

# Healthcare Provision in an Aging Society—The European Perspective

Peter Crome and Joanna Pleming

**Abstract** This chapter aims to set out an overview of current practice for the treatment of older patients in Europe. It focuses on established health services for the elderly and current prescribing practice in the context of European health policy. It details the roles of the professional health bodies within Europe including the European Medicines Agency (EMA) and European Union Geriatric Medicine Society (EUGMS) and patient charters including that of the PREDICT partnership. It explores some of the overprescribing and underprescribing issues in older people specific to Europe. The healthcare system for older people in England is described in some detail and compared to a number of other European countries, thereby providing a context for prescribing opportunities and challenges in the continent.

**Keywords** Healthcare in Europe • EUGMS (European Union Geriatric Medicines Society) • EMA (European Medicines Agency) • NICE (National Institute for Health and Care Excellence) • PREDICT

## Introduction

Physicians treating older people and older people themselves have long been concerned about the risks and benefits of pharmacotherapy. Issues of adherence, polypharmacy, potentially inappropriate medications, high rates of adverse events, and altered kinetic and dynamic responses, together with the poor evidence base for

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treatment in the over-75s and those with multimorbidity, all make prescribing problematic. These factors need to be considered in the context of improved diagnosis (e.g. scans), new medicines for newly identified conditions, the increased prevalence of conditions such as diabetes (although others are in decline), national policies and guidelines and the greater emphasis on secondary prevention for conditions such as stroke and heart disease. These issues have gained more prominence as the result of demographic changes and the growing recognition that older people are not a homogenous group (see Box 1). In this chapter some of these issues are explored from a European perspective.

## **Older People in Europe**

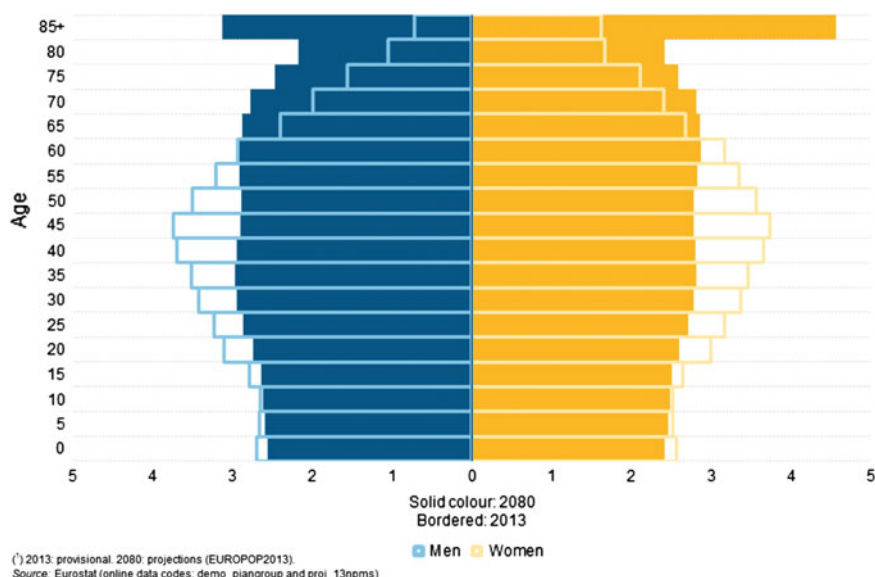
### ***Demography of Aging in Europe***

Europe is aging, and as it does so, it pulls a larger and larger proportion of the population out of work and into retirement. Life expectancies in European countries are some of the highest in the world and continue to increase. Over the last 50 years, life expectancy at birth in the 28 European Union Countries (EU-28) has increased by approximately 10 years and between 2001 and 2013, the median age of the population in Europe increased in all of the EU-28 countries, from a minimum of 2.1 years in Lithuania and up to 6.4 years in Estonia [1].

The aging population is, in part, contributed to by low birth rates. Fertility rates in the EU-28 have decreased since the baby boom of the 1940s–1960s and stayed relatively low. This trend is partly explained by European families having fewer children and parents waiting longer before starting families [2].

The aging of the population will also lead to an increase of the percentage of the population classified as the oldest old, >80 years. This proportion of the population is growing faster than any other and is projected to increase by more than twice as much again between 2013 and 2080 [3] (Fig. 1).

Life expectancy for women in Europe is, on average, longer than that of men, estimated at an extra 5.5 years of life in 2013. This longevity comes at a cost, however, with most of the later years being subject to activity limitations. The gap in “healthy life years” is much less significant between sexes, only equating to 0.1 years [4]. The growth in the elderly population has resulted in the elderly consuming an ever increasing proportion of health resources, with the over 65s accounting for 70 % of hospital bed days in the UK [5].



**Fig. 1** Projections of population spread with the *bordered color* representing actual figures from 2013 and the *solid color* the projections for 2080 (Source Eurostat)

### *Prevalence of Diseases/Disability in Europe*

The Dutch National Institute for Public Health and the Environment (RIVM) prepared a report to review the impact of chronic disease on the population of pre- and post-retirement age in the European Union. It reported the substantial burden of four main chronic diseases—cardiovascular disease, cancer, COPD, and diabetes. It notes the lack of good data on trend prevalence but states that the total number of people with chronic disease is expected to increase due to the aging population and the continued prevalence of lifestyle risk factors. It also notes significant differences between individual countries within the European Union [6].

In the UK, The Alzheimer's Society estimates that one in six people aged 80 or over have dementia at a financial cost of £26 billion per annum. It also estimates that only 44 % of people with dementia in the UK receive a diagnosis. The prevalence is increasing. By 2015 there will be 850,000 people with dementia in the UK and this number is expected to rise to 1 million people by 2025 [7]. Alzheimer Europe used projections from UN populations statistics for 2012 to estimate that dementia affects on average 1.5 % of the entire population of the European Union, the lowest in Romania and Slovakia at 1.07 % and highest in Italy at 2.09 %. It also notes that as more than half of dementia goes undiagnosed, these figures are in all likelihood, much higher [8].

There are also 157,000 new strokes per year in the UK [9]. The increase in prevalence of stroke in the elderly is paralleled in other European countries. Engstad et al.'s literature review in 2012 highlighted that, in Nordic countries, prevalence has increased due to a combination of improvement in care quality causing decreased lethality and a slower fall in incidence than increase in the proportion of the oldest old in the population [10].

European countries vary in the percentage of their GDP that is spent on health. OECD data shows that the proportion of GDP spent on health rose from 7.3 to 8.3 % between 1998 and 2008. There was almost twofold variation between countries with France spending 11 % of their GDP on health, whereas it was only 6 % in Cyprus and Romania [11]. The financial issues facing European health services as a consequence of the 2008 recession coupled with inflationary pressures (including their drug budgets) are obvious. Maximizing efficiency in a time of resource limitation whilst improving health in later years is a public priority across Europe. Keeping costs down whilst at the same time developing a national fiscal environment that encourages pharmaceutical innovation remains a challenge.

## Medication Use in Europe

### *An Introduction to Overprescribing and Underprescribing*

Medication use in older people and its regular review formed one of the pillars of the UK National Policy on Older People [12] that suggested that older people should be broadly categorized into three groups [12]:

- (1) Active and independent older people—those entering old age
- (2) Transitional Phase—the bridge between 1 and 3
- (3) Frail older people with a higher level of care needs and increased vulnerability.

We have illustrated the difference in care needs between these groups with two vignettes (Box 1).

**Box 1** The Diverse Faces of Aging: Two case vignettes highlighting the differences in health needs and prescribing considerations between two older patients

#### **THE DIVERSE FACES OF AGEING** **Older Person 1**

##### *Personal Situation*

65-year-old married female office worker. Works part-time and plans to retire in about two years. Two children and three small grandchildren. Her mother, 87, lives in a retirement apartment. Plays an active role in grandparenting and wishes to continue this. Life expectancy 20 years.

*Medical Conditions*

Type 2 diabetes and hypertension. No physical or mental health complaints. Slightly overweight. Blood pressure usually about 150/90. Osteopenia on dexam scanning.

*Drug Treatment Issues*

Realizes that she may need treatment for hypertension, diabetes, and osteopenia.

Wants to know what the risks are without drug treatment and what the benefits are for people like her, not for the entire population.

Prepared to put up with mild side-effects if there is substantial benefit.

Wants a simple drug regime that fits in with life style.

**Older Person 2***Personal Situation*

85-year-old widow. Admitted to a nursing home following a fall in which she fractured her right femoral neck. Limited mobility. Can only walk with the help of a walker. Her children are now retired. She enjoys visits from her grandchildren and great-grandchildren. Can only leave the home in a wheelchair. Life expectancy 3 years.

*Medical Conditions*

Type 2 diabetes, hypertension, and osteoporosis. Blood pressure usually about 150/90. Glucose slightly raised.

*Drug Treatment Issues*

Concerned about side-effects, particularly risk of hypoglycaemia and whether the drugs will produce worthwhile benefits.

The requirements in health provision differ greatly between these two groups. A lack of recognition that these two groups of patients have different care needs and medication requirements can create issues with overprescribing or underprescribing. Older Person 1 will benefit from active primary care for example, interventions to help her maintain a healthy BMI, actively manage cardiovascular risk factors, and monitor bone density, intervening when necessary. These interventions will keep her healthier for longer, keeping her out of hospital, limiting her cardiovascular risk and improving her quality of life. She is motivated to accept treatment but requires the time to be informed of benefits and risks to improve adherence. She will be on most of this medication for the rest of her life with no notable change to how she feels on a day-to-day basis. It may be tempting to restrict some medications as she is an older adult but this may lead to underprescribing for someone who may live for a further 30 years. Older Person 2 requires multidisciplinary comprehensive geriatric assessment with focus on maintaining and strengthening

existing function, regular medication review and advanced care planning. Antihyperglycaemic medication is indicated to prevent a hyperosmolar state but care should be taken that glycaemic control is not too strict as the long-term benefits will not be realized with a limited life expectancy and the risk of hypoglycaemia is higher and more dangerous. Overprescribing should be avoided with consideration made of quality of life and a shift in focus made from broad cardiovascular prevention to targeted prevention (e.g., bone protection in a patient at risk of falls) and symptom control.

Medications are prescribed by the general practitioner, hospital doctors during hospital admissions and other health professionals. This can lead to a lack of empowerment by any one professional to review an individual's medications meaning that medications are started and not stopped, or that an indication that has changed is not recognized, for example anticholinergics for benign prostatic hypertrophy continued after a long-term catheter has been inserted, increasing the risk of falls and delirium with no further benefit to the patient. In hospital there is a focus on short-term treatments, the acute care setting is not conducive to chronic medication review, and general practitioners may feel disempowered to change specialist prescription started sometimes decades previously, e.g., antidepressants. There can be limited communication between primary and secondary care [13].

In a study performed in 2005, Fialova et al. showed that polypharmacy (graded as 9 or more medications) was reported by 22 % of adults >65 years in home care in Europe [14].

## **Health Services for Older People**

### ***Discussion of Public Health Services with Individual Country Examples***

There is a general consensus in Europe that the provision of health services for older people is a national rather than an individual responsibility. How this is organized varies from country to country and even within countries from region to region. There is also a scheme that allows citizens or residents from one country to receive health care in another European country as if they were a citizen/resident of that country. To facilitate this, a European Health Insurance Card is available for travelers.

In the UK, the National Health Service (NHS) is free at the point of use for both primary and hospital health services. It is primarily funded by general taxation; there is no hypothecated health tax. The method of funding varies throughout Europe with some countries using state funding to cover the cost of health care, others use mandatory health insurance (both for profit and not for profit insurers) and top-ups or co-payments may be required. Private health care is used to a variable degree in all European countries and often allows greater flexibility to

choose the care provider, e.g., consultant or hospital, and chose the timing of appointments.

Every person in the UK is registered with a general practitioner (GP). These doctors work from community-based practices which contain from one to several GPs. GPs are generalists and act as gatekeepers to hospital outpatient services, referring patients to secondary care, usually via a paper or web-based referral form. If cancer is suspected, the NHS has a “two—week wait” pathway in which patients are triaged and seen by the specialist team within two weeks from the date of referral. Specialist secondary care is practiced in hospitals, generally not geographically placed within primary care centers. Some specialist referrals, for example specialist Parkinson’s disease clinics, are set in a multidisciplinary outpatient department with patients being seen by doctors, specialist nurses and physiotherapists within the same outpatient hospital visit. Specialty referral to geriatric medicine can be to several discrete outpatient services, for example, falls clinics, old age psychiatric services, or general geriatric outpatients. Some hospitals provide admission avoidance services. These can offer, for example, direct access by GPs to a consultant geriatrician via telephone for advice or to take a referral to see an older person in a specialist clinic to avoid what would otherwise lead to an admission to hospital. Admission avoidance appointments are typically longer and have access to occupational therapists, physiotherapists, and in some cases social services to organize home care packages, blood tests, and scans on the same day. Some departments have links with community-based nursing packages, through which nurses visit patients in their homes to administer intravenous medications and measure observations.

In the UK, most older people with care needs are cared for in their own home. Social care services in the UK are means-tested with those who have higher need care-packages prioritized. Occupational therapists in the community and allied to hospitals make recommendations as to the safest and best place for care to be delivered, making home visits to assess whether equipment or adaptations would enable living at home for longer. Older people who require more supervision can be offered sheltered or residential housing with a warden on site to make regular calls to check on residents. Nursing homes are usually a final step providing 24 h nursing care for those with severely disabling illness and requiring round the clock assistance. Medical care to nursing homes is provided either by GPs or, in some countries (e.g., the Netherlands) by nursing home physicians. In England, social care is facilitated by the Local Authority. In those who cannot pay, this is fully funded. There is a wide spectrum of social care outside the UK with significant reliance on informal care in some countries, depending on culture and GDP.

On admission to hospital in England, a decision to admit or discharge must be made within four hours. There are specialist pathways for some conditions, for example, fractured neck of femur and stroke, mobilizing members of the multidisciplinary team early, to decrease morbidity and mortality. Throughout the UK, geriatricians are involved in the care of older surgical patients and orthopedic patients, with a proven benefit to outcomes [15, 16].

A key focus of NHS reform in the UK in recent years has centered around integrated care—the development of a more holistic, person-centered system avoiding the fragmentation and compartmentalisation of different care episodes. Integrated care aims to deliver care to a patient in a location best suited to the patient, meeting their physical, mental, and social care needs. Geriatric patients are well suited to this approach, and their health and social care needs will increasingly be met through integrated care. Over time, changes in the way health care is financed and regulated will promote provision of integrated care. Admission avoidance and ambulatory care clinics, increasingly present in UK hospitals, provide an increased range of services to outpatients so that they can remain out of hospital or be discharged home earlier [17, 18].

Alongside the move to integrated care, there will be a shift in provision of care and prescribing away from hospital specialists and toward other health workers in the community, including specialist nurses. This will mirror the shift to nurse-led care that has already been seen in other disciplines. An example of nurse-led care which has been highly successful and widely adopted throughout the NHS is in the treatment of heart failure. Specialist heart failure nurses are usually allied to cardiology departments and work within hospitals or from a community base, also performing domiciliary visits. Nurse practitioners provide coordination of care with a multidisciplinary approach combining patient education, dietetics, medication review, and prescription including up titration of heart failure medications. Nurse-led intervention in this area, particularly in elderly and isolated patients, has shown benefits not only in clinical and cost-effectiveness, but also in quality of life [19].

There is much variation in the number of physicians and the division between general practitioners and specialists in Europe [20]. Throughout Europe there are 3.3 physicians/1000 population, the highest number being in Greece (6/1000) and the lowest in Turkey (1.5/1000). There is even greater variation in the proportion of physicians who are general practitioners—54.5 % in Romania, 4.5 % in Greece, with an overall European figure of 25 % [11].

## **Prescribing for Older People**

### ***National Guidelines and Cost-Effectiveness Arrangements***

The responsibility for prescribing for long-term conditions varies by country (Table 1). In the UK, the management of long-term conditions is the responsibility of the general practitioner (e.g., essential hypertension, Type 2 diabetes, hypercholesterolaemia, COPD, and hypothyroidism). Some specialist (and usually more expensive) medications are prescribed by specialists in hospital (e.g., chemotherapeutic agents, monoclonal antibodies, and drugs for HIV/AIDS). Shared care guidelines are in existence whereby treatment is initiated by specialist and then



**Table 1** Simplified comparison of key features of health services for older people in seven European Countries (excluding private sector)<sup>a</sup>

	UK	Germany	Italy	Belgium	Netherlands	Cyprus	Lithuania	Czech Republic	Greece
If an older person becomes ill whom do they see in the public health service? (Non-emergency)	GP	GP or specialist	GP	GP or specialist	GP	GP	GP	GP	GP
Who pays for the consultation?	State	Health insurance	State	Health insurance	Health insurance	Mostly state	State	Health insurance	State
Are there co-payments?	No	No	No	Yes (25 % paid out of the pocket by the patient)	No	Yes (3 euro co-payment)	No	Sometimes but not usually	No
If drugs are prescribed, does the patient have to pay?	No	Yes 10 Euro per drug prescribed up to a ceiling of a total healthcare expenditure of 3 % of the family income per year, reduced to 1 % of the family income in individuals with chronic conditions	No If the patient wants a brand instead of a generic one then he has to cover the difference in price	Yes Depending on drug, e.g., diabetes drugs are free but tranquilizers are not reimbursed	Yes At least 300 euro own risk for all insured patients, this includes also costs for medicines. For some drugs all costs have to be paid for depending on the insurer	0.5 euros per drug	Partly	Varies according to drugs	No

(continued)

**Table 1** (continued)

	UK	Germany	Italy	Belgium	Netherlands	Cyprus	Lithuania	Czech Republic	Greece
Are there any restraints on what the GP/primary care physician can prescribe?	If approved by NICE, drugs have to be provided by health service. Local formularies may vary from district to district	No (but the insurance company will ask questions if prescribing costs are very high, and the GP has to justify costs)	Yes Many drugs require a specialist prescription	Some Only a few very expensive drugs	Yes All GPs are not allowed to prescribe all drugs, health insurance companies have a preferred list of medicines that are allowed to be prescribed, these lists could be different from company to company	Some Restricted list of drugs stipulated by state	Some GP prescribing is monitored. Some medications can be prescribed only by specialists	Yes Some drugs are prescribed by specialists controls by health insurers	No Drugs usually prescribed by brand name
Do specialists provide primary care?	No	Yes	No	No	No	No	No	No	No
Who monitors chronic conditions?	GP	GP and specialists	GP	GP and specialists	GPs and specialists	GP	GP	GPs and specialists	GP

(continued)

Table 1 (continued)

	UK	Germany	Italy	Belgium	Netherlands	Cyprus	Lithuania	Czech Republic	Greece
Do GPs have financial incentives to prescribe?	Yes For GPs to meet targets for prescribing preventive treatments	No (but the insurance will ask questions if prescribing costs are very high, and the GP has to justify costs)	No	No	Yes Incentives from health insurance companies to prescribe the cheapest drugs	No	No	No GPs leave prescribing to specialists if possible	No
How do patients see geriatricians?	On referral from GP	Only in hospital	Mainly only available in the hospital with a GP referral or as a private visit	Mostly in hospitals	Mostly in hospitals	Self-referral or by doctors' recommendation	On referral from GPs	Only in hospital	Not a developed specialty
How is geriatric medicine practice different from the UK?		Only provided in hospital. No community geriatricians, no visits to nursing homes and no day hospitals	Mainly provided in the hospital. Few specialists are available in the community and in nursing homes	Geriatric day hospitals in every hospital. Mandatory internal medicine liaison	Only provided in hospital Geriatricians visit nursing homes at the request of nursing home physicians	Few private geriatricians only	Few geriatricians	Only in hospital—mainly university hospitals	As above

(continued)

**Table 1** (continued)

	UK	Germany	Italy	Belgium	Netherlands	Cyprus	Lithuania	Czech Republic	Greece
In hospital are there any constraints on prescribing?	Hospital formularies and policies e.g. antibiotic prescribing	No	No	Different formulary in every hospital	Yes, some hospitals do not allow prescription of very expensive drugs, most of the time this not relevant for geriatricians	Restricted formulary stipulated by state	No	No	Local hospital formulary. Essentially all drugs and brands are available
Are there financial incentives to prescribe?	Quality and outcomes framework (QOF)	No	No	No	No	No	No	No	
Who pays for hospital care?	State. No co-payments	Insurance	State. No co-payments	Insurance plus out of pocket payment by the patient (25 %)	Insurance	Either the state pays fully, or partially and patient makes modest contribution, or pays full cost (various criteria e.g. income, chronic illnesses, number of children)	State	Health insurance	State

(continued)

Table 1 (continued)

	UK	Germany	Italy	Belgium	Netherlands	Cyprus	Lithuania	Czech Republic	Greece
Who pays for drugs in hospital?	State. No co-payments	Insurance plus 10 euro per day hotel costs up to a ceiling of a total healthcare expenditure (also include prescriptions, travel to hospital, etc) of 3 % of the family income per year, reduced to 1 % of the family income in individuals with chronic conditions)	State. No co-payments	The hospital	Insurance	As above	State	State	State

<sup>a</sup>There may be differences in how services are provided for between different regions in the same country, e.g., at Laender level in Germany and at country level in the UK

devolved to GPs (e.g., cholinesterase-inhibitors for Alzheimer's Disease and novel oral anticoagulant medications).

Older people are exempt from prescription charges. At a practice level there are incentives for GPs to prescribe some medications in order to qualify for additional payments by meeting defined thresholds. Examples include anti-osteoporosis medication, antihypertensives, and lipid lowering drugs.

The ability of physicians to prescribe within state health systems is controlled by a variety of mechanisms. For example, in England and Wales, the National Institute of Health and Care Excellence ([www.nice.org.uk](http://www.nice.org.uk)) assesses the clinical and cost-effectiveness of new medications. As a general rule those drugs which are above the £20,000–£30,000 per quality adjusted life year (QALY) Incremental Cost-Effectiveness Ratio threshold will not be approved. At the present time manufacturers of anticancer drugs can apply to a special Cancer Drug Fund if their application to NICE is rejected. NICE approved drugs have to be made available through the NHS. In addition to its appraisal role NICE also produces evidence-based guidelines for the management of common geriatric medicine problems, e.g., delirium, dementia, falls, and continence. In France, the Haute Autorité de Santé is an independent organization evaluating both the health system and health care products as well as the organization of health systems including public health ([www.has-sante.fr](http://www.has-sante.fr)). Hospitals will have local formularies listing which drugs are recommended for what conditions and in some countries these controls will apply to community prescribers as well.

The cost of medications is a major health issue in Europe. The number of prescriptions in the community has increased to 1000.5 million in 2012, a 62.2 % increase over 2002. The total ingredient cost actually fell compared to 2011 largely due to the expiry of patents on widely prescribed drugs (e.g., atorvastatin). Free prescriptions accounted for 90 % of prescriptions of which 60 % were older people [20].

In most countries there is a conflict between the desire to reduce costs of medications (whether paid for by the state, insurers or the public directly) and the desire to promote the pharmaceutical industry as a source of employment and tax revenue.

In most European countries co-payment for prescriptions is required, often varied according to the cost of the drug or to the wealth of the patient (see Table 1). A useful summary of how prescribing is monitored is found at [http://www.icf.uab.es/es/pdf/publicacions/DU\\_inventory\\_countries.pdf](http://www.icf.uab.es/es/pdf/publicacions/DU_inventory_countries.pdf).

## European Actions

### Human Rights

Physicians in many European countries have taken the view that many of the issues surrounding drug treatment in older people can be considered within the framework of Human Rights. The European Convention on Human Rights, ratified after the events of the Second World War, includes the Right to Life (Paragraph 1),

The Right for Respect for Private and Family Life (Paragraph 7) and the Prohibition of Discrimination (Paragraph 14) [21]. National law is subject to this convention but not all rights are absolute and interpretation varies. All of these principles may be violated if governments do not set in place systems to ensure that older people are not denied safe and effective mediations. The European Union contains within its charter on fundamental rights at Article 25 “the Union recognizes and respects the rights of the elderly to lead a life of dignity and independence and to participate in social and cultural life” [22].

The EU Charter of Patient’s Rights (2002), although not specifically addressed to older people, affirms a patient’s right to fundamental rights when applied to healthcare. Article 35 of the Charter provides for a right to health protection as the “right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices”. Article 35 also specifies that the Union must guarantee “a high level of protection of human health,” meaning health as both an individual and social good, as well as health care. This formula sets a guiding standard for the national governments: do not stop at the floor of the “minimum guaranteed standards” but aim for the highest level, notwithstanding differences in the capacity of the various systems to provide services.

These conventions have served as models for the development of other charters that are more specific as regards the health of older people. The European Charter of the Rights and Responsibilities of Older People in need of long term care and assistance states at article 1.2.9 “protection from all medical and pharmaceutical abuse, maltreatment or drug use or denial of treatment” [23].

## European Medicines Agency

The European Medicine Agency (EMA) is the body that regulates medicines in almost all European Countries (i.e., European Union and the European Economic Area). It has two principal functions in relation to medicines for older people—the authorization for marketing and pharmacovigilance. Information about the EMA is available on its website [www.ema.org.eu](http://www.ema.org.eu). Some medications may also be authorized through national licensing bodies.

An important step in the development of European Medicines policy for older people was the publication of the report on adequacy of guidance [24]. This report analyzed the data submitted for 10 new drugs and compared the data submitted to standards recommended by the International Commission on Harmonization [25]. It concluded that in general, dossiers were compliant with the guidance, however there was scope for improvement. Amongst the suggestions were for professional bodies to define elderly, very-elderly, and frailty, the need for further discussions on increasing the number of older people recruited into studies and to systematically appraise the exposure of older people to a medication.

The EMA has produced a geriatrics medicine strategy which has its vision "... ensuring that medicines used by geriatric patients are of high quality, and appropriately researched and evaluated, throughout the lifecycle of the produce, for use in this population" and "improving the availability of information on the use of medicines for older people, thereby helping informed prescription" [26]. Amongst the actions advocated in the report is to give advice on numbers of older patients to be included in studies, the special needs of older people, age-specific end points, the identification of validated tools to measure safety in and effect in "frail" older people. Postmarketing monitoring in people with comorbidities was also recommended. To assist in this work a "virtual" geriatric expert group has been established [27]. One piece of work this group is taking forward is to develop definitions of physical and mental frailty and of comorbidity to guide drug development for these import subgroups of older people.

Recent reports on the implementation of the strategy have reviewed scientific guidelines and product information [28, 29].

An analysis of 28 guidelines produced in 2011–2013 showed that two were fully compliant with ICH E7. Of the 18 guidelines which were adopted over this period, one-third did not take into account comments made to rectify the situation [28].

The report on product information contains a more detailed account of information deficiencies and the responses of manufacturers. Examples included the need for further cardiovascular safety data, the requirement for post-authorisation follow-up because of the small number of older people included in the original submission, warnings about the lack of safety information about older people and the requirement to include a specific warning about falls risk [29].

Thus it can be seen that the EMA is taking on board the concerns of professionals about the present state of information about drugs in older people and addressing issues within their areas of competence. The EMA is producing a further reflection paper covering scientific literature, practical issues, and a gap analysis describing how existing authorisations do not meet the needs of older people. This is due to be published in 2016.

## **Actions on Representation of Older People in Clinical Trials**

As has been described above, the EMA has taken some steps to increase the number of older people in clinical trials of investigational medical products. However the issue goes beyond solely new products to affect both existing drugs and devices. The underrepresentation of older people in trials has been reported upon by a number of investigators. As an example, in 2011, Cherubini et al. [30] found that a quarter of clinical trials for heart failure had an arbitrary upper age limit and that over 40 % had one or more unjustified exclusion criteria [30]. The European Union Geriatric Medicine Society, the umbrella group for European societies, has established a pharmacology special interest group that lobbies on this and other issues with the EMA and other agencies [31].



European geriatricians have also undertaken collaborative research on this issue. For example the PREDICT study has reported on both professional and patient/carers views on the under-representation of older people [32, 33]. This work led to the production of a European Charter on Patients, Rights in Clinical Trials that has been endorsed by many European Geriatric Medicine Societies and other professional organizations (Box 2).

### **Box 2** Key Elements of the PREDICT Charter

- Older People have the right to access evidence-based treatments—they should demonstrate effectiveness in people of their age.
- Older people should not be discriminated against in recruitment for clinical trials.
- Research Ethics Committees, Sponsors, medical Journal Editors, and regulators should review all studies critically for unjustified exclusion based on age, other illnesses, disability, and other drug treatments.
- Clinical trials should be designed so that older people can participate easily.
- Researchers should be trained to conduct clinical trials in subjects with communication, sensory, mobility, or cognitive problems.
- Trial sponsors should recognize that older people may need extra support to participate in clinical trials.
- Clinical trials in older people should be as safe as possible.
- Outcome measures should be relevant to older people.
- Clinical trial sponsors should involve older people and carers in the design of clinical trials.
- Researchers should respect the values of each older person as an individual.
- Older people should be able to withdraw from a clinical trial without detriment to other treatment and their overall care.

The European Forum on Good Clinical Practice, a multidisciplinary organization that brings together academics, clinicians and the pharmaceutical industry, has produced a report on Medical Research For And With Older People In Europe (EFGCP) [34]. This report is targeted toward clinical trials undertaken for regulatory purposes. However, it is of relevance to all clinical trials (drugs and non-drugs) and covers ethical issues such as consent/assent, and risk assessments as well as topics such as numbers needed, inclusion and exclusion criteria, and outcome measures.

The European Union Geriatric Medicine Society (EUGMS) is a federation of national societies that is also promoting the inclusion of older people in clinical trials ([www.eugms.org](http://www.eugms.org)). Its pharmacology section's goals include promoting the inclusion of older people in clinical trials, to promote appropriate prescribing including the STOPP and START criteria (see below) and to develop pharmacogenetic research in older people. It has lobbied the EMA to establish additional requirements for

authorisation for drugs that will be used in older people. These would require the recruitment of very old people as well as those with multimorbidity and disability. They have suggested that companies that comply with additional recommendations might be “rewarded” with a longer patent for their product [31].

## **Actions on Inappropriate Prescribing and Failure to Prescribe Appropriate Medications**

The repeated finding that older people are more susceptible to the side-effects of drugs led to the development of lists of drugs which were deemed inappropriate outright or for specific conditions. The most widely employed and studied are the Beers criteria which have regularly been reviewed, most recently in 2012 [35]. Other investigators have developed alternative lists of medications to be avoided. [36] reported on the prescribing of inappropriate medication in six European countries using both the STOPP criteria and the then Beer’s criteria [36]. They reported that the overall prevalence of potentially inappropriate medications ranged from 34.7 % in a Czech hospital to 77.3 % in a Swiss hospital whilst for the Beer’s criteria the range was 22.7–43.3 % in the same two hospitals. These authors also reported that potential prescribing omissions averaged 59.4 % across the six European hospitals [36]. Since this paper was published there has been a further update of the STOPP/START criteria [37].

One of the criticisms of the use of criteria is that there has not been robust clinical trial evidence that using criteria such as STOPP/START or Beers has improved patient outcomes. This is now being tested in a controlled six nation trial in Europe funded by the EU (SENATOR study—<http://www.senator-project.eu/>). In this study 1800 patients will be randomized to have their medication assessed against a computerized version of the STOPP criteria or to standard care. A range of outcomes will be measured.

## ***Prescribing Toward End of Life***

Whilst there is consensus that prescribing drugs other than those that will provide symptomatic relief for those older people in their last few days of life is futile there is debate as to whether the same principle is true for patients in their last years of life. There are practical and ethical difficulties for physicians who have extolled patients to take statins and antihypertensive drugs for years only to tell patients that on reaching a certain age or a certain stage in their disease that they should stop the drugs as they are no longer necessary.

The process of “de-prescribing” has been operationalized by Garfinkel in Israel and has been taken up by physicians in Europe [38]. Garfinkel et al. undertook a systematic deprescribing exercise in nursing home residents with what they called the “geriatric-palliative” methodology [38]. An example quoted was to stop nitrates if there had been no chest pain for 3 months. Although not a randomized trial they found that the one year mortality in the study group was 21 % compared to 45 % in the control group. Acute care referral was also reduced—30 % in the control group and 11.8 % in the study group. They discontinued 332 drugs in 119 patients and had to reintroduce 33 drugs in 21 patients. Antihypertensives, H<sub>2</sub> blockers, and nitrates were the drugs most frequently discontinued [38]. Garfinkel and Mangin [39] have also described successful drug discontinuation in community-dwelling older people [39]. Scott et al. have advocated a similar approach with a 4-step decision tree: no benefit, harm outweighs benefit, symptoms stable, or non-existent, preventive drug benefits unlikely to be realized because of short life expectancy [40].

## Conclusion/Discussion

Older people and their families want access to the most effective and safest medications. Within health care systems, where there is co-payment for prescription drugs, then they want such co-payments to be reasonable. What might be considered reasonable will vary from country to country. Evidence from the PREDICT study shows that older people want their drugs to be tested by clinical trials with relevant outcomes. Trials may need to be modified to meet the needs of older people with multiple morbidities and frailty. “Real-life” trials with minimum exclusion criteria and simple meaningful outcomes such as, e.g., AD2000 or PDMed, or adaptive trials which allow for modification of design and the introduction of new drugs, are two ways to improve recruitment of older people into trials. There also needs to be recognition that taking medication does pose physical and psychological burdens in addition to financial burden. Toward the end of life consideration needs to be given to reducing or stopping medications for which there is unlikely to be benefit. These factors also need to be set in the context of governmental concerns about the costs of medication and the need to have a thriving manufacturing and research arms for their pharmaceutical industry, for there are still many conditions of later life for which there are no drug treatments with any significant benefits.

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