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Challenges in the Management of Hypertension in Older Populations

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Abstract

The prevalence of hypertension increases with age making it a significant health concern for older persons. Aging involves a range of physiological changes such as increases in arterial stiffness, widening pulse pressure, changes in renin and aldosterone levels, decreases in renal salt excretion, declining in renal function, changes in the autonomic nervous system sensitivity and function and changes to endothelial function all of which may not only affect blood pressure but may also affect individual response to pharmacotherapy used to manage hypertension and prevent end organ damage and other complications associated with poor blood pressure control.

Unlike many chronic conditions where there is limited evidence for management in older populations, there is good evidence regarding the management of hypertension in the elderly. The findings from multiple large, robust trials have provided a solid evidence-base regarding the management of hypertension in older adults, showing that reduction of blood pressure in older hypertensive populations is associated with reduced mortality and morbidity. Diuretics, agents action on the renin angiotensin system, beta blockers and calcium channel blockers have all been well studied in older populations both in view of the benefits associated with blood pressure lowering and the risks associated with associated adverse events. While all antihypertensive agents will lower blood pressure, when managing hypertension in older persons the choice of agent is dependent not only on the ability to lower blood pressure but also on the potential for harm with older persons. Understanding such potential harms in older populations is essential with older persons experiencing increased sensitivity to many of the adverse effects such as dizziness associated with the use of antihypertensive agents.

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Despite the wealth of evidence regarding the benefits of managing hypertension in the old and very old, a significant proportion of older individuals with hypertension have suboptimal BP control. While there is good evidence supporting blood pressure lowering in older antihypertensive agents, these have not yet been optimally translated fully into clinical guidelines and clinical practice. There appear to be considerable differences between guidelines in terms of the guidance given to clinicians. Differences in interpretation of the evidence, as well as differences in study design and populations all contribute to differences in the guideline recommendations with respect to older populations, despite the strength of the underlying scientific evidence. Differences around who is considered "old" and what BP targets and management are considered appropriate may lead to confusion among clinicians and further contribute to the evidence-practice lag.

Keywords
Hypertension • Pharmacotherapy • Guidelines • Antihypertensive • Aged • Older • Drug therapy

Hypertension is the leading modifiable cause of mortality worldwide. The prevalence of hypertension increases with age making it a significant health concern for older persons. Unlike many chronic conditions, there is good evidence regarding the management of hypertension in the elderly exists and pharmacotherapy is the mainstay of treatment for most patients. Given predicted international increases in the elderly population and the wealth of evidence regarding management of hypertension in the elderly, understanding how the risks associated with hypertension increase with age as well as how physicians currently manage older patients with increased blood pressure is important. Furthermore, insight into current barriers to the provision of optimal management is essential if we are to meet the health needs of the growing older population.

1 Who Is Old?

Internationally the proportion of the population that is considered older is increasing. In 1950, 8 % of the population was aged over 65 years, this increased to 10 % in 2000 and is predicted to exceed 20 % by 2050.(Department of Economic and Social Affairs United Nations 2002) It has been estimated that life expectancy for those aged 65 years has increased by 19 years for men and 17 years for women over the past century.(Rai and Mulley 2007) Projections indicate that by 2050 there will be over 2 billion older persons worldwide.(Halter 2009) However while there is international agreement that the population is aging there is less agreement regarding who should be considered "old". (Gambert 1994) Aging encompasses a number of domains and different definitions focus on different aspects of the aging process. Chronological age is the simplest and most commonly used parameter to define age and refers simply to the number of years since birth. Yet aging is multidimensional and not just related to the duration of time in an individual's life. Physiologically, aging refers to the general and gradual changes that human body experiences over time. Physiological aging is characterized by declining functional capacity, decreasing fertility and increased mortality all of which may vary from individual to individual. (Kirkwood and Austad 2000; Masoro and Austad 2006) Such variation among older populations and how it affects their response to

pharmacotherapy is one of the challenges facing clinicians in the management of hypertension among older populations.

2 Hypertension and Aging

Population aging presents a number of healthcare challenges. There are implications in terms of resources and funding, as well as in the type of care that is delivered. Non-communicable chronic diseases such as cardiovascular disease currently account for almost two-thirds of deaths worldwide. (Mathers and Loncar 2006; Daar et al. 2007) Cardiovascular disease contributes significantly to the disease burden, disability and death in both developed and developing countries (Beaglehole et al. 2008; Murray and Lopez 1997; Yang et al. 2008) with an increasing burden among the elderly..(Daar et al. 2007; Murray and Lopez 1997) Despite predicted increases in population aging, The World Health Organization (WHO) has predicted that ischemic heart disease and stroke will remain among the leading causes of death worldwide. (Mathers and Loncar 2006) Hypertension is a major risk factor for cardiovascular disease (Menotti et al. 2004; Lim et al. 2013), affecting up to one billion individuals internationally (Chobanian et al. 2003) (Kumar 2013). It is one of the leading cause of death worldwide (The World Health Organisation 2016). The prevalence of hypertension increases with age (Fagard 2002), with approximately 30 % of the population aged under 60 years being considered hypertensive. Once we start looking at older populations, the prevalence of hypertension doubles to over 60 % for those aged over 60 years, with even higher prevalence with further aging as demonstrated by data from both the UK Framingham study (Kannel and Gordan 1978; Vasan et al. 2002; Beckett et al. 2012) and the US National Health and Nutrition Survey (NHANES) (Lloyd-Jones et al. 2005). The NHANES data demonstrates that increases in hypertension prevalence begin in adulthood, with the prevalence doubling between the ages of 20 and 40 years, and doubling again between 40 and 60 years (Kannel and Gordan 1978), while the Framingham study showed that this pattern continues with ongoing aging, with the prevalence of hypertension increasing from 27.3 % in those aged $\geq$ 60 years to 74.0 % in those aged over 80 years (Vasan et al. 2002).

Gender differences in the prevalence of hypertension have been noted in both younger and older populations. A number of studies have shown found that while the prevalence of hypertension is higher in younger males, this reverse after the age of 60, when the prevalence in females is greater than that in males (Halter 2009; Franklin et al. 1997; Mann 1992; Hajjar and Kotchen 2003; Primatesta and Poulter 2004; Trenkwalder et al. 1994; Gambassi et al. 1998).

Differences in the hypertension phenotype with respect to increases in systolic (SBP) compared with diastolic blood pressure (DBP) have also been reported in older hypertensive populations. Both systolic (SBP) and diastolic blood pressure (DBP) increase with age, (Franklin et al. 1997) however it has been proposed that DBP may plateau or even decrease from the age of 60 years, leaving the SBP to increase (Franklin et al. 2001). Such differences may account for the increase in isolated systolic hypertension that is noted among older populations. Increases in hypertension among older persons may be due to pathophysiological changes associated with aging such as increased peripheral vascular resistance due to arterial stiffening (Franklin et al. 1997; Mitchell et al. 2004). This increase in arterial stiffness with ageing is proposed to alter the normal hemodynamic patterns causing an increase in pulse wave velocity which is an index of arterial stiffness and a widening pulse pressure may account for age related decreases in DBP and increases in SBP (Mann 1992; Mitchell et al. 2004; Pinto 2007; Mackey et al. 2002). Other age related factors such as the changes in renin and aldosterone levels, decreases in renal salt excretion, declining in renal function, changes in the autonomic nervous system sensitivity and function and changes to endothelial function may further contribute to the increases in hypertension seen with aging (Halter 2009; Weinberger 1996; Fliser and Ritz 1998; Wallace

et al. 2007). Age related life style changes such as decreased physical activity, changes in body fat composition, high sodium intake and obesity may further contribute to the development of hypertension among older persons. Moreover a synergistic effect on the risk of hypertension has been observed when multiple factors exist together (Halter 2009; Carretero and Oparil 2000; MacMahon et al. 1984; Barreto et al. 2001).

3 Pseudohypertension

Pseudohypertension is occasionally observed in older persons. In pseudohypertension, measurement of blood pressure using a sphygmomanometer results in a falsely elevated reading.(Kleman et al. 2013) This phenomenon is more common in older persons due to increased arterial stiffness, which results in falsely high reading upon blood pressure measurement due to the inability of the arteries to compress. Pseudohypertension is estimated to affect up to 7 % of patients with resistant hypertension (Kleman et al. 2013) and should be considered when older patients presenting with consistently elevated blood pressure over time but who show no signed of end organ damage or in those who treatment with antihypertensive agents result in ongoing symptoms of hypotension. In patients for whom pseudohypertension is suspected an intra-arterial blood pressure measurement is required.

3.1 Pharmacological Management of Hypertension in Older Populations

Unlike many conditions where limited evidence exists for management of those aged over 65 years due to the exclusion of older populations from clinical trials,(White 2010; Devlin 2010) the findings of multiple large, robust trials have provided a solid evidence-base regarding the management of hypertension in older adults. Adverse outcomes associated with poor blood pressure (BP) control in older persons have been well documented. A Cochrane review of 12 clinical trials showed that the management of hypertension in people aged 60 years and over was associated with a reduction in mortality (Relative Risk (RR)) = 0.9, 95 % confidence interval ((CI) 0.84–0.97).(Musini et al. 2009) The same review reported pharmacological management of hypertension in older adults was associated with significant reductions in both cardiovascular (RR = 0.77, 95 % CI 0.68–0.86) and cerebrovascular mortality (RR = 0.66, 95 % CI 0.53–0.82). (Musini et al. 2009) While life-style interventions are generally considered first-line for the management of all persons with hypertension, the majority of hypertensive patients, including older persons, will require pharmacotherapy to adequately control their blood pressure (Wallace et al. 2007). There have been a number of large well-conducted clinical trials exploring pharmacological management of hypertension in older populations and there is good evidence for the use of a variety of different antihypertensive agents in the management of hypertension in older persons (Pimenta and Oparil 2012).

3.1.1 Thiazide and Thiazide – Like Diuretics

Thiazides diuretics are one of the oldest drug classes used in the treatment of hypertension. (Huebschmann et al. 2006) Evidence of their effectiveness in lowering BP and preventing the cardiovascular and cerebrovascular adverse outcomes associated with hypertension in older people has been provided by several clinical trials, including the Hypertension in the very elderly trial (HyVET) (Beckett et al. 2012), the Swedish Trial in Old Patients with Hypertension (STOP) (Dahlöf et al. 1991; Hansson et al. 1999) and the Antihypertensive and Lipid-Lowering Treatment to prevent Heart Attack Trial; (ALLHAT) (Officers et al. 2002) studies While not all of these studies specifically recruited older participants, the mean participant age for all 3 was over 65 years, making their findings particularly pertinent to older populations.

Use of thiazide and thiazide like diuretics for the management of hypertension in older persons

has declined over the past decade (Primatesta and Poulter 2004; Trenkwalder et al. 1994; Triantafyllou et al. 2010; Prencipe et al. 2000; Psaty et al. 2002). There are a number of factors that may have contributed to this decline including increased use of other non-thiazide diuretics, particularly by older persons with complicated hypertension (Van Kraaij et al. 1998) the advent of newer antihypertensives such as Calcium channel blockers (CCBs) and agents acting on the Renin Angiotensin System (RAS) and caution by prescribers due to increased risk of potential adverse drug reactions associated with the use of thiazide diuretics in frail, older persons (Onder et al. 2001; Moser 1998). Despite this general decline, the use of thiazide diuretics for the management of hypertension in the older individual remains high (Bromfield et al. 2014; Rodriguez-Roca et al. 2013; Tu et al. 2006), especially in fixed-dose combination products where they are among the most commonly used antihypertensive agents (Primatesta and Poulter 2004; Trenkwalder et al. 1994; Triantafyllou et al. 2010; Prencipe et al. 2000; Rodriguez-Roca et al. 2013; Svetkey et al. 1996).

3.1.2 Agents Acting on the Renin-Angiotensin System (RAS)

There are three main three antihypertensive classes that act on the RAS. These are the angiotensin blocking agents (ARBs), the Angiotensin converting enzyme inhibitors (ACEI) and the direct renin inhibitors (DRI). The use of both ARBs (Triantafyllou et al. 2010; Bromfield et al. 2014; Rodriguez-Roca et al. 2013) and ACEIs (Primatesta and Poulter 2004; Trenkwalder et al. 1994; Triantafyllou et al. 2010; Psaty et al. 2002; Bromfield et al. 2014; Rodriguez-Roca et al. 2013; Svetkey et al. 1996; Barker et al. 1998; Prince et al. 2012) in older populations has increased over recent years and now surpasses the use of many other antihypertensive classes. The increase in use of these agents for the management of hypertension in older populations has been supported by clinical trials such as the Second Australian National Blood Pressure (ANBP2) (Wing et al. 2003). ANBP2 demonstrated that ACEI were superior to thiazide diuretics in terms of cardiovascular outcomes in a population comprising 6083 older persons aged between 65 and 84 years. Despite benefits in cardiovascular outcomes no difference between ACEI and diuretics in terms of all cause mortality was observed. (Wing et al. 2003) In addition to increased use as monotherapy for the management of hypertension among older individuals, the use of ACEIs and ARBs in combination with other antihypertensive medications has also increased over recent years (Primatesta and Poulter 2004; Trenkwalder et al. 1994; Triantafyllou et al. 2010; Rodriguez-Roca et al. 2013; Svetkey et al. 1996). In contrast the uptake of aliskiren, a direct renin inhibitor has been slow. Aliskiren has been approved for use in older populations with hypertension since 2007 yet use of daily practice is limited in comparison to other antihypertensive agents (Bromfield et al. 2014; Rodriguez-Roca et al. 2013). The slow uptake of aliskiren for use among older persons may be in part due to concerns around limited efficacy and a poor safety profile (Parving et al. 2012; Gheorghiade et al. 2013).

3.1.3 Calcium Channel Blockers (CCBs)

Since the introduction of CCBs, the prescribing pattern of this antihypertensive medication class in older populations has increased both as monotherapy and combination therapy (Trenkwalder et al. 1994; Prencipe et al. 2000; Bromfield et al. 2014; Svetkey et al. 1996; Barker et al. 1998) and use remained steady until the mid 1990s (Psaty et al. 2002). Despite publication of the findings from the Systolic Hypertension in the Europe Trial (Syst-Eur) in 1997, which showed that treating 1000 patients for 5 years with a CCB prevented 29 strokes or 53 myocardial infarctions (MI), a decline in the use of CCB has generally been noticed in older and the very old patients since the mid-1990s. (Primatesta and Poulter 2004; Triantafyllou et al. 2010; Rodriguez-Roca et al. 2013) This decline may in part be due safety concerns with the use of CCBs older populations, including increased risk of cancer, MI and gastrointestinal haemorrhage with long-term use (Pahor et al. 1996a, b; Maclure et al. 1998).

3.1.4 Beta Blockers (BBs)

Beta blockers have been among the most commonly prescribed antihypertensive agents since their introduction into hypertension treatment (Psaty et al. 2002; Svetkey et al. 1996; Barker et al. 1998) However in recent years, use in older persons has declined following publication of a meta-analysis questioning the efficacy of the BB for hypertension and highlighting safety concerns, with an increased risk of stroke reported with use as monotherapy. (Larochelle et al. 2014) Consequently use of BBs for the management of hypertension in older populations has declined particularly as monotherapy for uncomplicated hypertension management. (Primatesta and Poulter 2004; Trenkwalder et al. 1994; Triantafyllou et al. 2010; Prencipe et al. 2000; Onder et al. 2001).

3.1.5 Alpha Blockers

While several studies have shown a slight increase in the use of alpha blockers in the management of hypertension in the old and very old (Psaty et al. 2002; Bromfield et al. 2014) in general, there has been a downward trend in the use of these agents (Trenkwalder et al. 1994; Rodriguez-Roca et al. 2013; Svetkey et al. 1996; Barker et al. 1998). This decline in use may be due to the poorer adverse effect profile of the alpha-blockers for older persons in comparison to newer agents such as the ACEI and ARBs, as well as to a lack of mortality evidence when compared with other antihypertensive agents.

3.1.6 Nitrates

While nitrates have an important role in the management of coronary artery disease, the lack of studies in older populations using nitrates for the management of hypertension have resulted in these drugs no longer having a major role in the management of hypertension. There has been some discussion around the potential benefit of nitrates for the management of hypertension in older populations, however to date they are not currently recommended in the main hypertension guidelines (Weber et al. 2014; Mancia et al. 2013a).

3.1.7 Choice of Antihypertensive Agent in Older Populations

While all antihypertensive agents will lower blood pressure, when managing hypertension in older persons the choice of agent is dependent not only on the ability to lower blood pressure but also on the potential for harm with older persons showing an increased sensitivity to many adverse effects. In general low dose thiazides, calcium channel blockers or agents acting on the renin angiotensin system appear to present the lowest risks for older populations.

3.2 Barriers to the Optimal Management of Hypertension in Older Persons

Despite the wealth of evidence regarding the benefits of managing hypertension in the old and very old, a significant proportion of older individuals with hypertension have suboptimal BP control (Falaschetti et al. 2014). A number of barriers to optimal blood pressure control in older persons have been identified. These barriers can be considered as system, prescriber or patient related (Alhawassi et al. 2015).

System–related barriers affecting blood pressure control in older populations include the variability in treatment recommendations for this population. (Schäfer et al. 2012; Psaty et al. 1995). While a number of clinical trials have been conducted in older populations, the extent to which this evidence has been incorporated into treatment guidelines and translated into practice remains unknown.

While older persons are often excluded from clinical trials for many conditions (Gross et al. 2002; Heiat et al. 2002), multiple large, well-designed trials exploring hypertension in older persons have been conducted (Dahlöf et al. 1991; Bulpitt et al. 2011). A Cochrane review published in 2009 reported 15 studies ($n = 24{,}055$ subjects) exploring the management of hypertension in those aged over 60 years (Musini et al. 2009). These findings demonstrated the considerable benefits of actively managing hypertension in older populations, as well as

providing evidence regarding appropriate blood pressure (BP) targets and pharmacotherapy for this population.

Physician related barriers include differences in physician attitudes towards the risks and benefits of managing hypertension in older persons as well as differences in interpretation of the evidence. (Trenkwalder et al. 1994; Rodriguez-Roca et al. 2013).

Establishing the evidence is the first step in ensuring optimal care, yet it is well documented that there is a considerable lag in the translation of scientific evidence into current clinical practice. Moreover, incorporating the latest evidence into daily practice is something many physicians often find problematic (Spranger et al. 2004). One strategy aimed at minimizing the evidence-practice gap is the development and implementation of evidence based guidelines. Guidelines have the potential to improve care and improve patient outcomes (Grimshaw and Russell 1993) and multiple international guidelines for the management of hypertension exist.

Management of hypertension in older persons is one area where there appear to be considerable differences between guidelines in terms of the guidance given to clinicians. Differences in interpretation of the evidence, as well as differences in study design and populations all contribute to differences in the guideline recommendations with respect to older populations, despite the strength of the underlying scientific evidence. Differences around who is considered "old" and what BP targets and management are considered appropriate may lead to confusion among clinicians and further contribute to the evidence-practice lag and a recent systematic review of international hypertension guidelines found considerable variation in recommendations regarding the management of hypertension (Alhawassi et al. 2014).

4 Who Is Considered "Older" in International Guidelines?

In the 13 international guidelines for the management of hypertension included in the systematic review, three different age ranges were used to define older populations. Approximately half of the guidelines defined older populations as those aged 80 years or older, while other guidelines defined older populations as those above 65 years and one guideline included individuals aged over 60 years as older. To further add to the discussion, In the American Society of Hypertension/International Society of Hypertension (ASH/ISH) guideline (Weber et al. 2014), recommendations were given for the "middle aged to elderly population" which was defined as 55–80 years. The European Society of Cardiology (ESC) (Mancia et al. 2013a) and National Institute of Clinical excellence (NICE) (Jaques et al. 2013) guidelines referred explicitly to differing needs among older persons and provide recommendations for older populations aged below 80 years and those aged above 80.

5 BP Targets for Older Persons in the International Guidelines

In most international guidelines the same BP targets were used for younger and older populations. (Alhawassi et al. 2014) For the guidelines that did define hypertension, there was consensus that a higher BP reading was more acceptable in older persons with hypertension and that tighter blood pressure control could be considered for older populations. The majority of guidelines that provided specific BP targets for older populations defined a BP of 140/90 mmHg to be consistent with hypertension. The only guideline to provide a different BP target was the ASH/ISH guideline which specifying a slightly higher target BP of 150/90mmHG (Weber et al. 2014).

Despite the plentiful evidence supporting active management of hypertension in older persons, no guidelines specifically dedicated to the management of hypertension in the older populations were identified in the review. Specific information regarding the diagnosis and management of hypertension in older populations was included in all of the international hypertension guidelines included in the review,

however there was considerable variation in the depth and scope of the recommendations. Such variation may reflect differences in the populations included in the landmark hypertension in older population studies. The HYVET (Hypertension in the very Elderly) (Bulpitt et al. 2011) recruited participants aged over 80, while the SHEP (Systolic Hypertension in the Elderly) (Perry et al. 1989) recruited those 60 years and over, and the STOP study (Swedish Trial in Old patients with Hypertension) those aged between 70 and 84 years (Dahlöf et al. 1991).

In general, there is consistency across all guidelines regarding recommendations that treatment be commenced in older individuals when systolic BP readings were above 140–150 mmHg and treatment titrated to achieve a target BP at the same level. However, despite the guideline recommendations debate continues regarding the optimal BP targets in older populations. Two Japanese studies, the JATOS (Japanese trial to assess optimal systolic BP in older hypertensive patients) (Group 2008) and VALISH (Valsartan in Elderly Isolated Systolic Hypertension) (Ogihara et al. 2010) studies failed to show an additional benefit in treating older individuals to a target of 140 mmHg systolic compared to a target of 160 mmHg, highlighting the clinical uncertainty in this area.

The major international hypertension treatment guidelines (Weber et al. 2014; Jaques et al. 2013; National Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee) 2010; James et al. 2014; Mancia et al. 2013b; Dasgupta et al. 2014; Luehr et al. 2012; Shimamoto et al. 2014) all support the use of pharmacotherapy for the management of hypertension in the elderly reflecting the findings of a 2008 meta-analysis that concluded that the benefits of pharmacotherapy for managing hypertension in older individuals is comparable to that in younger persons (Turnbull et al. 2008).

While most guidelines mentioned that tolerability of pharmacotherapy may be an issue for older persons, only two guidelines in this review discussed specific adverse effects in the elderly such as orthostatic hypotension or falls. Antihypertensive medications have been linked with adverse outcomes in a number of studies (Tinetti et al. 1995; Rejnmark 2013; Sato and Akazawa 2013)

Given global increases in life expectancy, there is a need to re-consider how we define "older" populations as well as a need to ensure they are represented in clinical trials and included in evidence based clinical treatment guidelines.

6 Adverse Reactions and Antihypertensive Medications in the Elderly

One potential age related barrier associated with antihypertensive pharmacotherapy is an increased risk of adverse reactions (Monane et al. 1997). Adverse drug reactions (ADRs) are a significant health care problem, associated with significant morbidity and mortality worldwide. The World Health Organization (WHO) define an ADR as "the response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease, or for modification of physiological function". (National Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee) 2010) ADRs have a significant impact on heath, with between 5 and 7 % of all hospitalisations being due to an ADR and with a further 10–20 % of all hospitalized patient experiencing an ADR during their hospital admission (Davies et al. 2007, 2009; Pirmohamed et al. 2004). The burden associated with ADRs is considerable. Up to 6 % of all ADRs are fatal or have serious consequences (Moore et al. 1998; Wester et al. 2008; Lazarou et al. 1998; White et al. 1999).

Older persons have been shown to be at a high risk of ADRs. (Alhawassi et al. 2014) A systematic review estimated that at least one in ten older persons admitted to hospital will experience an ADRs, either leading to hospitalization or during hospitalization (Alhawassi et al. 2014). The very old, those aged over

80 years of age, are at an even higher risk of experiencing an ADR with up to 40 % of older adults medicine users experiencing an ADR. (Edwards and Aronson 2000; Talbot and Waller 2004) The increased risk of ADRs associated with aging is multifactorial. Physiological changes affecting pharmacokinetics and pharmacodynamics as well as increased clinical complexity, multimorbidity and polypharmacy have all been associated with an increased risk of an ADR in the elderly (Alhawassi et al. 2014).

Cardiovascular medicines, including antihypertensive medications have been associated with an increased risk of ADRs in the general adult population (Pirmohamed et al. 2004; Bond and Raehl 2006; Onder et al. 2002; Grossman and Messerli 2006; Stas et al. 2006; Bates et al. 1999; Field et al. 2004; Gribbin et al. 2010; Tinetti et al. 2014; Rende et al. 2013). One study found that over two thirds of adults using antihypertensive therapy has experienced an adverse reaction to their medication (National Heart Foundation of Australia (National Blood Pressure and Vascular Disease Advisory Committee) 2010; Olsen et al. 1999). Side effects associated with antihypertensive agents are well documented in the product information for each medication and it is well known that older persons are more sensitive to a number of antihypertensive side effects, such as hypotension. The Hypertension Detection and Follow-up Program study, although not mainly designed to study ADR, found that about 33 % patients had experienced at least one drug side effect and required antihypertensive medications discontinuation (Curb et al. 1985).

There have been a number of concerns regarding both the role of poorly controlled blood pressure and the use of antihypertensive agents with a number of common conditions in the elderly such as dementia and falls (Dharmarajan and Dharmarajan 2015). The use of centrally acting ACEI has been associated with reduced rates of cognitive decline (Gao et al. 2013). A systematic review of 18 observation studies comprising 1.3 million older individuals reported similar findings, suggesting that the benefits in terms of cognitive function appeared associated with both CCBs and those medicines affecting the renin angiotensin system (Rouch et al. 2015). Given that these findings are based upon observational data it remains uncertain if the observed benefit in terms of cognitive decline is directly due to the use of the individual antihypertensive agents or if it is a benefit of optimising blood pressure control in older individuals.

Falls are a common adverse occurrence that increases in prevalence with age. While multiple factors such as cognitive function, comorbid conditions, functional status and environment may play a role in falls (Dharmarajan and Dharmarajan 2015), antihypertensive medications have long been recognised as contributing factors (Butt et al. 2013; Callisaya et al. 2014; Gribbin et al. 2011; Lee and Goeres 2015). However the evidence around the role of antihypertensive medications in falls is conflicting. A large meta-analysis exploring if any of the commonly used antihypertensive agents (thiazide diuretics, ACEI, ARBs, CCBs and BB) were associated with an increased risk of falls failed to confirm the association. Despite these findings there has been multiple studies demonstrating a dose dependent significant increase in the risk of falls with the use of antihypertensive medications across multiple antihypertensive agents (Butt et al. 2013; Callisaya et al. 2014; Gribbin et al. 2011; Lee and Goeres 2015). Given that all antihypertensive medications may cause hypotension, and that older persons appear to have an increased sensitivity to such effects, balancing the benefits of optimal blood pressure control with minimization and avoidance of adverse effects remains a challenge in clinical practice.

7 Conclusions

Antihypertensive medications are widely used by older persons and have critical role in decreasing hypertension related mortality and morbidity for older persons. However, achieving optimal blood pressure control may be challenging among older populations. Despite considerable high quality evidence regarding the benefits of blood pressure management in older persons, translation of this

evidence into treatment recommendations in clinical guidelines remains problematic internationally. Furthermore increased medication related harm and adverse reactions associated with the aging further add to complexity to the optimal management of hypertension in older populations.

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