Chapter 1

General introduction
Introduction
Falls are one of the leading causes for disabilities in older adults, despite that up to 40% of falls appear preventable [1-3]. Most fall prevention programs target persons that have fallen in the past, whereas timely primary intervention in individuals at risk of falls might be more beneficial and cost-effective. To identify these individuals at risk, the assessment of balance and gait quality holds promise [4, 5]. Fall prevention interventions often stimulate physical activity to increase endurance, balance or muscle strength and decrease fall risk. However, recent studies suggest that physical activity indeed decreases the risk of falls in community-dwelling adults, but increases fall risk in frail older adults [1-3, 6]. This may suggest an interplay between the quality and quantity of physical activity and fall risk. Therefore, this thesis focuses on the assessment of gait quality and the quantity of daily activity and their predictive value for falls in older adults. This work could reveal targets for intervention and might help to efficiently select individuals at high risk of falls for prevention purposes.

Falls and their consequences
Falls are a common hazard for older adults due to their high incidence and older adults’ susceptibility to injuries. Each year, one-third of the older adults falls and half of these persons fall more than once [7-11]. The prevalence of falling increases with age and frailty. Almost half of the older adults over 75 years of age falls once per year, and older adults living in residential care and nursing homes fall two to three times more often than community-dwelling older adults [11-15]. A broad range of definitions for falls is used in literature [16]. In this thesis, a fall is defined as an unexpected event in which a person comes to rest on the ground or other lower level [17].

The consequences of falls can be devastating. Falls are among the main causes of functional impairments, admission to residential care facilities, hospitalization and mortality in older adults [14, 18, 19]. Around one-third of the falls result in minor injuries such as bruises or abrasions, and 15% of falls cause serious injury such as fractures and head injuries [9-11, 13-15, 20]. In the Netherlands, fall injuries in persons aged 65 and older led to 84,000 emergency room visits, 44,000 hospital admissions and 2,503 deaths in 2012 [21]. Expressed per day, this means that almost 7 older adults die because of the consequences of a fall. Since fall incidence is likely to increase due to the ageing population, the number of fall-related emergency room
visits, hospital admissions and deaths is expected to increase by more than 60 percent in the next 28 years [21, 22]. As a consequence, the direct medical costs of falls will increase from the current 820 million euros per year to a striking 1.400 million euros by 2030 [21]. Even when a fall does not result in a physical injury, it can affect the quality of life of the person involved. Older individuals that have fallen often experience fear of falling, activity restriction and a decline in social interactions [18, 23, 24]. Early identification of individuals at risk of falls and subsequent prevention is therefore of upmost importance.

**Risk factors for falls**

Because of the high societal costs and their impact on quality of life, a lot of effort is directed towards identifying risk factors for falls. Over the past 50 years, numerous epidemiological studies explored risk factors for falls and over four hundred factors associated with falls have been identified [7, 9, 15, 25-40]. These factors include history of falls, age, gender, cognitive impairments, depression, fear of falling, gait and balance impairments, use of assistive devices, grip strength, vision impairments, certain medications, medical conditions, limitations in activities of daily living, sedentary behavior and environmental factors [7, 9, 15, 25-39]. The diversity in risk factors indicates the multifactorial nature of falls, and illustrates the challenge for prevention.

Risk factors for falls are often classified as intrinsic or extrinsic factors. Intrinsic risk factors affect one’s ability to maintain balance and avert falling. These relate mainly to physical capacities, but also describe psychological and behavioral characteristics. The strongest intrinsic risk factors for falls are muscle weakness, gait and balance impairments, poor vision, cognitive and functional impairments and the use of certain medication [9, 15, 29]. Of these factors, gait and balance impairments are suggested to be most sensitive to fall risk [29, 41].

Extrinsic fall risk relates to the presence of environmental hazards such as slippery flooring, obstacles, dimmed lighting and inapt footwear [19, 42, 43]. These hazards are often encountered during daily ambulation, but are difficult to quantify as one encounters different environments during a day. However, the amount of physical activity a person performs might reflect the extrinsic fall risk. For example, consider two persons with equal impairments of balance; yet, one of these persons is very active, while the other is sedentary. One might expect that the active person is more likely to experience a fall, even though they exhibit similar intrinsic fall risk.
However, in the long term this person might be protected from further physical decline. This suggests that the relation between physical activity and fall risk can only be clarified if intrinsic fall risk is taken into account.

**Fall risk assessment**

In clinical settings, fall risk is often assessed using questionnaires or functional tests of physical abilities. Such questionnaires are frequently self-reported and identify the presence of risk factors such as those mentioned in the previous section. Examples of questions are ‘Do you experience difficulties with mobility?’ or ‘How many minutes a day are you physically active?’ Responses to these questions can be subjective, qualitative and are often dichotomized, which hampers discriminative ability. Nevertheless, questionnaires achieve moderate identification of future fallers, but improvement is desirable [41, 44, 45]. Functional tests, such as the Timed-Up and Go test and the Berg Balance Scale, are a more objective way to assess one’s physical abilities or intrinsic fall risk. These tests can discriminate fallers from non-fallers with moderate accuracy [46-49]. However, they lack responsiveness to small balance impairments and provide low precision in populations with relatively good health [4, 47, 49-51]. Laboratory-based measurements can provide qualitative and responsive measures for fall risk [4, 5]. Unfortunately, these measurements often require expensive equipment and are usually time consuming, which limits their integration in clinical settings.

Recent advancements in inertial sensors allow for ambulatory assessment of body accelerations. If these small, wearable sensors, such as accelerometers, can capture fall risk, their integration in clinical settings seems promising. Several researchers have already integrated wearable sensors in functional tests to enhance precision [52-54]. For example, accelerometry is used to automatically detect the start and end of the sit-to-stand movements, eliminating the observer’s response time [52-56]. More advanced applications of accelerometry revealed differences in acceleration patterns between fallers and non-fallers during gait and sit-to-stand movements [5, 53, 54, 56-63]. Nowadays, inertial sensors can be worn unobtrusively during daily life over longer periods of time, allowing for assessment of fall risk under daily-life conditions.

**Gait quality**

Walking is an important means of everyday transportation. However, the ability to
walk usually declines with ageing or development of disease and most falls occur during gait [11, 14, 64-67]. Older adults often experience difficulties with balance control or directing attention during walking, which suggests that increased control of balance is required [68]. Laboratory-based studies have revealed differences in gait patterns between fallers and non-fallers. Fallers usually walk slower, with reduced stride length, increased step width and increased double support time [65, 69-72]. This pattern is similar to that seen in patient populations, and is suggested to indicate a more cautious gait pattern to increase stability and decrease fall risk [70-72].

More information on gait control can be obtained by looking at variations in gait parameters. Walking, just like all human behavior, is inherently variable and thus each cycle is slightly different from the previous. This stride-to-stride variability was assumed to originate from random noise, until Hausdorff et al. [73] revealed its deterministic origin. Later, they and others showed that older individuals at risk of falls exhibit higher variability in step duration under controlled settings [5, 61, 69, 71, 74, 75]. There are a lot of different manners to quantify gait variability. In this thesis, variability of stride timing, variability of trunk accelerations [76-78] and the inverse of variability, regularity [79], were assessed. Depending on the context and characteristic under study, increased or decreased variability has been associated with falls [74, 80, 81]. Moreover, solely assessment of variability provides limited insight into the underlying mechanisms responsible for a loss of balance when walking. Therefore, additional information might be gained from nonlinear or frequency-based dynamical measures.

Promising measures in this regard are orbital stability, local dynamic stability, harmonic ratios and the index of harmonicity. Orbital stability provides information on the effects of small perturbations from one cycle to the next [82]. It is assessed using Floquet multipliers, but although they are theoretically sound, recent insights suggest that Floquet multipliers are not related to fall risk [82-87]. Local dynamic stability is considered to capture the response of the neuromuscular system to small perturbations that occur naturally during gait for example due to irregularities in flooring and neuromuscular noise [76]. Its estimation is based on that of Lyapunov exponents with adaptations to suit gait data [76, 88-90]. Usually two exponents are estimated, the short-term exponent over 0 to 1 steps and the long-term exponent quantifying reactions between 4 to 10 strides. Only short-term dynamic stability has been shown to be affected by ageing, disease and fall history, while results for long-term dynamic stability are more ambiguous [59-61, 76, 91-98]. Nevertheless, since
these results are observational and based on retrospective falls, the sensitivity of these measures to balance impairments and their predictive ability for falls remains unclear. The harmonic ratio is a measure of gait symmetry [99]. It describes the ratio of the even and odd harmonics and is affected by ageing, disease, fall history and fall risk [59, 62, 70]. The index of harmonicity reflects gait smoothness [100]. The power in the dominant frequency is divided by the power in the dominant frequency and its harmonics. The index of harmonicity has been associated with fall history [59]. However, none of these gait quality measures have yet been related to prospective falls and as fear of falling might bias retrospective associations [71, 101], the predictive ability of these gait quality measures for future falls remains to be elucidated.

Since the valid estimation of these gait characteristics generally requires long data series, they are usually assessed during several minutes of steady state treadmill walking [102, 103]. However, daily ambulation occurs over ground and differences in variability and stability have been reported between over ground gait and treadmill walking [104]. Accelerometry can be used to assess gait characteristics during over ground gait [5] and allows for the assessment of gait outside of the laboratory. This enables bypassing the white coat effect, and may provide a better understanding of an individual’s daily-life functioning. In addition, large numbers of strides might be more easily obtained during daily-life ambulation than in the lab. However, while gait quality under controlled settings seems related to intrinsic fall risk, this does not directly imply that gait quality in daily life also quantifies fall risk. Extrinsic factors, such as dual tasking or irregularities in flooring, might affect gait quality measures and could limit their predictive ability for fall risk. Thus, despite the apparent advantages of ambulatory measurements, the sensitivity and reliability of gait characteristics based on trunk accelerometry needs to be tested.

**Physical activity**

Physical activity generally declines with age [105, 106] and is often encouraged in fall prevention interventions. The beneficial effects of physical activity on health are well known [107-110]. Habitual physical activity is considered to decrease intrinsic fall risk by increasing physical capacity by improving endurance, balance or muscle strength. However, both high and low levels of physical activity have been associated with increased risk of falls [27, 31, 32, 107, 111-113]. An explanation for these inconsistent findings could be that besides decreasing intrinsic fall risk, the amount of daily activity also reflects the amount of exposure to extrinsic risk factors.
The latter would increase fall risk if there is a mismatch between one's intrinsic fall risk and the amount of physical activity. Some support for this notion is provided by intervention studies, which suggest that although physical activity decreases the risk of falls in community-dwelling older adults, it increases fall risk in frail older adults [2, 3, 6]. In addition, an observational study suggested that physical activity can be a protective factor for fall-related fractures in older adults without mobility limitations, but is a risk factor in older adults with mobility limitations [114]. This suggests an interaction between one's intrinsic fall risk and the amount of physical activity, which needs to be investigated.

Previous research often used questionnaires to quantify the amount of physical activity. However, self-reports of daily activity are subjective, and can be affected by recall bias [115, 116]. Moreover, these questionnaires apparently fail to capture irregularly performed physical activity at lower intensities, comprising most of the activities in older adults [117, 118]. Studies comparing questionnaires to more objective measurements, such as double labeled water, step counters and accelerometers, found that questionnaires overestimated as well as underestimated daily physical activity in older adults by up to 120 percent [119]. Hence, objective assessment of daily physical activity is required. Body-worn sensors can be used to quantify the amount of physical activity [120]. Several devices are currently available, such as step counters and inertial sensors. Step counters are relative simple devices that detect steps or stepping-like behavior such as biking. They provide easy means to gain insight in the amount of physical activity, but also have some downsides. As step counters usually detect steps based on a threshold of the intensity of the movement, they do not provide information on the timing, duration or intensity of activity bouts. In addition, their validity is low in frail older adults, as gait intensity often does not exceed the set threshold [121]. Inertial sensors, consisting of for instance accelerometers, barometers, magnetometers or gyroscopes, likely provide a better alternative. Because of current battery limitations, usually only accelerometers are incorporated in sensors for long-term ambulatory assessments.

Physical activities and intensities fluctuate within and between days [122, 123]. Hence, to obtain reliable estimates of the amount of daily physical activity the accelerometer has to be worn during multiple days and for a substantial part of the waking hours [122-128]. Previous studies suggested that one to six days of measurement are required to obtain reliable estimates of walking and lying duration and energy consumption in older adults [122, 123]. However, these studies were based on daytime measurements only and other parameters that might be relevant
for fall risk assessment, such as the number of transitions from sit-to-stand or stand-to-sit or the duration of gait episodes, were not taken into account. Therefore, to be able to take the amount of physical activity and its interaction with gait quality into account for determining fall risk, the reliability of physical activity monitoring needs to be assessed.

**Aim and outline of this thesis**

The aim of this thesis was to develop a method for ambulatory assessment of fall risk. To achieve this aim, this thesis consists of two parts. In the first part, methodological aspects of trunk accelerometry to assess gait quality and quantity of daily activity were studied. In the second part, the predictive value for falls of parameters derived from daily-life trunk accelerometry was evaluated in an observational study, the FARAO (FAll Risk Assessment in Older adults) study.

First, validity and reliability of promising gait quality measures were studied. In Chapter 2, sensitivity of gait quality measures to balance impairments was tested. Balance was manipulated in healthy young participants and gait stability and variability with and without balance impairment was compared. In addition, the feasibility of using these measure for screening of fall risk was explored. In Chapter 3, the reliability and smallest detectable differences of local dynamic stability was studied by comparing repeated measurements. In Chapter 4, the question was addressed whether gait quality measures could be obtained from short bouts of gait, as would be available during daily life. In Chapter 5, the reliability of ambulatory assessment of the amount of daily activity was studied in an observational study. The minimum number of measurement days to reliably assess the amount of daily activity on group and individual levels were determined.

In the second part of this thesis, the ability of accelerometry-derived quality and quantity of gait to detect fall risk was studied in the FARAO cohort study. In Chapter 6, a comparison between associations with fall incidence obtained by recall or during follow-up was made. In addition, a prediction model for falls was tested when adding parameters on quality and quantity of daily activities to questionnaires concerning depression, cognition, fear of falling, grip force, processing speed and executive function.

Finally, in Chapter 7, a general conclusion is drawn with respect to methodological aspects and predictive value of falls using trunk accelerometry, and implications for clinical practice and directions for future research are discussed.