10mg/dL	0.85 (0.74 - 0.99)	0.030	0.95 (0.84 - 1.08)	0.46
LDL-C, per 10mg/dL	0.98 (0.93 - 1.04)	0.52	1.0 (0.95 - 1.05)	0.94
History of hypertension	1.6 (1.01 - 2.4)	0.047	1.2 (0.78 - 1.9)	0.39
History of diabetes	1.5 (0.97 - 2.3)	0.069	0.75 (0.44 - 1.3)	0.31
Systolic BP, per 10mmHg higher	1.0 (0.91 - 1.1)	0.99	0.96 (0.88 - 1.1)	0.44
Diastolic BP, per 10mmHg higher	1.05 (0.87 - 1.3)	0.60	0.89 (0.73 - 1.1)	0.27
Cardiovascular disease	1.7 (1.1 - 2.5)	0.011	1.07 (0.72 - 1.6)	0.74
Cardiovascular mortality				
Current/prior smoking	1.4 (0.62 - 3.0)	0.44	0.90 (0.45 - 1.8)	0.78
BMI, per kg/m²	0.98 (0.92 - 1.05)	0.60	1.0 (0.95 - 1.06)	0.94
Total cholesterol, per 10mg/dL	1.0 (0.94 - 1.07)	0.98	0.96 (0.89 - 1.03)	0.24
HDL-C, per 10mg/dL	0.86 (0.70 - 1.07)	0.17	0.90 (0.73 - 1.1)	0.30
LDL-C, per 10mg/dL	1.01 (0.93 - 1.09)	0.87	0.96 (0.88 - 1.05)	0.39
History of hypertension	1.6 (0.82 - 3.2)	0.16	0.97 (0.51 - 1.8)	0.91
History of diabetes	1.5 (0.79 - 2.8)	0.21	0.93 (0.41 - 2.1)	0.87
Systolic BP, per 10mmHg higher	0.96 (0.83 - 1.1)	0.61	0.99 (0.86 - 1.1)	0.88
Diastolic BP, per 10mmHg higher	1.1 (0.82 - 1.5)	0.49	0.89 (0.65 - 1.2)	0.47
Cardiovascular disease	2.2 (1.2 - 3.9)	0.010	1.3 (0.71 - 2.5)	0.38

Abbreviations: HR, hazard ratio; CI, confidence interval; BMI, body mass index; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; BP, blood pressure.

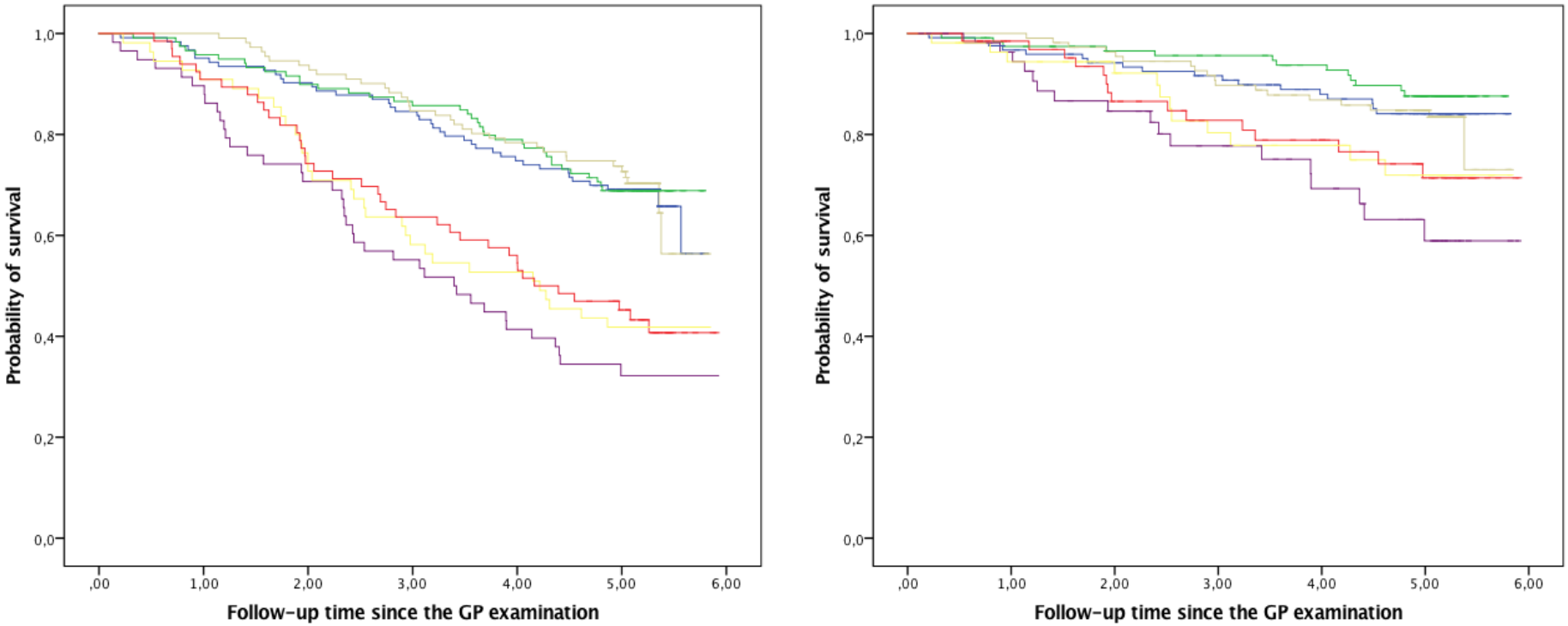
All HR were adjusted for gender, age and level of education.

*, frail according to the Fried criteria OR the Puts model OR the Groningen Frailty Indicator.

Figure 1.

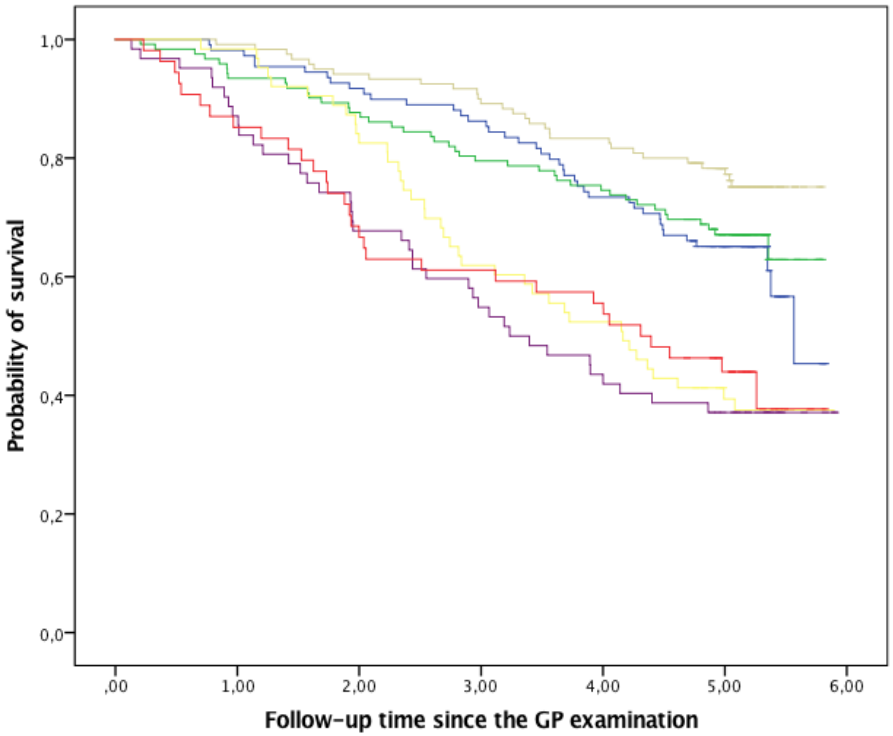
All-cause mortality	Cardiovascular mortality

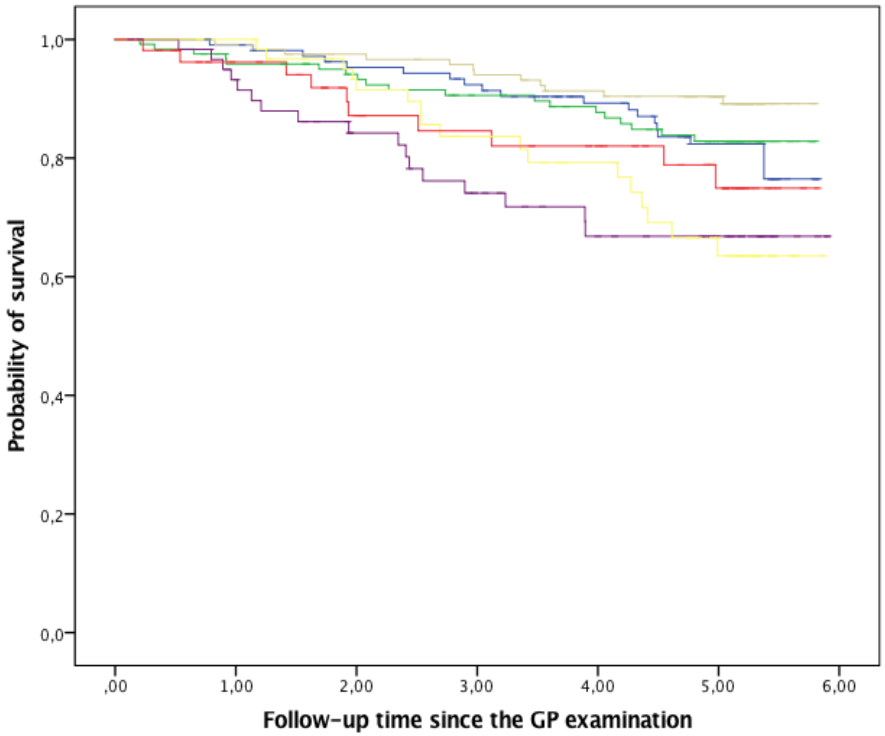
Total cholesterol



Robust and lowest tertile of total cholesterol (<179mg/dL)
Robust and middle tertile of total cholesterol (179 - 218mg/dL)
Robust and highest tertile of total cholesterol (>218mg/dL)
Frail and lowest tertile of total cholesterol (<179mg/dL)
Frail and middle tertile of total cholesterol (179 - 218mg/dL)
Frail and highest tertile of total cholesterol (>218mg/dL)

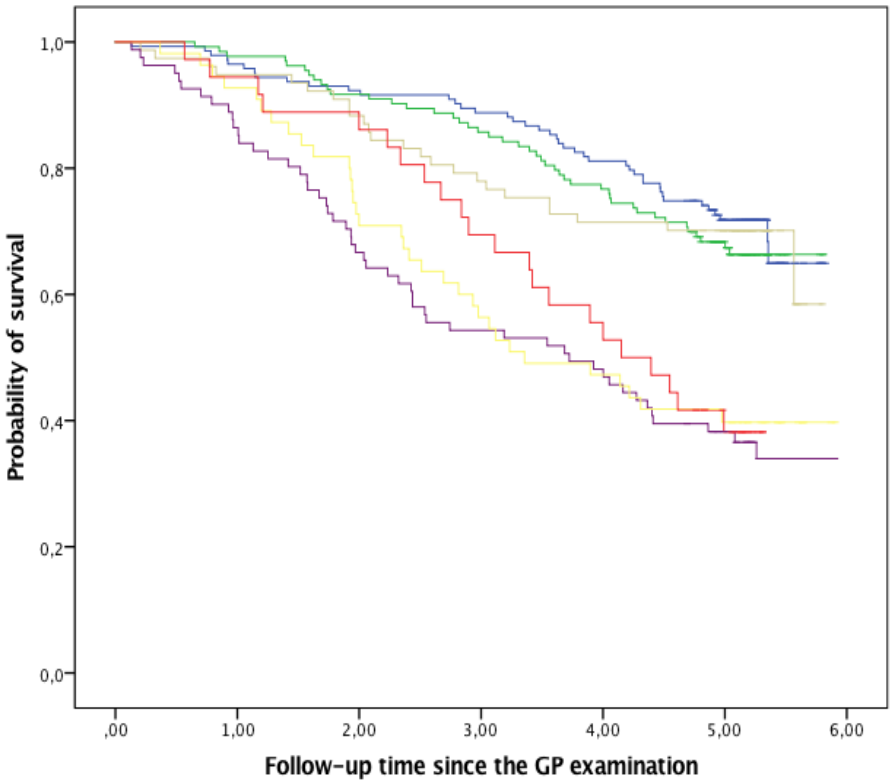
HDL cholesterol

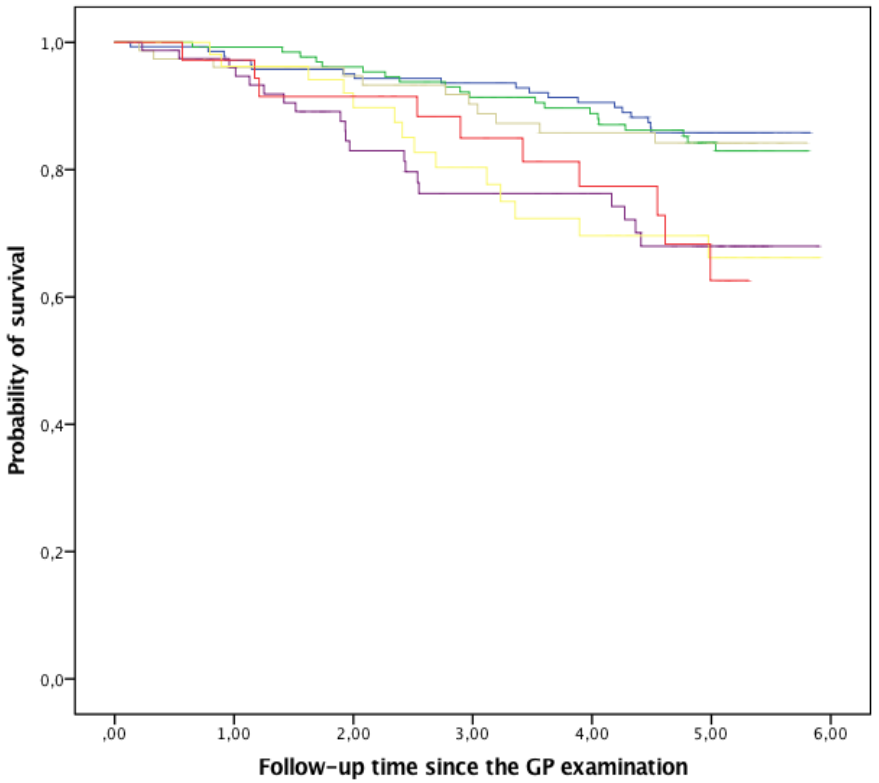




Robust and lowest tertile of HDL-C (<48mg/dL)
Robust and middle tertile of HDL-C (48 - 60mg/dL)
Robust and highest tertile of HDL-C (>60mg/dL)
Frail and lowest tertile of HDL-C (<48mg/dL)
Frail and middle tertile of HDL-C (48 - 60mg/dL)
Frail and highest tertile of HDL-C (>60mg/dL)

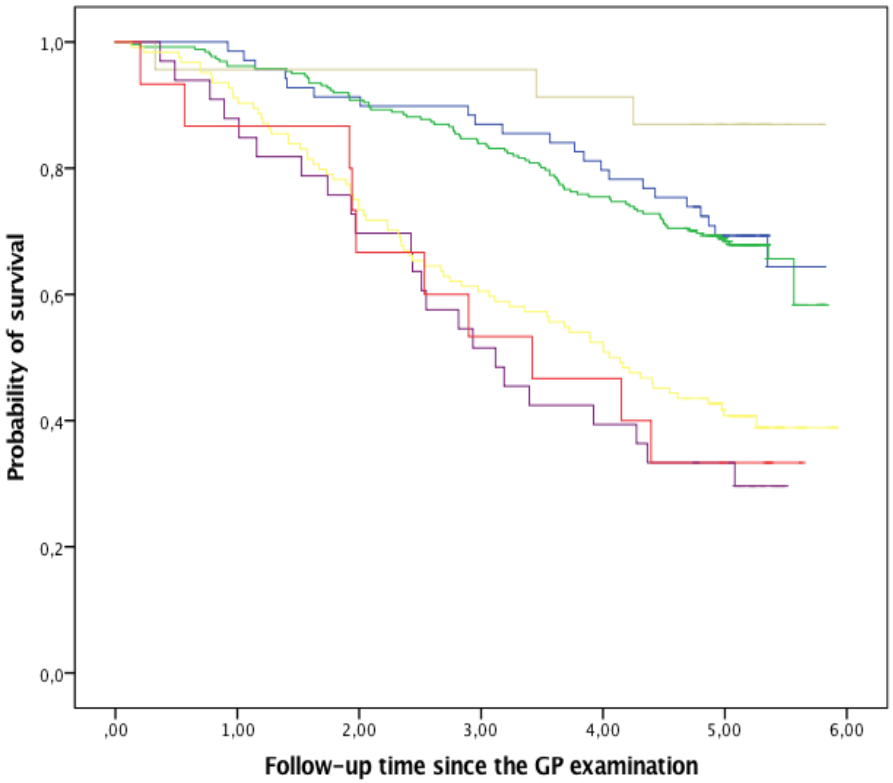
Systolic blood pressure

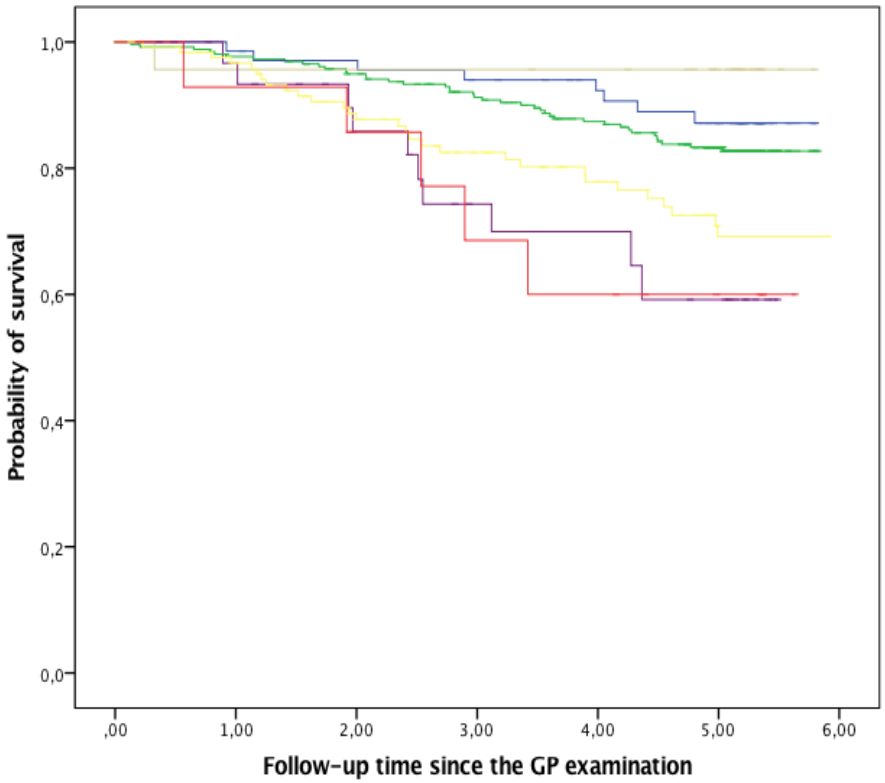




Robust and systolic BP <140mmHg
Robust and systolic BP 140-160mmHg
Robust and systolic BP ≥160mmHg
Frail and systolic BP <140mmHg
Frail and systolic BP 140-160mmHg
Frail and systolic BP ≥160mmHg

Diastolic blood pressure





Robust and diastolic BP <70mmHg
Robust and diastolic BP 70-90mmHg
Robust and diastolic BP ≥90mmHg
Frail and diastolic BP <70mmHg
Frail and diastolic BP 70-90mmHg
Frail and diastolic BP ≥90mmHg

APPENDIX

Supervisory Committee on Medical ethics approval

Aan: Bert Vaes;

CC: David Depoortere;

English version below

Geachte Heer/Mevrouw

De Opleidingspecifieke Ethische Begeleidingscommissie van de opleiding "Master in de huisartsgeneeskunde (Leuven e.a.)" heeft uw voorstel tot Masterproef "Een geïndividualiseerd bloeddrukbeleid gebaseerd op frailty in de oudste ouderen" onderzocht en gunstig geadviseerd. Dit betekent dat de commissie van oordeel is dat de studie, zoals beschreven in het protocol, wetenschappelijk relevant en ethisch verantwoord is. Dit gunstig advies van de commissie houdt niet in dat zij de verantwoordelijkheid voor de geplande studie op zich neemt. U blijft hiervoor zelf verantwoordelijk. Indien u van plan bent uw masterproef te publiceren kan deze e-mail dienen als bewijs van goedkeuring.

Dear Mr/Ms

The Supervisory Committee on Medical ethics of the "Master in de huisartsgeneeskunde (Leuven e.a.)" programme has reviewed your master's thesis project proposal "Een geïndividualiseerd bloeddrukbeleid gebaseerd op frailty in de oudste ouderen" and advises in its favour. This means that the committee has acknowledged that your project, as described in the protocol, is scientifically relevant and in line with prevailing ethical standards. This favourable advice does not entail the committee's responsibility for the planned project, however. You remain solely responsible. If you intend to publish your master's thesis, this e-mail may be used as proof of the committee's consent.

Met vriendelijke groeten

Opleidingsspecifieke begeleidingscommissie van de opleiding Master in de huisartsgeneeskunde (Leuven e.a.)

Protocol

mp05280	Een geïndividualiseerd bloeddrukbeleid gebaseerd op frailty in de oudste ouderen

Student(en):
David Depoortere (david.depoortere@student.kuleuven.be)
Promotor:
Bert Vaes (Bert.Vaes@med.kuleuven.be - u0087897 - Acad. Centr. voor Huisartsgeneeskunde)
Hoofdonderzoeker:

Faculteit:
Geneeskunde
Opleiding:
Master in de huisartsgeneeskunde (Leuven e.a.)
Het onderzoek is:
monocentrisch
De opdrachtgever is:
academisch (universiteit,...)

Het onderzoek is:
Literatuurstudie.

Bijkomende gegevens:

Achtergrond:

Een geïndividualiseerd bloeddrukbeleid gebaseerd op frailty in de oudste ouderen

Patienten stratifiëren volgens frailty om optimale bloeddrukcontrole te bekomen

Tot dusver kunnen we uit de literatuur de volgende zaken weerhouden:

1. Dat de huidige richtlijnen betreffende antihypertensieve therapie bij ouderen niet kunnen geëxtrapoleerd worden naar de categorie van de oudste ouderen (80+): zij vertonen een dusdanig complex beeld van multipele comorbiditeiten, gewijzigde psychosociale en biologische status (het concept van immunosenescentie), dat een geïndividualiseerd beleid bij deze patiënten meer dan noodzakelijk blijkt.

2. Dat in deze groep van oudste ouderen, hogere bloeddrukwaarden een protectief effect lijken te hebben naar mortaliteit en cognitieve achteruitgang, en niet (of minder) gepaard gaan met de schadelijke effecten zoals men die bij jongere personen kan aantonen (zoals het effect op nierfunctie); en dat lagere bloeddrukwaarden (vooral diastolisch) eerder gepaard gaan met een verhoogde mortaliteit en cognitieve achteruitgang. De studies hieromtrent variëren echter sterk in hun resultaten.

3. Dat het concept van 'frailty' als indicator van kwetsbaarheid in de oudere patiënt een belangrijke impact heeft op de relatie tussen leeftijd en mortaliteit/cognitieve functie; het besef groeit dat biologische leeftijd, veel meer dan chronologische leeftijd, de weerstand van een individu tegen fysieke en cognitieve achteruitgang bepaalt.

4. Dat, in deze groep van oudste ouderen, de associatie tussen bloeddruk enerzijds en fysieke en cognitieve achteruitgang anderzijds duidelijk beïnvloed wordt door de aan- of afwezigheid van frailty.

De relatie tussen bloeddruk en frailty is complex. Aan de ene kant is het duidelijk dat ongecontroleerde hoge bloeddruk op jongere leeftijd een belangrijke risicofactor is voor frailty op latere leeftijd, o.a. door het in de hand werken van cardiovasculaire comorbiditeiten. Aan de andere kant zien we wel dat het mogelijks protectief effect van een hoge bloeddruk op hogere leeftijd (80+) sterk afhankelijk is van de kwetsbaarheid (frailty) van het individu.

Frailty is echter een vaag concept, en verschillende studies gebruiken verschillende methodes om dit te definiëren. Tot dusver zijn er geen eenvoudige tools ter beschikking om een aanpassing van het antihypertensieve beleid bij de oudste ouderen aan te passen volgens de frailty van het individu.

Vraagstelling:

We proberen na te gaan welke indicatoren/predictoren gerelateerd aan frailty (klinisch, psychosociaal, biochemisch…) het meest relevant zijn voor het sturen van dit geïndividualiseerd bloeddrukbeleid bij de oudste ouderen; m.a.w.: Welke factoren kunnen ons helpen in het bepalen of deze 80-plusser nood heeft aan een strikte bloeddrukcontrole (zoals we die toepassen bij de 'jongere' ouderen) dan wel meer baat heeft bij hogere bloeddrukwaarden, teneinde de achteruitgang van de cognitieve functies tegen te gaan?

Methodologie:

Het opzet van deze studie is een cross-sectionele gegevensanalyse gebruik makend van de BELFRAIL-database, een prospectieve, observationele, populatie-gebaseerde cohort studie van patiënten van 80 jaar en ouder in België. Deze database was opgesteld met onder andere bedoeling een beter inzicht te verkrijgen in de relatie tussen gezondheid, frailty en disability, en bevat zowel medische achtergrond, klinische gegevens psychosociaal functioneren als lichamelijk functioneren, en biedt ons zo een unieke tool om de dynamische interacties tussen deze factoren te bestuderen. A

Referenties:

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