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STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria

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Abstract

Introduction: STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) is a new, systems-defined medicine review tool. We compared the performance of STOPP to that of established Beers' criteria in detecting potentially inappropriate medicines (PIMs) and related adverse drug events (ADEs) in older patients presenting for hospital admission.
Methods: we prospectively studied 715 consecutive acute admissions to a university teaching hospital. Diagnoses, reason for admission and concurrent medications were recorded. STOPP and Beers' criteria were applied. PIMs with clear causal connection or contribution to the principal reason for admission were determined.
Results: median patient age (interquartile range) was 77 (72–82) years. Median number of prescription medicines was 6 (range 0–21). STOPP identified 336 PIMs affecting 247 patients (35%), of whom one-third ($n = 82$) presented with an associated ADE. Beers' criteria identified 226 PIMs affecting 177 patients (25%), of whom 43 presented with an associated ADE. STOPP-related PIMs contributed to 11.5% of all admissions. Beers' criteria-related PIMs contributed to significantly fewer admissions (6%).
Conclusion: STOPP criteria identified a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events than Beers' criteria. This finding has significant implications for hospital geriatric practice.

Keywords: *inappropriate prescribing, elderly, STOPP, screening tool*

Introduction

Older people often experience multiple co-morbidities and are prescribed multiple medications thereby increasing the risk of adverse drug events (ADEs), drug–drug and drug–disease interactions [1, 2]. This risk is heightened by age-related physiological changes, which influence pharmacokinetics and pharmacodynamics [3]. Particular drugs pose special risks to older people as a result of these changes, e.g. prolonged sedation and increased risk of falls with long-acting benzodiazepines [4] or increased risk of upper gastrointestinal bleeding with non-steroidal anti-inflammatory drugs [5]. Prescription of such drugs is potentially inappropriate, particularly where safer alternatives exist.

Various criteria have been devised to identify potentially inappropriate medicines (PIMs) in older people [6–10], the most frequently cited being Beers' criteria [6]. Though often used to detect PIMs in large-scale epidemiological studies, some of Beers' criteria are controversial [11]. There is disagreement over the designation of certain drugs as inappropriate, e.g. amitriptyline [12] and nitrofurantoin [13], and almost half of the PIMs in Beers' criteria are unavailable in European formularies [14]. Furthermore, few studies report a tangible benefit to patients in terms of clinical outcome from using Beers' criteria [15]. Therefore, the general clinical relevance and applicability of these criteria is uncertain. Nonetheless, quality and safety of prescribing in older people remains a global healthcare concern and further endeavours to improve appropriateness in medication selection for older people are warranted.

We have devised a new screening tool of older patients' medicines called STOPP (Screening Tool of Older People's potentially inappropriate Prescriptions). Validation of STOPP is described in detail elsewhere [16]. Briefly, 18 experts in geriatric pharmacotherapy with recognized credentials in their specialist areas were recruited to establish the

content validity of STOPP by a Delphi consensus method [17]. The panel comprised nine physicians in geriatric medicine, three clinical pharmacologists, three senior hospital pharmacists with an interest in geriatric pharmacotherapy, two senior academic primary care physicians and one psychiatrist of old age. Sixty-eight potentially inappropriate prescribing practices in older people were presented to the panel, supported by relevant references. Panellists were asked to rate their level of agreement with each statement and to suggest any additional inappropriate prescribing practices. Sixty-five of 68 criteria were included in STOPP following two rounds of the Delphi process, with strong consensus. STOPP incorporates commonly encountered instances of potentially inappropriate prescribing in older people including drug–drug and drug–disease interactions, drugs which adversely affect older patients at risk of falls and duplicate drug class prescriptions (Appendix 1, available at *Age and Ageing* online). STOPP criteria are arranged according to relevant physiological systems for ease of use, as is the case in most drug formularies. Each criterion is accompanied by a concise explanation as to why the prescription is potentially inappropriate. Inter-rater reliability of STOPP criteria is good with a kappa co-efficient of 0.75 [16].

The objective of the present study was to prospectively evaluate the performance of STOPP and Beers' criteria (Appendix 2, available at *Age and Ageing* online) in terms of identifying PIMs with a clear causal connection to, or which are recognised major risk factors for, the main presenting problem in consecutive, non-selected, acutely ill, older patients requiring admission to a university teaching hospital.

Methods

Study population

We prospectively studied 715 consecutive older patients admitted with acute illness to a university teaching hospital over a 4-month period in 2007. All patients were aged 65 years and over and were admitted via the Emergency Department following referral by their general practitioner (GP) or self-referral. All were admitted under the care of the general medical or surgical services as required, similar to the admission policies of the National Health Service in the United Kingdom. The local Clinical Research Ethics Committee approved the study protocol.

Data collection

Standard demographic details, principal clinical reason for admission, medical co-morbidities, concurrent medications, serum biochemistry and electrocardiograph results were abstracted from each patient's admission document and cross-referenced with the GP referral letter, except in those who had self-referred to hospital. Supplementary information was obtained from the patient, GP, community pharmacist and hospital record when necessary, e.g. precise dose and duration of therapy, analgesic history, baseline renal function and blood pressure profile. Recorded medications were those that were prescribed before hospital physician intervention. Non-prescription medications were excluded, as the study focussed on the relationship between adverse prescribing practices and acute illness requiring hospital admission.

Trained geriatric clinical judgement (P.G., D.O'M.) was used to identify adverse effects of medications that were clearly causal or contributory to the principal reason for admission. Such associations had to have previous bibliographic descriptions and were not included if aetiological alternatives were evident. Every effort was made to establish whether or not there was a clear temporal relationship between prescription of the drug and onset of presenting symptoms. STOPP and Beers' criteria were used to identify PIMs on admission. The proportion of PIMs with clear causal connection or contribution to the principal reason for admission was calculated for each tool. Statistical analysis was performed using SPSS for Microsoft version 14. Descriptive statistics included median and interquartile range for non-parametric variables. Tests of association were performed using the chi-square statistic. The Mann–Whitney U and Kruskal–Wallis tests were used to determine independence of two or more non-parametric variables, respectively. Multivariate logistic regression was used to examine the influence of gender, age and number of medications on PIM-related admissions. A probability value of <0.05 was considered statistically significant.

Results

Data were prospectively collected from 715 consecutive patients, of which 386 (54%) were females (Table 1). The median age (interquartile range) was 77 (72–82) years, the overall range being 65–94 years. The most common presenting conditions included falls with resultant injury such as fracture (27%), ischaemic heart disease (12%), respiratory tract infection (10%), stroke/transient ischaemic attack (7%), cardiac failure (6%) and delirium (5%). The most prevalent co-morbidities included hypertension (40%), ischaemic heart disease (29%), atrial fibrillation (18%), stroke (16%), diabetes mellitus (16%), dementia (10%) and depression (8%).

A total of 4,403 medications were prescribed in this cohort with a median of 6 and a range of 0–21 medications (Table 1). Forty-eight per cent ($n = 341$) of patients were prescribed ≤ 5 medications and 41% ($n = 293$) were prescribed between 6 and 10 medications. High-level polypharmacy, i.e. > 10 medications, was identified in 11% ($n = 81$) of patients. There was no significant difference between numbers of medications prescribed in males and females ($P = 0.515$) or across the three age categories ($P = 0.733$).

Potentially inappropriate medicines

Three hundred and thirty-six medicines were potentially inappropriate according to STOPP criteria (Table 2). These were distributed amongst 35% ($n = 247$) of the study population with 180 patients (25%) receiving one PIM, 49 (7%) receiving two PIMs, 14 (2%) receiving three PIMs, 3 receiving four

Table 1. Characteristics of the study population ($n = 715$)

	Male	Female	Total
Number of patients	329 (46%)	386 (54%)	715
Age distribution (years)			
Median age (IQR)	75 (70–81)	78 (73–83)	77 (72–82)
65–74	142 (43%)	127 (33%)	269 (37%)
75–84	143 (44%)	184 (48%)	327 (46%)
85–94	44 (13%)	75 (19%)	119 (17%)
Morbidities			
Hypertension	133 (40%)	156 (40%)	289 (40%)
IHD	113 (34%)	93 (24%)	206 (29%)
CCF	33 (10%)	33 (9%)	66 (9%)
Atrial fibrillation	60 (18%)	67 (17%)	127 (18%)
Stroke/TIA	56 (17%)	60 (16%)	116 (16%)
Dementia	31 (9%)	44 (11%)	75 (10%)
Depression	23 (7%)	35 (9%)	58 (8%)
Single fall	67 (20%)	115 (30%)	182 (25%)
Recurrent falls	18 (5%)	33 (9%)	51 (7%)
Osteoporosis	9 (3%)	54 (14%)	63 (9%)
COPD	36 (11%)	34 (9%)	70 (10%)
Diabetes mellitus	57 (17%)	58 (15%)	115 (16%)
PUD	40 (12%)	28 (7%)	68 (10%)
Prescribed medications			
Patients prescribed regular medication	306 (93%)	365 (95%)	671 (94%)
Median number of medications (IQR)	6 (4–9)	6 (3–9)	6 (4–9)
Number of patients prescribed cardiovascular medications	236 (72%)	220 (57%)	456 (64%)
Number of patients prescribed psychoactive medications	112 (34%)	150 (39%)	212 (36%)

IQR, interquartile range; IHD, ischaemic heart disease; CCF, congestive cardiac failure; TIA, transient ischaemic attack; COPD, chronic obstructive pulmonary disease; PUD, peptic ulcer disease.

PIMs and 1 patient receiving five PIMs concurrently. The most common PIMs identified by STOPP included (i) psychoactive medications such as long-acting benzodiazepines, tricyclic antidepressants (TCAs) with clear-cut contraindications and first-generation antihistamines; (ii) medications that increase the probability of falls in those already prone to falls, e.g. benzodiazepines, neuroleptics and vasodilator drugs known to cause hypotension in patients with persistent postural hypotension; (iii) inappropriate use of NSAIDs and opiates and (iv) duplicate drug class prescriptions including two ACE inhibitors, two NSAIDs, two selective serotonin re-uptake inhibitors (SSRIs) or dual antiplatelet therapy without indication. Beers' criteria identified 226 PIMs (Table 3) distributed amongst 177 patients (25%) with 135 patients (19%) receiving 1 PIM, 26 patients (5%) receiving 2 PIMs, 5 patients receiving 3 PIMs and 1 patient receiving 4 PIMs concurrently. There was a significant difference in the numbers of PIMs detected by STOPP (35%) and by Beers' criteria (25%) despite the latter containing more criteria for potentially inappropriate prescribing than STOPP (Mann–Whitney $Z = -8.28$; $P < 0.001$).

Adverse effects of prescribed medications

An adverse effect of a prescribed medication was identified as clearly causal or contributory to the principal reason for admission in 90 patients (12.5%) independent of STOPP and Beers' criteria. Eighty-two of these 90 patients (91%) were prescribed a STOPP criteria PIM that was causal or contributory to admission, e.g. overt digoxin toxicity with high-dose digoxin and renal impairment, upper gastrointestinal bleeding with inappropriate NSAID use and falls with inappropriate psychotropic use (Table 2). Forty-three of these 90 patients (48%) were prescribed a Beers' criteria PIM that was causal or contributory to admission (Table 3). STOPP identified a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events than Beers' criteria (Mann–Whitney $Z = -15.33$; $P<0.001$). Neither STOPP nor Beers' criteria identified any false positive ADE-related acute admissions in this study. Therefore, the specificity of STOPP and Beers' criteria in detecting potential ADE-related admissions was equal. ADE-related admissions not identified by STOPP criteria included first presentations of SSRI-induced hyponatraemia ($n = 2$), thiazide-induced hyponatraemia ($n = 1$) and excessive anticoagulation secondary to warfarin ($n = 5$).

Multivariate regression analysis accounting for age, gender and numbers of medications showed that females were more likely to be admitted with a PIM-related adverse event than males (STOPP criteria odds ratio 1.87 (95% CI 1.14–3.07); $P = 0.014$; Beers criteria OR 2.53; 95% CI 1.24–5.15; $P = 0.01$). Patients prescribed five or fewer medications were less likely to present to hospital with a PIM-related adverse event than those prescribed six or more medications [STOPP criteria OR 0.59 (95% CI 0.37–0.96); $P = 0.032$, Beers' criteria OR.44 (95% CI.22–.86) $P = 0.016$].

Discussion

STOPP identified significantly more PIMs than Beers' criteria [6] and almost twice as many PIMs with a causal or contributory relationship to hospital admission in this non-selected sample of 715 acutely ill older patients. This highlights the potential for STOPP to be used not only as a screening tool for PIMs but also as a method of identifying potential ADEs in older people, which often present with non-specific symptoms such as confusion, falls or constipation [19]. STOPP, though clearly not a substitute for clinical assessment and judgement, encourages clinicians to consider medications as a possible cause of such symptoms in older people thereby avoiding unnecessary and potentially harmful prescribing cascades, e.g. prescription of an anticholinergic to treat extrapyramidal effects of neuroleptic medication in an older patient with dementia and behavioural symptoms.

Concerns over the suitability of Beers' criteria for use outside of the United States are re-enforced by the present study [10, 12, 14]. Many of the proscribed drugs in Beers' criteria are rarely used in Western Europe, e.g. trimethobenzamide,

Table 2. Potentially inappropriate prescriptions as determined by STOPP criteria

Criterion	*n*	Adverse effect of PIM as a causal or contributory factor to admission
Cardiovascular system		
Digoxin >125 μg per day with impaired renal function	4	1 (digoxin toxicity)
Thiazide diuretic with history of gout	1	0
β-blocker with COPD	12	3 (recurrent exacerbation of COPD)
Diltiazem or verapamil with NYHA class III or IV heart failure	1	1 (severe CCF)
Calcium channel blockers with chronic constipation	2	0
Dipyridamole as monotherapy for cardiovascular secondary prevention	1	0
Aspirin with history of PUD without histamine H2 antagonist or PPI	2	1 (PUD)
Aspirin ≥150 mg/day	1	0
Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event[a]	14	0
Central nervous system		
TCA with dementia	2	2 (delirium, fall and fractured femur)
TCA with cardiac conductive abnormalities	1	0
TCA with constipation	1	0
TCA with prostatism or history of urinary retention	1	0
Long-term, long-acting benzodiazepines	65	26 (fall 9; fall + fracture 8; fall + head injury 1; benzodiazepine overdose 1; cognitive decline 7)
Long-term neuroleptics in those with Parkinsonism	1	0
Prolonged use of first generation antihistamines	9	4 (fall + fracture 2; cognitive decline 2)
Gastrointestinal system		
Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause	2	0
Diphenoxylate, loperamide or codeine phosphate for severe infective gastroenteritis, i.e. bloody diarrhoea, high fever or severe systemic toxicity	2	0
PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks	29	0
Respiratory system		
Theophylline as monotherapy for COPD	4	0
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate–severe COPD	4	1 (exacerbation COPD + osteoporotic vertebral fracture)
Musculoskeletal system		
NSAID with history of PUD or gastrointestinal bleeding, unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol	3	1 (PUD)
NSAID with moderate to severe hypertension	20	3 (GI bleed 2; PUD 1)
NSAID with heart failure	1	0
Long-term NSAID for relief of mild-moderate joint pain in osteoarthritis	9	1 (PUD)
Warfarin and NSAID together	12	1 (GI bleed)
NSAID with chronic renal failure	9	1 (acute renal failure)
Long-term corticosteroid as monotherapy for rheumatoid or osteoarthritis	1	0
Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol	3	1 (GI bleed; also on warfarin–counted above)
Urogenital system		
Bladder antimuscarinic drugs with dementia	6	3 (delirium 2; fall and fractured femur 1)
Antimuscarinic drugs with chronic prostatism	1	0
Endocrine system		
β-blockers in those with diabetes mellitus and frequent hypoglycaemia	2	2 (falls 2, fracture 1)
Drugs that adversely affect those who are prone to falls		
Benzodiazepines	37	20 (recurrent falls 7, falls + fracture 13)
Neuroleptic drugs	6	3 (fracture femur 2, fracture radius 1)
Vasodilator drugs with postural hypotension	4	2 (orthostatic hypotension)
Long-term opiates in those with recurrent falls	1	1 (fall + fracture femur)
Analgesic drugs		
Use of long-term powerful opiates, e.g. morphine or fentanyl as first-line therapy for mild-moderate pain	13	3 (fall + fracture femur)
Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives	6	0
Long-term opiates in those with dementia unless indicated for palliative care or management of moderate/severe chronic pain syndrome	2	2 (delirium 1; fall + fracture femur 1)
Duplicate drug class prescriptions	43	
Total	336	82 (11.5% of all 715 admissions)

PIM, potentially inappropriate medicine; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; CCF, congestive cardiac failure; PUD, peptic ulcer disease; PPI, proton pump inhibitor; GI, gastrointestinal; TCA, tricyclic antidepressant; NSAID, non-steroidal anti-inflammatory drug.

[a]Prescriptions for aspirin in those with well-controlled hypertension and target organ damage, diabetes or atrial fibrillation were considered appropriate as per British Hypertension Society Guidelines [18].

Table 3. Potentially inappropriate prescriptions as determined by Beers' criteria [6]

Criterion	*n*	Adverse effect of PIM as contributory factor to admission
Independent of diagnosis		
Doxazosin	22	1 (hypotension)
Amiodarone	15	0
Digoxin > 125 μg/day	14	1 (digoxin toxicity)
Methyldopa	1	0
Long-acting benzodiazepines	43	17 (fall + fracture 8; fall + head injury 1; recurrent falls 3; benzodiazepine overdose 1; cognitive decline 4)
High-dose short-intermediate acting benzodiazepines	11	1 (fall)
Amitriptyline	16	4 (fall + fracture 3; recurrent falls 1)
Fluoxetine	4	0
Doxepin	7	0
Chlorpheniramine	4	0
Nitrofurantoin	7	0
Non-COX selective NSAID	6	1 (upper gastrointestinal bleed)
Ferrous sulphate > 325 mg/day	1	0
Considering Diagnosis		
Bladder Outflow Obstruction		
Antidepressant	2	0
Anticholinergic	1	0
Depression		
Long-term benzodiazepine use	20	0 (4 had falls, but are counted in syncope/falls category)
Syncope/Falls		
Short –intermediate acting benzodiazepines	29	16 presented with falls as reason for admission
Tricyclic antidepressants (imipramine, doxepin and amitriptyline)	6	4 (counted under amitriptyline independent of diagnosis)
Cognitive impairment		
Antispasmodic	1	0
Anticholinergic	9	1 (temporal relationship to cognitive decline)
Chronic constipation		
Tricyclic antidepressant	1	0
Calcium channel blocker	1	0
Gastric or duodenal ulcers		
NSAID and aspirin	3	1 (upper gastrointestinal bleed)
COPD		
Long-acting benzodiazepine	1	0
Total	226	43 (6% of all 715 admissions)

guanadrel or meprobomate. Furthermore, the designation of certain drugs as inappropriate by Beers' criteria is debatable, e.g. avoidance of amiodarone and doxazosin in older people regardless of the diagnosis [6]. Amiodarone may be the only agent for effective control an arrhythymia, and although not often a first-choice agent, may be entirely appropriate in particular cases. Doxazosin may be appropriate in patients with resistant hypertension. Similarly, nitrofurantoin may be the only antimicrobial to which an infecting pathogen is sensitive and would therefore be appropriate to prescribe. Beers' criteria identified 44 patients as 'inappropriately' receiving these drugs, though they were justified in all but one case. STOPP contains 33 instances of potentially inappropriate prescriptions not found in Beers' criteria, 28 of which were identified in the present study. These include long-acting benzodiazepines such as nitrazepam and prazepam, excessive duration and dose of proton pump inhibitor therapy and duplicate drug class prescriptions all of which add unnecessarily to cost and complexity of drug regimes for older people without providing additional therapeutic benefit.

Beers' criteria list three specific TCAs to be avoided in older people: doxepin, amitriptyline and imipramine [6]. In contrast, STOPP highlights the clinical situations where it is potentially inappropriate to prescribe any TCA, e.g. in older patients with dementia, glaucoma, cardiac conductive abnormalities or constipation, thus allowing freedom to prescribe a TCA in situations where it may be indicated, e.g. low-dose amitriptyline in chronic pain syndromes. All 16 patients prescribed amitriptyline in this study were on low-dose amitriptyline for management of neuropathic pain. STOPP identified 5 of these patients as inappropriately receiving amitriptyline, thus allowing the treatment to proceed in the remaining 11 patients who were tolerating the low-dose TCA effectively and without any adverse effect. We believe that this approach is more flexible than that of Beers' criteria. Similarly, STOPP details particular instances where prescription of NSAIDs is potentially inappropriate, e.g. with peptic ulcer disease, heart failure, hypertension, prolonged treatment in osteoarthritis or gout. STOPP identified more admissions related to adverse effects of NSAIDs

($n = 7$) than Beers' criteria ($n = 2$). In fact, only one of the non-COX selective NSAIDs (naproxen) listed in Beers' criteria was encountered in this population.

Falls with a resultant injury were among the most common reasons for hospital admission in this study. Though falls are clearly multifactorial in nature, medication review is an essential component of comprehensive falls assessment [4]. STOPP identified 48 patients with a history of falls receiving potentially inappropriate psychoactive or vasodilator medications. In addition, STOPP identified several inappropriate prescriptions in patients presenting with an isolated fall, e.g. long-acting benzodiazepines ($n = 17$), first-generation antihistamines ($n = 2$) and inappropriately prescribed opiates ($n = 4$). Beers' criteria identified considerably fewer patients whose falls risk was increased as a result of inappropriately prescribed medication ($n = 35$).

A limitation of this study is that assessment of PIM-related causality or contribution to the presenting complaint was based on trained geriatric clinical judgement as opposed to the criteria of a validated ADE causality assessment tool such as the Naranjo algorithm [20]. However, such judgement replicates everyday clinical practice. As this was an observational study with no interventional component, rigorous ADE-causality assessment criteria involving dechallenge and rechallenge of a drug over time in addition to placebo-response and serum drug-level measurement were not applicable. Such criteria for establishing true ADE causality are rarely practicable in the everyday clinical setting.

Balancing safety and quality of prescribing with appropriate treatment of all co-morbidities is complex and challenging. Geriatrician input and pharmacist review can improve drug appropriateness in older people [15, 21]. However, it is not feasible, in most health services, for a geriatrician to assess all older patients. STOPP can be used in a time-efficient manner by all disciplines involved in the care of older patients, e.g. primary care, secondary care, psychiatry, general or orthopaedic surgery to assess appropriateness of drug treatment, with the intention of minimising the risk of ADEs and associated morbidity. STOPP was designed to be used in conjunction with START (Screening Tool to Alert doctors to Right, i.e. appropriate indicated Treatment) [22] to afford a comprehensive appraisal of older patients' medications, i.e. errors of prescribing commission could be identified at the same time as errors of omission. We acknowledge that the criteria will need regular updating in line with emerging evidence. Whether STOPP/START used as an intervention can significantly improve prescribing appropriateness or reduce drug-related morbidity or mortality remains to be seen. Clearly, substantial randomised controlled trials are required to address these important questions.

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Key points

- Potentially inappropriate prescribing is highly prevalent in older patients presenting for hospital admission.
- STOPP criteria identified at least one potentially inappropriate medication in 35% of older patients requiring admission to hospital.
- Well-recognized adverse effects of inappropriately prescribed medicines were casual or contributory to hospital admission in 11.5% of patients when screened with STOPP criteria compared to 6% when screened with Beers' criteria.
- STOPP criteria are more sensitive in identifying patients coming to harm as a result of inappropriately prescribed medicines than Beers' criteria.

Supplementary data

Supplementary data for this article are available online at http://ageing.oxfordjournals.org.

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