Interventions towards reducing adverse drug reactions among geriatric population in Africa: A scoping review of the literature from 1990-2016

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Abstract

Adverse drug reactions (ADRs) are an important health concern among the geriatric population, considering their negatives impact on the patients' health outcomes. Many interventions to reduce ADR among this segment of the population have however been proposed. This scoping review aims to discuss these interventions among the elderly African. A literature search was conducted to identify literature published in English between 1990 and 2016 on google scholar, Ebscohost, PubMed and African Journal Online (AJOL) databases. The search was conducted using the following keywords: "geriatric", "adverse drug reaction", "inappropriate prescribing" "polypharmacy" "drug interactions" "intervention" "Africa" alone or in combination. Thirty-two articles were reviewed, out of which only 9 (28.1%) observational studies were included. Studies on ADRs amongst the geriatric population in Africa settings have essentially been limited to the prevalence of the risk factors. The majority of the studies using the explicit prescribing criteria showed that potential inappropriate prescribing (PIP) is rife in Africa and is a major risk factor for ADRs among the African geriatric population, there is, however, no interventional study towards reducing the ADRs. The validity of the explicit criteria and their relevance in predicting and preventing ADRs among the African geriatric patients has also not been reported. There is a dire need for interventional studies on strategies to reduce ADRs among the geriatric population in Africa.

Keywords: Adverse drug reactions, side effects, African, geriatrics

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Introduction

Adverse drug reactions (ADRs) are an important health concern among the geriatric population, considering their negatives impact on the patients' health outcomes. An ADR is defined as 'any response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of diseases, or for the modification of physiological functions (WHO, 1972). Several risk factors for ADRs among the geriatric population have been identified. These include the inability of the health workers to correctly identify ADRs among the geriatric population, polypharmacy, drug interactions and potential inappropriate medicine prescribing (PIP) (Salwe et al., 2016; Patterson et al., 2012; Viktil al., 2007; Rochon et al., 2005). There are serveral issues linked to the occurrence of ADRs in the elderly people; these include the screening and identification thereof; the appropriateness of the tools used as well as the effectiveness of intervention as explained below.

Identification and screening for ADRs among the geriatric patients

Many health workers lack the technical skill to correctly identify ADRs, especially among the geriatric population. In many cases, ADRs are attributed to 'geriatric syndrome' or diagnosed with a new ailment. The inability to distinguish ADRs from definitive diagnosis of diseases, most times results in the prescribing of another medicine, which increases the likelihood of drug–drug interactions, and aggravate the ADRs (Rochon et al., 2005). Many methods of determining the causality association between a drug and ADR in a specific patient are presently being used in practice. These ADR causality assessment tools are either in form of short validated questionnaires or algorithms. However, the World Health Organisation (WHO) causality assessment tool, developed in conjunction with the Collaborating Centers for International Drug Monitoring, the Uppsala Monitoring Center (WHO-UMC), and the Naranjo probability scales are the most widely applied in clinical practice due to their simplicity (Agbabiaka et al., 2008). The reliability of the Naranjo tool has, however, been a subject of debate among researchers in recent times (Garcia-Cortes et al., 2008). Gallagher et al (2011), using the tool found that some questions in the tool were inappropriate and that the questions contributed significantly to the artificial lowering of the overall score. The implication of this is that many definite ADRs are missed.

Screening of patients at risk of ADRs

The use of ADR risk scores to screen geriatric patients for the identification of the group at risk of ADRs has been proposed. The Brighton Adverse Drug Reactions Risk (BADRI) and the GerontoNet ADR risk score are also commonly used models in clinical practice today (Petrovic et al., 2016). These tools assess many risk factors relating to ADR, with significant consideration for the number of medicines. A "de-prescribing strategy" and the use of "aspirational target method" have also been proposed to reduce polypharmacy in the elderly. De-prescribing is a process of gradual withdrawing or tapering of inappropriate medications to mitigate ADRs (Thompson and Farrell, 2013). Gnjidic et al (2012) in their review of evidence from randomised controlled trials that applied de-prescribing as an intervention strategy to reduce ADRs among the geriatric population revealed that de-prescribing decrease medication usage and cost in some studies but observed that several other intervention studies found no differences in patients' health outcomes and mortality. Evidence for its feasibility in clinical practice is also at present inadequate. Scott and Jayathissa (2010) proposed a strategy which limits the number of drugs to be prescribed to the vulnerable geriatrics to five. This aspirational target has however been shown to contradict many current clinical guidelines for the management of diseases (Topinkova et al., 2012).

Development of screening tool for potential inappropriate prescribing to the geriatrics

It should be noted that explicit criteria that defining potential inappropriate medicines (PIM) in the geriatric populations have been developed to guide physicians towards evidence-based medicine use and prevention of ADRs among the geriatric population in American and Europe (Stephanie et al., 2010; Gallagher and O'Mahony, 2008; Barry et al., 2007; Beers, 1997). The oldest of the tools is the "Beers criteria" which were first developed in 1991. They have since undergone several revisions based on the currently available clinical evidence (AGS, 2015).

These criteria have been widely applied to determine the prevalence of PIP in different clinical settings (Nam et al., 2016; Budnitz et al., 2007; Egger and Bachmann, 2006). However, the relevance of the criteria in reducing ADRs among the elderly population has been very controversial. Many studies that specifically evaluated the association between drugs in the earlier Beers criteria list and the prevalence of ADRs, reported no significant association (Budnitz et al., 2007; Laroche et al., 2007; Onder et al., 2005). Other reports, however, contradict this negative finding (Budnitz et al., 2011; Franceschi et al., 2008; Passarelli et al., 2005; Chang et al., 2005). The lack of reproducibility and failure to produce a consistent association between the Beers criteria PIMs and ADRs in many studies tend to suggest that the criteria may not be adequate in defining ADRs in the geriatric population. The STOPP (Screening Tool of Older Person's potentially inappropriate Prescriptions) and START (Screening Tool to Alert doctors to the Right Treatment) which was developed in 2008 and later reviewed in 2014 identifies with the dual nature of inappropriate prescribing by the inclusion of potential inappropriate omission (PPO) checklist in addition to PIMs list.

Since the release of the criteria in 2008, it has been used to evaluate medication profiles in many settings, including community dwellings, ambulatory and inpatient geriatric care in Asia, Europe and North America (O'Mahoney et al., 2014; O'Connor et al., 2012; Wahab et al., 2012). Hamilton et al (2011) applied the criteria to evaluate the relationship between ADRs and PIM use and reported a significant association between the medicines in STOPP criteria and ADRs. An interventional study that applied the criteria within 3-days of admission also reported a significant reduction in the ADRs and the duration of hospital stay by 72 hours among the study geriatric patients (O' Connor et al., 2012). Other recent screening tools for PIP in the geriatric population include the FORTA (Fit FOR The Aged) list and the ACOVE project. FORTA which was developed in Germany categorises medicines into four based on the degree of evidence of their clinical benefits, efficacy and safety (Wehling, 2009). The tool, though validated by a panel of the geriatricians still need to be assessed for its impact on therapeutic outcome (Kuhn-Thiel et al., 2014). The Assessing Care of Vulnerable Elders (ACOVE) project, apart from specifying medicines that should not be prescribed or need to be carefully monitored after initiation, also identifies quality guides for appropriate medicine administration in the geriatrics (Shrank et al., 2007; Shekelle et al., 2001).

Another effort at reducing PIP is the development of a clinical decision supports system (CDSS) for evaluating the risk of PIM in geriatric primary care patients known as TRIM (Tool for reducing inappropriate medicines) (Niehoff et al., 2016). The tool, when supplemented with direct patient assessment and medical chart review, can generate patient-specific reports on problematic medications for the individual. However, further evaluation of the tool for specificity, reliability and practicability of use in the clinical settings is still needed. Many interventions to reduce

ADRs among the geriatric population have been developed and implemented in developed nations with varying degrees of success; however, to the best of the authors' knowledge, no review of such interventions have been documented in the African geriatric population. Hence, this study was carried out with a view to describe the trends in the prevalence of known risk factors for ADRs among the geriatric population in Africa; and to describe the interventions towards reducing ADRs that have been implemented in geriatric patients in Africa.

Methods

This scoping review was based on the Arksey and O' Malley's (2005) methodology and the modification proposed by Levac et al (2010). A review of the literature on the interventions to reduce ADRs among the geriatric population was carried out. A broad literature search was initially carried out to identify articles on the background to ADRs among the geriatric population in peer-reviewed journals, published in English between 1990 and 2016. The search was later narrowed down to the studies on the African geriatric population. Papers on the classified thematic areas were identified and studied for inclusion in the review. Two thematic areas were identified as being core to the review. They are: (a) the prevalence of the documented risk factors for ADRs among the geriatric population in Africa (b) the interventions targeting the risk factors towards reducing ADRs among the geriatric population. Thus, relevant systematic reviews and research articles on sub-thematic issues such as polypharmacy, drug-drug interactions, inappropriate medicine prescribing, prevalence and identification of ADRs, physicians and pharmacist-led medication chart review and its impact on ADR prevention or reduction were included in the initial search.

The search was conducted using the keywords, "geriatric" "adverse drug reaction", "inappropriate prescribing" "intervention" "irrational" together or as appropriate on google scholar and Ebscohost, PubMed and AJOL. Articles were included in the review if (1) it is a research article reporting primary data collected by the author(s) (2) published between January 1990-December 2016 in a peer-reviewed journal (3) published in English (4) the study populations are geriatric in Africa (5) 60 years and above (6) evaluates any of the identified sub-thematic issues. The selection was not limited to a study design. Articles were excluded if (1) duplicated, the most comprehensive were included (2) it is on economics implication of ADRs among the elderly (3) evaluates ADRs in a specific disease population (4) the full text of the articles were in languages other than English. (5) full text of the article was not accessible (6) Opinion papers or conference proceedings. The identified articles were studied by the principal author but the decision on the article to be included was a joint decision of both the principal author and the co-authors. The risk of bias in the included studies was however not assessed. Data were extracted into a data-charting form and later imported into Excel worksheet. Information extracted from each of the publications include author, year of publication, country of study, study design, population, the focus of the study, the criteria/tool used, outcomes measured, results and conclusion. A descriptive analysis was carried out.

Review findings

Search results

Out of the 216 reports that were initially identified only 32 reported on Africans; 9 (28.1%) of the 32 met the inclusion criteria; 2 (7.4%) which had full articles in French and Arabic were rejected (Figure 1).

Figure 1: The flow diagram for the selection of the included articles
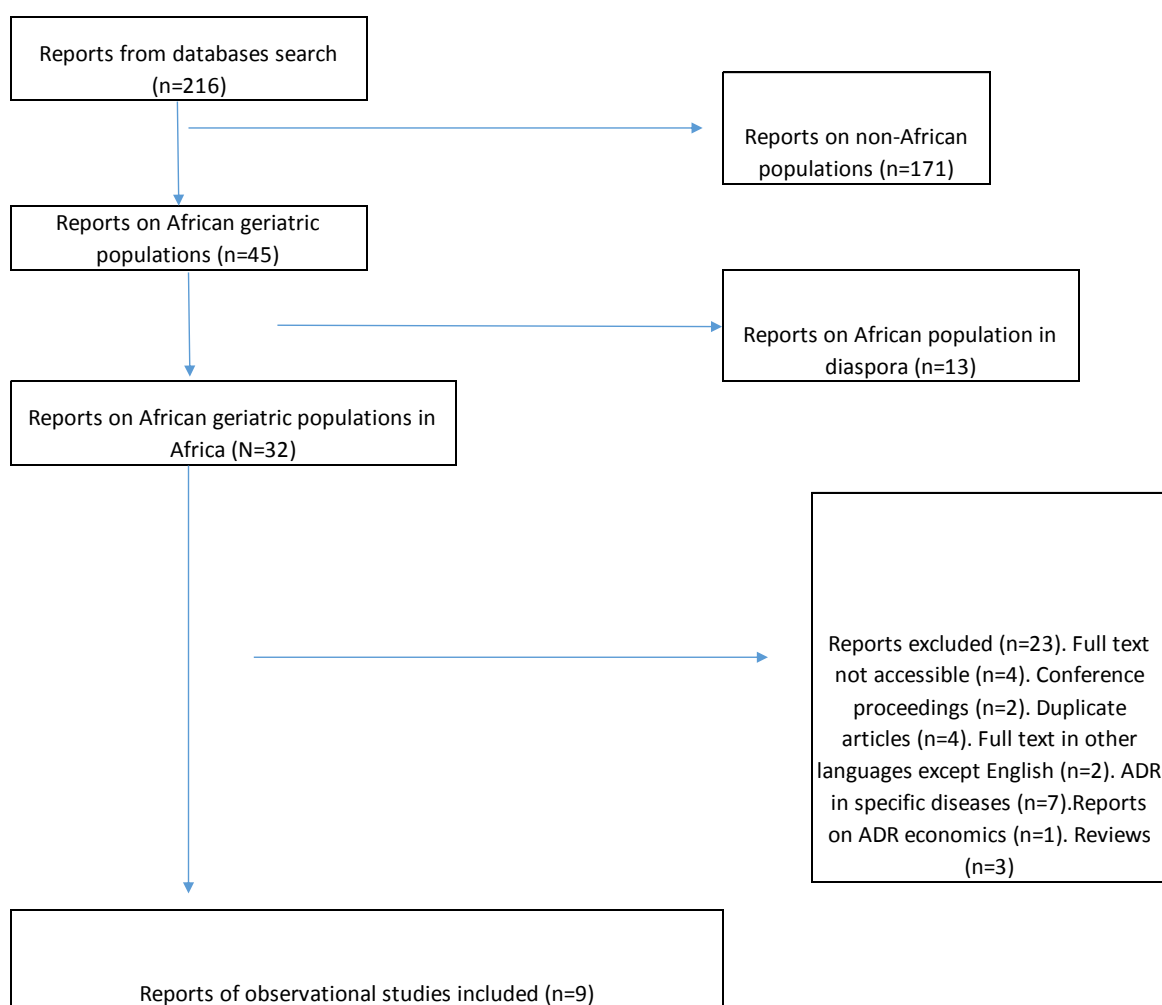
Study characteristics

The included articles 9 (100.0%) were cross-sectional and observational studies involving 2339 (2.1%) elderly outpatient prescriptions; 296 (0.3%) inpatients prescriptions and 109,830(97.6%) prescriptions from pharmacy database. The exact number of the study participants could not be determined due to the likelihood for cross-over between the participants included in the studies that used especially pharmacy database. Only 1(11.1%) articles evaluated the prevalence of drug-drug interactions; 3(33.3%) evaluated the prevalence of polypharmacy and PIP while 8(88.9%) assessed the prevalence of PIP among the elderly. Three (33.3%) articles were from Nigeria. Majority 6(66.7%) of the studies were carried out in a single centre (Table 1).

Table 1: Studies included in the review

Author (year)	Country	Study design	Population	Criteria used	Outcome Measured	Conclusion
Hamza et al (2012)	Egypt	Cross-sectional prospective (Interview and medical chart review)	395 outpatients ≥60 years	Beers criteria 2003	Polypharmacy And PIP	There is a significant relationship between Polypharmacy and PIP
Eze and Olowu (2011)	Nigeria	Retrospective (Chart review)	1000 outpatients' prescription ≥60 years	Beers criteria 2003	Potential inappropriate Prescribing	Prescribing to the elderly was suboptimal
Van Heerden et al (2016)	South-Africa	Retrospective (pharmacy database)	103,420 ≥65 years	Beers criteria 2012	Potential inappropriate Prescribing	PIP is common in elderly prescriptions
Getachew et al (2016)	Ethiopia	Retrospective	156 inpatients ≥65 years	2015 STOPP/START Criteria	Potential inappropriate prescribing of antithrombotic	PIP is less common in hospitalized patients

					therapy.	
Teka et al (2016)	Ethiopia	Cross-sectional (method used not indicated)	140 in-patients ≥60 years	Micromedex online drug interaction reference	Drug-drug interactions	Drug-drug interactions in prescriptions to the elderly is common in the resource-limited setting
Fadare et al (2013)	Nigeria	Cross-sectional prospective	220 outpatients ≥65 years	Beers criteria 2012	Polypharmacy and potential inappropriate prescribing	Polypharmacy and potential inappropriate prescribing are major therapeutic issues in Nigeria
Fadare et al (2015)	Nigeria	Cross-sectional Prospective	350 outpatients ≥65 years	Beers criteria 2012 and STOPP/START Criteria 2015	Potential inappropriate prescribing	Both tools detected potential inappropriate prescribing
Hanan and Hanan (2012)	Egypt	Retrospective	374 outpatients≥65 years	Beers criteria (version not stated)	Potential inappropriate prescribing	Potential inappropriate prescribing was high
Chetty and Gray (2004)	South-Africa	Retrospective	6,410 prescriptions	Beers criteria 1997	Potential inappropriate prescribing and polypharmacy	Potential inappropriate prescribing is rife. Women are more likely to receive inappropriate medicines than male

Discussion

Studies on the intervention to reduce ADRs among geriatric population in Africa are rare. This review did not identify any interventional study towards reducing ADRs among the African geriatric population. The paucity of research in this area in Africa is probably because Africa was regarded as a continent for the young until recently. Most of the studies identified by the review were carried out in the 2000's and it appears little or no reports were available about the topic in the 90's. This review, however, identified 9 observational studies on the prevalence of different risk factors for ADRs among the geriatrics in Africa

Poly-pharmacy

Hamza et al (2012) in a study to determine the prevalence of polypharmacy and PIM use among 395 elderly persons (≥60 years) in rural areas of Egypt showed that polypharmacy (defined as the use of 5 or more drugs) was more than half (56%) while PIM (as defined by 2003 Beers criteria) use was 41% in the population. Another prospective study in Nigeria appears to corroborate this finding. Fadare et al (2013) using a medical chart review of 220 outpatients aged 65 years and above in a rural hospital observed that almost 30% of the population received 5 or more drugs and concluded that polypharmacy was a major concern among the elderly. This review did not identify any reports that explored the relationship between polypharmacy and ADRs among the geriatric population in Africa and no intervention has been reported in this area

Drug interactions in prescriptions to the geriatric population

Polypharmacy is a prominently documented risk factor for ADRs among the geriatrics, majorly due to drug-drug interactions. Teka et al (2016) evaluated the prevalence and the determinants of drug-drug interactions among 140 geriatric patients (≥60 years) admitted to a medical ward of a referral hospital in Ethiopia in 2014. The concurrently prescribed medicines taken by the patients for at least 24 hours were evaluated. They reported that more than 60% of the population had taken drugs with at least one potential drug-drug interaction while 3.6% were exposed to contraindicated drug combinations. In addition, the researchers observed that polypharmacy defined as 5 or more drugs could potentially contribute to the higher risk of drug-drug interactions in the patients. Apart from the population sample size which may be considered small for this study, a prospective longitudinal study to determine the clinical importance of these interactions is needed. Studies on the prevalence of drug-drug interactions in outpatients' prescription are also needed. It is possible that the low prevalence of contraindicated drug combinations reported in this study may be due to special attention usually paid to the inpatients by many prescribers; a luxury not enjoyed by the outpatients in many health facilities in Africa.

Inappropriate medicines prescribing to the African geriatric population

Studies that applied the Beers criteria

The Beers criteria despite the criticism against the earlier versions of its use of "independent of diagnosis", limited transferability and failure to address common potentially inappropriate

prescribing (PIP) such as drug interaction has, nonetheless remains the cornerstone to the optimisation of geriatric therapy in many parts of the globe (Hill-Taylor et al., 2013). The criteria appear to be the mostly applied in the African settings compare to others. This review identified 7 studies that have applied the criteria in 3 different countries on the continent. Chetty and Gray (2004) applied the modified 1997 version of the criteria to prescriptions from the public primary health care facilities and old age homes in South-Africa and reported that 30% of the prescriptions included at least one PIP. Eze and Olowu (2011) evaluated 1000 outpatients' prescriptions in a Nigerian tertiary hospital using the 2003 Beers criteria and reported that more than 45% of the prescriptions contained at least one PIP. They also, in addition, observed that 82.7% of the PIM were medicines of high ADR severity as graded by the criteria. The prescription of PIM of high ADR severity grade in their study appears to be higher when compared with the observation of Hamza et al (2012) who reported 41% prevalence of PIM and 32% prevalence of medicines graded high ADR severity among the Egyptian elderly population (≥60 years) using the same version of the criteria. Hanan and Hanan (2012) in Egypt evaluated 375 outpatients' prescriptions from the family medicine in 2011 and reported that 38.1% of the prescriptions contained PIM. The prevalence of PIM use among the African elderly population in these reports appears to be comparable. This may be an indication of likely similar local prescribing habits and formularies, pointing to the feasibility of regional criteria.

The prevalence of PIM among geriatric population in Africa, however, appears to be on the downward trend judging from the latest reports. Fadare et al (2013) in a prospective study of 220 elderly general outpatients in a rural health facility in Nigeria using 2012 Beers' criteria showed that over a quarter of the patients had at least one PIM. Van Heerden et al (2016) also applied the 2012 version of the criteria on a database of the South African pharmaceutical benefit management company reported that 13% of the patients' prescriptions contained PIM. The authors also observed that female sex was more likely to receive PIMs than the male folk. The observed trend in PIM use among African elderly patients could have been due to likely more awareness of the criteria by the prescribers on the continent as well as the improved sensitivity of the newer versions of the Beers criteria. However, like other studies in other parts of the globe that evaluated the prevalence of PIM using the Beers' criteria, the included studies in this review are limited by their designs. Most were retrospective and use "independent of diagnosis" subset and the earlier versions of Beers criteria which transferability has been questioned (Nam et al., 2016)

STOPP/START criteria

The use of STOPP/START criteria to determine PIP though, very popular in the Europe appears to be relatively uncommon in Africa, probably due to its relative novelty. Only 2 included articles applied the criteria. Getachew et al (2016) applied the 2015 version of the criteria in a retrospective study of 156 hospitalised Ethiopian elderly who were on anti-thrombotic therapy. They revealed that more than 13% of the patients were prescribed at least one PIP. The study, however, did not evaluate the contribution of the PIM to the hospitalisation or patients' length of stay in the hospital. Due to the deficiencies of individual PIP screening criteria and there overlaps in several domains reported by many studies in Europe and America, it is not uncommon to find researchers applying both the criteria for a better identification of PIP (Formiga et al., 2016). It is not surprising to note that almost all the studies that applied Beers and STOPP/START in the

literature criteria were carried out in America and Europe and very little has been reported from the African continent. This probably because the tools were developed in these countries and appear to be specific for the countries of their origin.

Comparison of the Beers criteria and STOPP/START criteria

The review identified only one study that compared the explicit criteria in Africa. Fadare et al (2015) in a study to compare the 2012 Beers criteria with 2015 STOPP/START criteria in determining PIP among 350 elderly patients attending the outpatient clinics of two tertiary hospitals in Nigeria, reported that the Beers criteria detected more PIP than the STOPP/START criteria (30.3% against 15.7%). This contradicted many reports from the developed countries (Ubeda et al., 2012; Hamilton et al., 2011; Ryan et al., 2009; Gallagher et al., 2008). This observation by the Fadare and colleagues lays credence to the need for the validation of the criteria in the African settings. It is worthy of note that in all the studies that applied the Beers and STOPP/START criteria among African geriatric populations, the criteria were not validated. There are potential challenges associated with invalidated criteria in Africa. These include the possibility that of some of the medicines listed in the criteria may not be available on the African continent due to the difference in local prescribing habits and formularies. In addition, some of the listed medicines in the criteria may also not have the same adverse effect in the African population due to genetic and other variations. Furthermore, none of the studies evaluated the relationship between PIM listed in the criteria and the ADRs. The contributions of the drugs listed in the criteria to potential drug-drug interactions in diseased elderly patients were also not assessed. In addition, the perceptions and attitude of the prescribers on the continent towards the adoption and implementation of the criteria have not been evaluated.

Limitations

Studies/review of this nature can be difficult to understand for the reason to extend research results beyond the setting in which the study was conducted. It is difficult to establish validity, because to generalize results from already conducted studies to the general population may be difficult to compare.

Conclusions

Reports of intervention to reduce ADRs among the geriatric patients in Africa are limited. Many of the efforts in this regard have been on the identification of the causes of the ADR using the explicit criteria for PIP. Studies on the validity of the criteria and its relevance to predicting and preventing ADRs among the African geriatric patients are needed. The development of regional criteria from the modified Beers criteria (apparently the most applied criteria on the continent) will be a right step in the right direction. Intervention studies towards reducing the ADRs among the geriatric population on the African continent are also needed.

Declaration of conflict of interest

We declare that there is no conflict of interest in relation to this study.

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