

Do You Know What FRIDs Are?

By: Mr. Mohd Shah Rezan bin Hamzah & Assoc. Prof. Dr. Mahmathi Karuppanan

Falls present a noteworthy public health issue due to their association with many complications, including fall-related injuries, psychological and social consequences, increased healthcare costs, and mortality. In the United States (U.S.), it was reported that more than one out of four older people aged 65 and older fell annually [1]. According to the Centers for Disease Control and Prevention (CDC), death rates following falls for older people in the U.S. increased by 30% from 2007 to 2016, and were expected to rise by 2030, with the anticipation of seven fall deaths every hour. Falls among older people are a common source of high injury severity, such as broken bones and head injuries and mortality [2]. Falls are also the most common cause of traumatic brain injury in the U.S., which may result in death [3]. According to the CDC, 3 million older people are treated in emergency departments each year for fall injuries, and nearly 1 million older people are hospitalized each year for head injuries and hip fractures due to falls. This situation has resulted in the U.S. spending more than USD 50 billion on total medical costs associated with falls [4].

The occurrence of falls in older people can be attributed to factors such as advanced age, age-related health conditions, physical instability, limited mobility, the presence of numerous chronic illnesses, hazardous home or environmental conditions, and the use of medications. Among these factors, medications contribute to an increased risk of falls and are potentially modifiable. Exposure to two or more Fall Risk-Increasing Drugs (FRIDs) is associated with an elevated risk of falling [5]. Additionally, higher fall risk was observed in patients with polypharmacy, defined as the prescription of five or more medications [6,7], as well as in individuals taking only a few medications [6,8]. This was further supported by a study conducted among the elderly population of England, which found that the risk of falls was 21% higher among those taking five or more drugs and 50% higher among those taking more than ten drugs, compared to those who did not have polypharmacy [9]. These findings indicate that the combination of multiple prescription medications can potentially increase the risk of falling due to adverse reactions [10].

FRIDs encompass a range of medications that have been identified as posing an elevated risk of falls among older people. These medications include antihypertensives, anticholinergics, antihistamines, sedative-hypnotics, antipsychotics, antidepressants, opioids, and non-steroidal anti-inflammatory drugs (NSAIDs) [11]. These drugs increase falls mainly through their pharmacological actions which can adversely affect the central nervous system (CNS), cardiovascular system (CVS), and musculoskeletal systems (MSS) [12]. These medications act on the CNS and cause sedation, hypnosis, psychomotor impairment, and confusion. Anticholinergics such as antihistamines, antiemetics, and antispasmodic can cause cognitive and vision impairment, hence increasing the risk of

falling in older people [13]. Furthermore, medications that act on the CVS also put older people at higher risk of falling due to orthostatic hypotension effects. This includes beta-blockers, alpha-blockers, CCBs, diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and nitrates [14]. All drugs that can cause orthostatic hypotension are classified as orthostatic drugs (ODs) [15]. Antidiabetic agents such as insulin and oral insulin-secretagogues, particularly sulfonylurea, can cause hypoglycemia, thereby increasing the risk of falling in older people [12]. A case-control study was conducted in a specific country among fallers and non-fallers living in assisted living facilities to assess the relationship between medication use and falls. The study found that the use of vasodilators, diuretics, alpha-blockers, opioids, antipsychotics, and sedative-hypnotics was significantly more common in fallers than non-fallers [10].

Psychotropics

According to meta-analyses and systematic reviews, psychotropic medications such as antipsychotics, antidepressants, and benzodiazepines (BZDs) are associated with a significant risk of falling, with odds ratios (OR) ranging from 1.26 to 6.30 [16-19]. BZDs were identified as the most often prescribed FRIDs among older people residing in the community in Spain, accounting for 28.9% of prescriptions [20], and the risk of falling is increased with the concomitant use of different types of BZDs, sudden increments in BZD dosages, and the use of short-acting BZDs [21]. The utilization of BZDs such as lorazepam, alprazolam, and zolpidem were seen as potentially unsuitable for older people when above the maximum recommended doses for the geriatric population, as outlined in Beer's criteria [22].

Antihypertensives

The use of loop diuretics and alpha-adrenoreceptor antagonists has a significantly higher risk of falling in older people, as indicated by the adjusted OR of 1.36 (1.17–1.57) with $p = 0.002$ and 1.62 (0.76–3.45) with $p = 0.02$, respectively. The adjusted OR for beta-blocking agents, ACE inhibitors, and angiotensin II antagonists were 0.88 (0.80 - 0.97) with $p = 0.004$, 0.91 (0.78 - 1.08) with $p < 0.001$, and 0.87 (0.72 - 1.06) with $p = 0.004$, respectively, for the risk of falls in the elderly [23]. A similar study determined that there was no significant association between the use of calcium channel blockers (CCBs) and falling. This conclusion is supported by the adjusted OR of 1.00 (95% confidence interval: 0.80–1.24) and a p -value of 0.02 [23]. However, a research study conducted among older people residing in homes in Northern Finland discovered that the utilization of CCBs was associated with a relatively low likelihood of experiencing falls. This was evidenced by the incidence rate ratio (IRR) of 0.92 (0.64–1.33) [24].

Anticholinergics

Drugs with potent anticholinergic properties such as first-generation antihistamines, antipsychotics, tricyclic antidepressants, drugs for Parkinson's disease, and urological agents are recognized as potentially inappropriate for use by older people due to their increased risk of falls [25]. The aforementioned risks arise from the impact of these substances on the CNS, resulting in cognitive dysfunction, vertigo, a sensation of faintness, as well as mydriasis, which might potentially cause a decline in visual adaptation [26]. These side effects can significantly impact an individual's ability to maintain balance and navigate their environment safely, increasing the likelihood of falls. In addition, it should be noted that anticholinergic medications have the potential to impact peripheral systems, including the CVS and MSS. These treatments have been associated with the occurrence of orthostatic hypotension; a condition characterized by a decrease in blood pressure upon assuming an upright position. This physiological response can potentially exacerbate the risk of falls [25]. Additionally, anticholinergic drugs may induce muscle weakness and impair muscle tone, making it more challenging for older adults to maintain stability and prevent falls. Moreover, a prior systematic review and meta-analysis have demonstrated that the use of anticholinergic medications, such as antipsychotics (e.g., Olanzapine) and antidepressants (e.g., Trazodone), is associated with a substantial increase in the likelihood and susceptibility of falls among the elderly. The OR for antipsychotics in increasing the risk of falls among the elderly was found to be 2.16. Similarly, the risk ratio (RR) for antidepressants in increasing the risk of falls among the elderly was calculated to be 1.79 [27].

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