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Research paper

A survey of geriatric expertise in medicines evaluation at national regulatory agencies in Europe: There is still room for improvement!

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ABSTRACT

We investigated geriatric medicine input in national regulatory medicine licensing agencies across Europe, focusing on changes occurred since a previous survey published in 2011. A questionnaire was mailed to 22 national regulatory agencies in 2014. Four reminders followed: 16/22 (73%) answered. Currently only one agency (6%), i.e. the Swedish Medicines Authority, has a specific committee to evaluate medicines for older people, while previously, 2/21 agencies (10%) had a specific committee to assess medicines used by older people. The Swedish and Dutch regulatory agencies (13%) have binding policy on how to assess medicines for older people. On the other hand, nine national agencies (56%) follow external policies for the evaluation of geriatric medicines. Six agencies (38%) follow a policy concerning the inclusion of older people in clinical trials. Eight agencies (50%) have at least one geriatrician on their medical advisory boards, although this position is permanent at only three of them. Twelve agencies (75%) have access to ad-hoc geriatric advice. Compared to the previous survey, 6/21 agencies (28%) had a geriatrician on their medical advisory boards and 10/21 (48%) agencies provided for ad-hoc input of geriatricians into advisory board discussions. Finally, three regulatory authorities (19%), involve geriatricians in research on drug prescription in older people. This survey demonstrates that, despite some improvement from the previous investigation, there is still a need for promoting a greater involvement of geriatric expertise in medicines evaluation across Europe.

1. Introduction

Older people are the main users of drugs in Europe which consequently underlines the need for greater attention to the heightened risks associated with the use of medicines [1,2]. These heightened risks are frequently associated with multiple chronic diseases affecting older people that often result in polypharmacy. Potentially inappropriate prescribing, or the prescription of medicines for which the risks outweigh the benefits, occurs frequently in older people [3–5]. In spite of the above mentioned risks, relatively little data is generated about the efficacy and safety of medicines in older people. Older people, particularly those aged 75 years and older, are often underrepresented in clinical trials [6–8]. Those older people who are included in clinical trials seldom represent the complexity of patients with multimorbidity and/or frailty who need multiple medicines at the same time. Consequently, the evidence base for drug licensing and clinical practice in older people is weak. Moreover, it is inappropriate to expose patients to the risks of medicines based on how they work in a demonstrably different (i.e. younger, more robust) patient population. In the European Union (EU), all medicines must be authorised before they can be marketed and made available to patients. There are two main routes for authorising medicines: a centralised route and a national route.

The European Medicines Agency (EMA) is an agency of the European Union (EU) and it is responsible for the authorisation of medicines that are managed through the central authorisation procedure. The centralised procedure is compulsory for: (1) human medicines containing a new active substance to treat human immunodeficiency virus (HIV) or acquired immune deficiency syndrome (AIDS); cancer; diabetes; neurodegenerative diseases;

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[1] http://www.eugms.org/research-cooperation/special-interest-groups/pharmacology.html.

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auto-immune and other immune dysfunctions; viral diseases; (2) medicines derived from biotechnology processes, such as genetic engineering; (3) advanced-therapy medicines, such as gene-therapy, somatic cell-therapy or tissue-engineered medicines; (4) orphan medicines (medicines for rare diseases). The centralised procedure is optional for other medicines: (1) containing new active substances for indications other than those stated above; (2) that are a significant therapeutic, scientific or technical innovation; (3) whose authorisation would be in the interest of public or animal health at EU level.

National competent authorities, on the other side, are responsible for the authorisation of many of the medicines available in Europe that are not authorised by the European Commission on the recommendation of the EMA. The majority of medicines currently available in the EU were authorised at national level, either because they were authorised before EMA's creation or they were not in the scope of the centralised procedure. Each EU Member State has its own national authorisation procedures.

At a European level, the European Union Geriatric Medicine Society (EUGMS) has played an important role in raising the awareness on the need of a better evaluation of drugs in older patients [9].

In 2011, Martin et al. published a survey of 31 European regulatory agencies (with a response rate of 21/31, i.e. 68%) to understand if and how geriatric expertise was systematically incorporated in the evaluation of license applications. At that time, 90% percent of the national European agencies had neither committees nor policies for medicines use by older people [10].

The purpose of this study is to understand how the involvement of geriatric expertise has changed among national regulatory agencies in Europe since the baseline survey.

2. Methods

A follow-up closed-question survey was developed by the authors to investigating geriatric expertise availability in the committees and policies of national regulatory agencies, specifically policies on clinical trials inclusion and exclusion criteria, and the role of geriatricians at the agencies. The presence of geriatric expertise in in-house committees and policies were compared to answers for paediatric expertise, which served as a 'control' group. We chose paediatric regulatory measures as a 'control group' because this area is acknowledged as being a special patient population.

In March 2014, we administered the survey through an established network of geriatric experts, which had the task to contact national agencies in 22 European countries. This was followed-up with four reminders in 2014. The responses, provided by representatives of the national regulatory agencies, were collected over a period of 11 months until February 2015 to maximise the response rate.

3. Results

Representatives of 16 national regulatory authorities answered (response rate 73%). An overview of responses by agency can be found in Table 1.

Only one out of 16 agencies (6% of respondents), i.e. the Swedish Medicines Authority, has a specific committee to evaluate medicines for use by older people. This committee for older people was established in 2012 and includes geriatricians as members. In the Dutch and Hungarian regulatory agencies (13% of respondents), there are discussions underway to create a committee to assess geriatric medicines. In the 2011 survey, 2/21 agencies (10%) had a specific committee to assess medicines used by older people.

Only the Swedish and the Dutch regulatory agencies (13% of respondents) have their own binding policy on how to assess medicines for older people. In the 2011 survey, 2/21 agencies (10%) had a policy on how to assess medicines for older people.

However, nine national agencies (56% of respondents) (Belgium, Hungary, Ireland, Italy, the Netherlands, Norway, Portugal, Spain, the UK) do follow external policies for the evaluation of geriatric medicines and one agency did not answer this question.

Six agencies (38%) follow a policy concerning the inclusion of older people in clinical trials, including Belgium, Czech Republic, Hungary, the Netherlands, Spain and the UK; however, one of these did not specify the policy's details. Two of the five of these policies prohibit comorbidity or frailty as exclusion criteria; three policies require clinical trials to include a minimum of 100 patients over the age of 65, and prohibit age as an exclusion criterion; four policies require the inclusion of patients over the age of 75. In the 2011 survey, 5/21 agencies (24%) had a policy on participant exclusion on the basis of age.

Table 1
Overview of the inclusion of geriatric expertise from 16 national medicines regulatory authorities.

Countries	Presence of a committee to evaluate drugs used by older people	Presence of a binding policy on the evaluation of drugs for use by older people	Presence of a non-binding guidance on the evaluation of drugs for use by older people	Adherence to a policy on the inclusion of older people in clinical trials submitted to the agency	Presence of a geriatrician on medicines advisory board	Availability of ad-hoc advice from geriatrician for medicines advisory board
Austria	No	No	No	No	No	No
Belgium	No	No	No	Yes	Yes	Yes
Czech Republic	No	No	No	Yes	No	Yes
Estonia	No	No	No	No	No	No
Germany	No	No	No	No	No	No
Hungary	No	No	No	Yes	No	Yes
Iceland	No	No	No	No	No	Yes
Ireland	No	No	No	No	Yes	Yes
Italy	No	No	No	No	Yes	Yes
Luxembourg	No	No	No	No	Yes	Not answered
Netherlands	No	Yes	No	Yes	Yes	Yes
Norway	No	No	No	No	No	Yes
Portugal	No	No	No	No	No	Yes
Spain	No	No	No	Yes	Yes	Yes
Sweden	Yes	Yes	No	No	Yes	Yes
UK	No	No	No	Yes	Yes	Yes