1

*General introduction*
Introduction

Fall prevention has become a focal point of interest over the last decade in both public health care and science, which is not surprising given the potential impact of falls on individual lives and society. The ultimate goal and motivation behind the research presented in this thesis was to identify older adults with a high fall risk. Early identification may facilitate referral to and personalization of fall prevention programs. This goal was pursued by assessing fall risk through the analysis of gait. A new approach was taken by monitoring older adults’ gait in daily life instead of measuring their gait in a laboratory or in the clinic. The way older people walk in daily life may contain information about the occurrence of perturbations and their capacity to overcome these, which may be predictive of their fall risk. This introduction sets a starting point for the analysis of gait in daily life by sketching the background of fall risk assessment, gait analysis, and accelerometry, by explaining which chances and challenges to expect from monitoring gait in daily life, and by describing the approach taken in the remainder of this thesis to advance toward the goal of identifying older adults with a high fall risk.

Background

Fall risk

Falling is a major health and safety issue that is expected to grow in years to come, due to our aging population. Adults of 65 years and older are estimated to have a one in three chance of falling at least once per year (Campbell et al., 1990; O'Loughlin et al., 1993; Stel et al., 2004; Tinetti et al., 1988; Tromp et al., 1998). Based on demographic prognoses, the consequences of fall accidents are expected to grow in the Netherlands from 84 000 emergency room visits, 44 000 hospital admissions and 2503 deaths in 2012, to 140 000 emergency room visits, 73 000 hospital admissions and 3900 deaths in 2030 (VeiligheidNL, 2013). Consequently, the direct medical costs of falls will increase over the next two decades from an estimated 820 million to 1.4 billion euros per year (VeiligheidNL, 2013). These figures highlight the importance of fall prevention. Interventions such as physical exercise with a high intensity and a challenging balance component have been shown in systematic reviews to be
effective in reducing fall risk (Gillespie et al., 2012; Sherrington et al., 2011). The efficiency and effectiveness of such interventions may improve if fall risk can be detected early, i.e., before an actual, potentially injurious fall takes place. Moreover, identification of specific fall risk factors may enable tailored and more effective interventions.

Over the past decades, a great variety of fall risk factors have been identified, ranging from medical or physiological factors like medication, muscle strength, and balance to environmental or behavioral factors, such as having a pet and amount of alcohol consumption (Ambrose et al., 2013; Peeters et al., 2010). To assess these factors, various approaches have been pursued. Questionnaires, such as the LASA fall risk profile (Pluijm et al., 2010), or the Falls Efficacy Scale-International (FES-I, Yardley et al., 2005) provide efficient and validated tools for fall risk screening. However, they may be quite subjective as they are typically based on self-reported information. Physical assessments may provide more objective information on an individual’s mobility and physical performance and ability. Examples of these physical assessments are the Timed Up and Go Test (TUG, Shumway-Cook et al., 2000), Short Physical Performance Battery (SPPB, Guralnik et al., 1994), Berg Balance Scale (Berg, 1989), Tinetti’s Performance Oriented Mobility Assessment (POMA, Köpke, 2006; Tinetti et al., 1988), and the Physiological Profile Assessment (PPA, Lord et al., 2003). Gait analysis can be considered a specific type of physical assessment and is an obvious tool in fall prediction, because most falls are reported to occur during walking (Bergland et al., 1998; Robinovitch et al., 2013).

**Gait analysis**

The ability to walk is of great importance for the well-being of humans. Many people take great pleasure in walking, whether it is in the city, in the countryside or in the wild. On a more basic level, the ability to walk increases and facilitates our freedom to go where we wish, in service of our personal and social needs. A better understanding of the underlying mechanisms of our ability to walk may contribute to help in particular aging and patient populations to maintain this ability.
The analysis of gait in this thesis follows a more clinical approach, in the sense that attention is given to deviations or individual differences in the gait pattern rather than the common mechanisms behind our ability to walk. These differences may indicate fall risk and are analyzed by comparing characteristics of individual gait patterns.

**Accelerometers**

Monitoring human movement in daily life, including activities outside the home, is nowadays possible by the use of body-worn sensors. One of the most common and early used types of body-worn sensors is the accelerometer. This device, which records accelerations along one or more usually perpendicular axes, provides a view of its movement, and thereby of the movement of the person wearing it. Although the use of accelerometers for gait analysis was already proposed by Morris in 1973 (Morris, 1973), it took until the 1990s for many researchers to follow his lead and to further develop the application of these body-worn sensors in gait analysis (Auvinet et al., 1998; Currie et al., 1992; Evans et al., 1991; Moe-Nilssen, 1998). Nowadays, a variety of accelerometers is commercially available and they continue to improve in terms of battery-life and user-friendliness. This has led to rapid proliferation of the use of accelerometers in gait analysis. Initially their use was restricted to the laboratory, where subjects walked on a treadmill or a limited distance over ground. In daily life, accelerometers have been mainly applied to assess the amount and intensity or energy expenditure of different kinds of physical activities (e.g., Bouten et al., 1997a; Troiano et al., 2008).

**Estimating gait characteristics**

An important advantage of accelerometers is that they are easy to use and thus allow for low-effort acquisition of gait kinematics. However, the estimation of gait characteristics from accelerations is challenging; estimation methods depend on a variety of assumptions, partly related to limitations of the view provided on a person’s movement. For instance, a conversion of the recorded accelerations to positions requires the initial velocity, continuous orientation of the sensor, and corrections for integration of measurement errors. Since the early days of gait analysis using accelerometry, several characteristics have
been proposed, based on different estimation algorithms that typically depend on the accelerometer wearing location. The lower back may be considered a suitable location for assessment of stability of gait since it is close to the center of mass (Marschollek et al., 2011; Weiss et al., 2011), and is therefore the location used in this thesis. Standard gait characteristics like gait speed and step length can be readily measured with other instruments but require fairly advanced data analysis techniques when using an accelerometer. Zijlstra and Hof proposed a method assuming a compass gait type during each support phase and estimated step lengths by means of trigonometry from peak-to-peak height differences (Zijlstra and Hof, 2003). For other characteristics, such as step width, estimation from trunk accelerations may not be feasible at all. However, acceleration time series offer the possibility to estimate a variety of other characteristics that are sometimes more abstract and more difficult to imagine or define for a walking human, but that may still distinguish gait patterns and discriminate individuals. For example, movement intensity can be estimated as the root-mean-square of the acceleration signal (Menz et al., 2003), and stride-to-stride regularity as the normalized autocorrelation for one stride time delay (Moe-Nilssen and Helbostad, 2004). Gait symmetry and smoothness can be estimated from trunk accelerations by the harmonic ratio (Menz et al., 2003) and the index of harmonicity (Lamoth et al., 2002). Both measures are based on the signal’s power spectrum, in particular on the power of stride frequency harmonics. Local dynamic stability (i.e., Lyapunov exponents) and entropy are characteristics that have their origin in dynamical systems theory. Several competing methods for their estimation from time series such as recorded accelerations have been developed (Pincus, 1991; Richman and Moorman, 2000; Rosenstein et al., 1993; Wolf et al., 1985), and the optimal method to select for the evaluation of gait is an ongoing topic of discussion (Bruijn et al., 2012; Cignetti et al., 2012a, b; Leverick et al., 2014; Yentes et al., 2013).

**Validity of gait characteristics’ estimators**

Several gait characteristics that can be estimated from recorded trunk accelerations have proven to be associated with fall risk. Examples are gait speed, variability, stability, entropy and symmetry (Doi et al., 2013; Hamacher et al., 2011; Lockhart and Liu, 2008; Riva et al., 2013; Toebes et al., 2012;
VanSwearingen et al., 1998). However, the outcomes of studies on the relation between gait characteristics and fall risk do not always correspond (Hamacher et al., 2011). This raises the question to which extent these characteristics indeed represent valid measures of fall risk. Recently, Bruijn et al. (2013) proposed a scheme to assess the validity of a characteristic as a measure of gait stability, involving four different levels of validity: construct validity, predictive validity in a model, convergent validity in experimental studies, and finally predictive validity in observational studies. The latter indicates that a characteristic is different between prospective fallers and non-fallers. This is the level of validity addressed when assessing the added value of daily-life gait characteristics for the prediction of falls. The first three levels are more closely related to stability at a given instant and situation than to the risk of future falls. When assessing fall risk it is not only gait stability measures as validated by these first three levels that need to be examined. For example, a low gait speed has been reported to be associated with falling, even though gait speed is not a direct measure of stability. Although being a valid measure for gait stability makes a good candidate for fall risk prediction, it is not a necessary condition.

A different aspect of validity that is not directly related to stability or fall risk, but that forms a foundation of valid estimators in general, can be coined algorithmic validity. This tells whether the estimator for a measure provides a valid outcome, i.e., it estimates what it claims to. This type of validity is difficult to verify, particularly for the more abstract measures such as local dynamic stability and entropy when applied to physiological time series, as no gold standard reference values exist against which these measures can be validated.

**The wild side**

Fall risk assessment by the observation of human gait in the 'wild', i.e., in daily life, rather than in the laboratory or clinic is a new and emerging research topic. This section provides an overview of the chances and challenges that may be expected when entering this unexplored area, and of the route planned for the investigations.
**Chances and challenges**

Analysis of gait in daily life for the purpose of fall prediction may have the advantage over laboratory-based estimates that it occurs in the actual environments that people face every day, and may therefore incorporate information on the exposure to challenging situations that can induce falling. Gait analysis performed in a controlled setting likely provides an index of someone’s abilities. For example, it may indicate how fast, regular or symmetric someone walks under specific conditions. What one cannot glean from these analyses is information about whether or not people encounter different (challenging) situations in daily life and how demanding these situations are in relation to someone’s abilities, which may be another important factor in fall risk.

The question of algorithmic validity of gait characteristics may be more pronounced when estimated in daily life than in controlled settings in a laboratory. The validity may depend on measurement conditions, which can be controlled in the laboratory, but not in daily life. Estimation methods that have been successfully developed for gait characteristics in controlled laboratory settings were only recently applied in the analysis of daily-life gait (van Schooten et al., 2015; Weiss et al., 2013). Several potential problems exist that may interfere with the estimates’ validity and reliability in daily life. In contrast with laboratory settings, there is no full control over behavior and wearing compliance of participants. Variability in if, when and how they wear the accelerometer may affect the estimations. In addition, the situations and behavior of people may vary from day to day. It is therefore unclear whether a limited time such as a week of measurements is sufficient to reliably estimate gait characteristics that are representative for an individual’s gait pattern. Furthermore, in daily life, general exposure to challenging situations might be expressed by the most common value of gait characteristics such as the median over a day, whereas specific high-risk situations may be expressed by extreme values of gait characteristics. In this manner, the variation of gait characteristics between episodes of walking might provide additional insight into fall risk, and gait analysis in daily life may provide a unique opportunity to retrieve information on situational fall risk factors. On the other hand, the difference in conditions between individuals and over time raises the question to what extent gait analysis in daily life can be used to assess walking ability.
**The route**

This thesis presents a number of studies focusing on the feasibility of gait analysis based on daily-life accelerometry, and its potential for fall prediction.

First, a method was developed for the evaluation of algorithmic validity of estimation algorithms for characteristics of dynamical systems such as a walking human. This method was applied to Lyapunov exponents as measures of local dynamic stability, to support the selection of an optimal estimator, which may improve the feasibility and potential contribution of this characteristic to fall risk assessment (Chapter 2).

Second, feasibility of estimation of gait characteristics in daily life was investigated in Chapters 3, 4 and 5. The limited control over and potential variability of sensor positioning in daily-life measurements may affect the feasibility of daily-life gait analysis. The consequences of this limited control were assessed by investigating the effects of differences in sensor positioning on estimates of gait characteristics (Chapter 3). Furthermore, the potential added value of daily-life measurements over controlled measurements in fall prediction was explored by a comparison between gait characteristics estimated during daily-life gait and during treadmill walking served as a first step in investigating the sensitivity of the gait characteristics to situations and behavior (Chapter 4). The reliability of gait characteristics estimated in daily life was determined by comparing estimates of two different weeks (Chapter 5).

Third, the predictive value of the daily-life gait characteristics for falls was investigated in Chapters 5 and 6. The potential as a fall risk indicator of gait characteristics estimated in daily life was assessed by their association with fall history (Chapter 5). Finally, a fall prediction model was developed, based on a combination of questionnaire data, monitored activities and gait characteristics estimated in daily life, and the added value of extreme values of gait characteristics during daily life for this model was tested (Chapter 6).

A summary and general discussion of the findings of the presented studies can be found in Chapter 7.
General introduction