Chapter 7

Epilogue
Summary

The aim of this thesis was to develop a method for ambulatory assessment of fall risk. To achieve this aim, this thesis consisted of two parts. In the first part, methodological aspects of using trunk accelerometry to quantify gait quality and the amount of daily activity in real-life and real-life mimicking situations were studied. In the second part, the predictive ability of daily-life trunk accelerometry for fall risk was evaluated. In this chapter, the results and conclusions from these studies will be summarized and revisited. Furthermore, the limitations of this thesis will be discussed and recommendations for clinical practice and future research will be given.

Part one: Methodological aspects of trunk accelerometry

The assessment of gait quality holds promise for estimating fall risk. However, most evidence comes from observational studies that associated gait quality with retrospective falls, while fear-of-falling and compensational strategies might bias results. In Chapter 2, we investigated validity of gait quality measures, i.e. orbital stability, local dynamic stability and mediolateral trunk variability, by experimentally inducing balance impairments during gait. Healthy young participants wore inertial sensors (accelerometer and gyroscope) on their back and both feet, and walked on a treadmill at slow, fast and preferred speed. Balance impairments were induced by galvanic stimulation of the vestibular system so that, in contrast with most observational studies, within-subject comparisons could be made. All gait quality measures were significantly affected by galvanic vestibular stimulation, but only short-term local dynamic stability and mediolateral trunk variability showed effects of the induced balance impairments. The effect of these balance impairments was small, i.e. 11% for local dynamic stability and 20% for mediolateral trunk variability. Nevertheless, local dynamic stability and mediolateral trunk variability allowed for correct classification of the presence or absence of balance impairments on an individual basis in approximately 80% of the trials. The results of this study indicated that accelerometry-derived local dynamic stability and mediolateral trunk variability are sensitive measures of balance impairments.

To be able to use trunk accelerometry to identify persons with balance impairments, it should not only be able to capture these balance impairments but also be sufficiently reliable to detect differences on an individual level. In Chapter 3, we investigated the inter- and intra-day reliability of local dynamic stability. To mimic real life situations, measurements were performed during over ground walking. Healthy
young participants wore an accelerometer on their lower back and walked 500 m back and forth. The measurements were repeated 2-30 weeks later, and reliability at group and individual levels was assessed. Different estimation methods (i.e. different state space reconstruction methods) were employed and results were compared. We showed that the estimation method affected between-day reliability substantially and therefore recommended a standardized estimation method. With this method, within-day reliability of local dynamic stability was good and between-day reliability was moderate at group level. At individual level, differences of around 20% could reliably be obtained. The results of this study and the previous study indicated that accelerometry-derived local dynamic stability is a reliable measure, which can be used to detect effects of balance impairments on gait at the individual level.

In daily life, walking episodes are usually short, so we further investigated whether gait quality measures can be obtained from short bouts of gait. In Chapter 4, we compared local dynamic stability, mediolateral trunk variability and stride time variability based on short bouts to those based on a long distance. Healthy young participants wore an accelerometer on their lower back and walked a long reference trial of 500 m and 36 bouts of 20 m over ground. The short walking bouts were repeated, on average 2.6 months later, so that reliability at group and individual levels could be assessed. Stride time variability and mediolateral trunk variability were increased when walking short bouts and estimates did not correlate well with those obtained from a long distance. In addition, test-retest reliability of stride time variability and mediolateral trunk variability was low. Local dynamic stability did correlate highly between walking multiple short bouts and the long distance. We showed that a minimum of 15 bouts of 20 m (8 steady state strides) are required for concurrently valid and reliable assessment, and that reliability at both group and individual levels was comparable to when walking a long distance. The results of this study indicated that accelerometry-derived local dynamic stability can be estimated based on several short bouts, such as occur during daily-life gait.

Physical activity is usually encouraged in fall prevention interventions to improve physical capacity and decrease fall risk, but may also reflect time-at-risk and hereby increase the risk of falls. To reliably assess the amount of physical activity from daily-life trunk accelerometry, the accelerometer might need to be worn during multiple days. In Chapter 5, we investigated the minimum number of measurement days required to reliably obtain the amount of physical activity at group and individual levels. A group of 79 older adults wore an accelerometer on their lower back during daily life. Two weeks of measurements were obtained on average 3.5 weeks apart. We
calculated the duration of locomotion, lying, sitting and standing, and determined the movement intensity. In addition, the number of locomotion bouts, transitions to standing and the median and maximum duration of locomotion per day were determined. We showed that a period of 6 consecutive days of 24 hours resulted in good to very good reliability for all physical activity measures studied. Moreover, we determined that 2 consecutive days of measurements were sufficient to obtain reliable results at group level for all measures, except for the duration of lying and median locomotion bout duration, which require 3 and 5 measurement days, respectively. We also demonstrated that obtaining more than 4 days of measurements did not substantially increase reliability at the individual level. The results of this study indicated that one week of trunk accelerometry is sufficient to gain reliable insight in an individual’s habitual daily activities.

Part two: Predictive ability of daily-life trunk accelerometry for fall risk

Gait quality measures have been associated with falls, however, most studies identified fallers based on fall history while recall difficulties, sustained injuries and fear-of-falling might bias these retrospective designs. In addition, recent studies suggest an interaction between one’s intrinsic fall risk and the amount of physical activity. In Chapter 6, we investigated associations with retrospective and prospective falls for clinically used questionnaires and functional tests, as well as accelerometer-derived quantity of daily activities and gait quality. A group of 169 older adults wore an accelerometer on their lower back during one week in daily life. Based on accelerometry, daily activities were identified as either locomotion, sitting, standing, lying or unclassified. The total duration of these activities was calculated and for the locomotion bouts, variables describing gait quality were estimated. In addition, clinically used questionnaires on fall risk factors and functional tests of grip strength and executive functioning (trail making test) were obtained. Six-months fall incidence was collected retrospectively by recall and prospectively by fall diaries and monthly telephone contact. Of all participants, 35.5% had a history of ≥1 falls and 34.9% experienced ≥1 falls during follow-up. Logistic regressions showed that questionnaires, grip strength and trail making test, as well as gait quantity and quality, were significantly associated with falls. Significant associations differed between retrospective and prospective analyses, although odds ratios indicated similar patterns. In addition, we showed that low walking speed, low gait intensity, low local dynamic stability, low harmonic ratio and high index of harmonicity were associated with prospective falls. Furthermore, the prediction of falls based on
questionnaires, grip strength and trail making test (area under the curve of 0.68) improved substantially by including accelerometry-derived parameters of gait quality (local dynamic stability, gait smoothness and gait intensity), gait quantity (number of strides) and their interactions (area under the curve of 0.81). The interaction between gait quality and quantity implies that the amount of gait increases the risk of falls only for persons with balance impairments. The results of this study indicated that daily-life trunk accelerometry contributes considerably to the identification of individuals at risk of falls.

General discussion

From controlled settings to daily-life estimation of gait quality

In this thesis, we developed a method to assess gait quality, which was up until now mainly derived from laboratory measurements, from daily-life trunk accelerometry. For this achievement, several obstacles had to be taken. First, we studied whether gait quality could be assessed from short bouts of gait. Daily-life gait in older adults comprises mainly short bouts (Chapter 5), while previous studies showed that for valid and precise estimation of most gait quality measures continuous data series exceeding 200 strides are required [2, 3]. Our results indicated that short bouts of gait could be used to assess local dynamic stability although a substantial number of strides is still required (Chapter 4). During daily-life measurements in older adults, on average 1253 (SD 830) 10-second windows from 528 (SD 308) daily-life gait episodes could be extracted in Chapter 6. This suggests that sufficient episodes of gait are available during daily life of older adults to estimate gait quality.

Secondly, to obtain gait quality measures from daily-life trunk accelerometry, some modifications were made in the estimation methods used in the experimental studies of this thesis. The estimation methods for gait stability and variability initially required identification of gait cycles (Chapters 2-4). However, errors in step detection, such as missed or false steps, might be more common in data from fall-prone older adults and can thus cause bias. Therefore, we employed and developed estimation methods that do not require step detection ([59] and Chapter 6). In addition, the employed algorithm to estimate local dynamic stability changed during the course of this thesis. In the experimental studies (Chapters 2-4), the method of Dingwell et al. [76] based on the algorithm by Rosenstein et al. [90] was used. Recent insights [196-199] suggested that the algorithm by Wolf et al. [89] might be more suitable for data series length and signal-to-noise ratio as encountered in daily-
life accelerometry. Therefore, this method was used in Chapter 6. The correlation between both estimation methods is high for the data in Chapter 6 ($r=0.72$, $p<0.001$; see Figure 1) and the association of local dynamic stability based on the algorithm by Wolf et al. [89] with prospective falls was stronger than that based on Rosenstein et al. [90] ($p=0.005$ vs. $p=0.031$), but future research should further compare both methods.

Thirdly, we assessed whether variability of the measurement over time was small enough for use in a daily-life setting. We showed that test-retest reliability was moderate and our results suggested that accelerometer orientation differences between measurements negatively affected reliability (Chapter 3, Chapter 4). In a subsequent study, we showed that gait characteristics are quite robust against displacement of the accelerometer over the lumbar spine, but rotations around the body axis resulted in lower consistency between locations [193]. We developed a realignment method based on the sensor's orientation with respect to gravity and optimization of the left-right harmonics, and subsequently investigated whether one week of daily-life trunk accelerometry resulted in reliable estimates of gait quality. We showed that gait speed, stride time, several variability measures, stride
regularity, gait intensity, gait symmetry, gait smoothness and local dynamic stability could all be assessed with moderate to good reliability [59]. This suggested that extrinsic factors that have an effect on gait quality in daily-life assessment, such as dual tasking or irregularities in flooring, do not considerably affect reliability, and that one week of trunk accelerometry is satisfactory for the assessment of gait quality. Finally, since in daily-life settings extrinsic factors will affect gait quality, it may not only express intrinsic fall risk as is the case under controlled settings. Therefore, translating the association between fall risk and gait quality from controlled laboratory settings to daily life is not straightforward. Our results indicate that gait speed, stride time, gait intensity, gait symmetry, gait smoothness and local dynamic stability obtained during daily life are predictive of fall risk (Chapter 6), which is in agreement with earlier laboratory-based studies [60–62, 65, 69-72, 96]. However, in contrast with laboratory studies [5, 61, 69, 71, 74, 75], none of the variability measures obtained during daily life, i.e., variability of stride timing, variability of trunk accelerations and gait regularity, was associated with fall risk (Chapter 6). A possible explanation could be that during daily life compensations take place to decrease variability (Chapter 6), or that effects efface since variability depends on environmental factors (as suggested in Chapter 4). Only one other study, by Weiss et al. [77], investigated the relation between gait quality obtained from daily life and prospective falls. They showed an association between variability of anteroposterior trunk accelerations and recurrent falls. There were some dissimilarities in the selection of analyzed gait episodes between their and our study but it is more likely that differences arose because of the definition of fallers and non-fallers. They defined fallers based on recurrent falls, whereas we classified fallers based on a single fall. Possibly, intrinsic fall risk in recurrent fallers coincides with larger changes in gait variability that exceed the noise caused by extrinsic factors. However, more research is required to test this explanation. Comparison of gait quality estimated from controlled and daily-life settings might further aid in understanding discrepancies between these settings. We [200] and Weiss et al. [77] showed mild to moderate correlations between settings for both variability and other gait quality measures, which suggest that they quantify comparable constructs to some extent. Future studies should elucidate whether daily-life and laboratory measurements are complementary in the prediction of fall risk.
Usability of trunk accelerometry in older adults

For quantification of the amount of physical activity and the quality of gait by trunk accelerometry, it is important that the accelerometer is actually worn. We included in total 451 older adults within the observational study (follow-up still in progress at the time of writing), who wore the accelerometer for one up to 14 weeks. In total, we obtained 8365 days of trunk accelerometry. All participants were instructed to wear the accelerometer all the time during the measurement week, except during aquatic activities such as showering. One person lost the accelerometer and 8 others forgot to remove the accelerometer before showering which resulted in damage to the device. For future studies, a waterproof accelerometer or waterproof case is advised. Although some participants requested not to wear the accelerometer during nighttime, the overall acceptance was high.

For accurate estimation of the amount of physical activity and to a lesser extent the quality of gait, the accelerometer needs to be worn for a considerable part of the day. Previous studies suggested that a minimum wear time of 75 to 90 percent of the day results in representative estimates of the amount of physical activity [122, 126-128, 186, 187]. In Chapter 5, we evaluated the effect of these cutoffs and concluded that, since it virtually did not affect reliability (Chapter 5, Appendix A and Table 2), a minimum wear time of 75 percent of the day could be employed in subsequent analyses. Future studies could consider discriminating between not wearing during the night, which might not pose much of a problem, and not wearing during daytime. We explored this during analysis of Chapter 5, but observed that not wearing the accelerometer during the night often coincided with not wearing the accelerometer during daytime (90% overlap). Of the analyzed measurements days in Chapters 5 and 6, 91% complied with a minimum wear time of 75 percent per day. Overall, this suggests that daily-life measurement using trunk-worn accelerometers is feasible in the older population.

Fall risk and physical activity

Physical activity is often encouraged in fall prevention interventions to decrease intrinsic fall risk, although it may also increase the exposure to extrinsic risk factors and thereby increase fall risk. Previous studies that attempted to elucidate this relation often employed questionnaires to quantify the amount of physical activity. Most questionnaires fail to capture activities at low intensities that are irregularly performed and, especially in older adults, recall can cause bias [115-118]. Therefore, we decided to employ trunk accelerometry to objectively quantify
the amount of habitual physical activity. We found that physical activity was not univariately associated with fall risk, but did contribute to the prediction of fall risk in a multivariate model (Chapter 6). The amount of gait, i.e. number of strides taken, increased the risk of falls after correction for gait quality. We further identified an interaction between gait quantity and gait quality, indicating that for persons with low gait quality, the amount of walking poses additional risk, while for persons with high gait quality, the amount of gait is protective against falls. As walking comprises most of physical activity in older adults, this might explain why both high and low levels of physical activity have been associated with increased risk of falls [27, 31, 32, 107, 111-113]. Future studies should take the interaction between the amount and quality of physical activity into account when assessing fall risk and evaluating interventions.

![Figure 2: Fall risk from quantity of gait](image)

Our results suggest that the amount of physical activity should match one's balance ability. In Figure 2, the relative contributions of gait quality and quantity to fall risk, based on the prediction model developed in this thesis, are depicted for all participants included in Chapter 6. The axes are scaled equally and the graph is split into quadrants, to allow quick identification of persons with high or low risk originating from gait quality or quantity. It can be easily observed that a substantial
part of fall risk in fallers originates from the quantity of gait. Similar information is provided by Table 1 below. In this table, local dynamic stability and the number of strides are employed to represent gait quality and quantity and the percentage of fallers or non-fallers in each quadrant is reported. It can be observed that older adults with a high risk of falls more often exhibit low gait quality (see grey marking), as was expected based on literature and this thesis (Chapter 2 and 6 and [5, 60–62, 65, 69–72, 74, 75, 96]). Additionally, it can be noticed that older adults with a high fall risk more often exhibit low gait quality combined with high gait quantity (see bold marking). This might signify misjudgment of one’s own ability, which results in an increased risk of falls. Misjudgment might arise for instance due to cognitive decline [201–204] and, if confirmed by other studies, these results suggests that besides improvement of balance, some persons may also benefit from increasing awareness of their own capacities.

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<tr>
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<th>Low gait quality</th>
<th>High gait quality</th>
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<td><strong>Low gait quantity</strong></td>
<td>26% of non-fallers</td>
<td>22% of non-fallers</td>
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<tr>
<td></td>
<td>38% of fallers</td>
<td>9% of fallers</td>
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<tr>
<td><strong>High gait quantity</strong></td>
<td>14% of non-fallers</td>
<td>38% of non-fallers</td>
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<td>27% of fallers</td>
<td>26% of fallers</td>
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<td><strong>Total</strong></td>
<td>40% of non-fallers</td>
<td>60% of non-fallers</td>
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<td>65% of fallers</td>
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**Limitations of this thesis**

The studies described in this thesis had some limitations that should be taken into account. We did not correct for seasonal influences on physical activity, although periods of cold weather may decrease the amount of outdoor activities. Preliminary analysis in 308 of in total 451 older adults indicated that the amount of standing was lower in summer compared to winter ($p=0.02$), however for the amount and duration of gait no effects of season were observed (overall $p=0.41$). Moreover, although validity of the employed physical activity classification algorithm has been shown to be high for locomotion and lying and fair for sitting and standing [175–178],...
misclassifications might have occurred which could have affected both reliability and validity of quantity and quality of daily activities. Nevertheless, reliability was adequate (Chapter 5 and [59]) and characteristics describing quality and quantity of gait were associated with fall risk (Chapter 6). Future studies should further investigate the effects of seasonal influences and potential misclassifications on estimates of physical activity and quality of gait and their reliability.

The group in the observational study was a convenience sample of volunteers, which could have introduced a selection bias towards relatively healthy older adults. This may limit generalizability of the prediction model to frail or sedentary populations. Despite the potential selection bias towards healthy older adults, the amount of physical activity was low (only 23.2% of the participants in Chapter 6 exceeded the recommended 8,000 steps per day [190]) and the fall incidence was high (35% of the participants fell during 6 months follow-up). In addition, when applying the prediction method to the participants in the lowest quartile of grip strength (average of left plus right for men 52 kg and women 29 kg), an indicator of frailty [205], the AUC was 0.87 (95% CI 0.73–1.0). This is not different from the AUC of 0.81 (95% CI 0.74–0.88) obtained for the total population (Chapter 6). Nevertheless, future studies should validate this method in more frail and sedentary populations.

The prediction model was not externally validated, hence over-fitting might bias results. However, the sample on which the model was created was large and the number of variables in the model is appropriate for the number of cases. After analysis in Chapter 6, we have obtained fall incidences and analyzed data of an additional 26 participants. Preliminary validation of the prediction model in these participants yielded a correct classification of 72.0%, with a sensitivity of 71.4% and a specificity of 72.7%. This is barely lower than the correct classification of 73.2%, sensitivity of 73.5% and specificity of 72.7%, obtained in Chapter 6 and may indicate that with some fine tuning of the regression coefficients and cutoff values the prediction model can be used to identify older adults at high risk of falls. However, a larger validation study is required, which upon completion of data collection can be performed within the FARAO cohort.

Clinical implications
Currently, fall risk in clinical settings is often assessed using questionnaires or functional tests, which can be subjective and lack responsiveness in healthy populations [4, 5]. In this thesis, we developed a method for ambulatory assessment
of fall risk. We showed that accelerometry-derived quantity and quality of gait had additional predictive value for falls over clinically used questionnaires and functional tests (Chapter 6). The resulting prediction model for fall risk comprised fall history, local dynamic stability, gait intensity, the amount of gait (number of strides), depression score, gait smoothness and the interaction between gait intensity and gait smoothness and the amount of gait. Its predictive ability was quantified by the area under the receiver operating curve (AUC) also called c-statistics. The AUC quantifies the area below the 'sensitivity against 1-specificity for all possible cutoff values of predicted probability'-curve, and ranges from 0.5 (chance) to 1 (perfect classification). The AUC of our prediction model was 0.81 (95% CI 0.74-0.88), which is very high in comparison with other fall risk assessment methods, which generally achieve AUCs ranging from 0.55 to 0.74 [41, 44, 45]. The cutoff value employed in Chapter 6 was optimized to achieve the best combination of sensitivity and specificity, although more optimal cutoffs may be possible. For instance, misclassification as a faller probably has less adverse consequences, high sensitivity may be more valuable than high specificity. Cost-effectiveness analysis can also aid in the decision of a cutoff between those to treat and those not to treat. When the fall risk prediction model is further developed and externally validated, it can be used for early identification of older individuals at risk of falls and selection of these individuals for fall risk interventions. Furthermore, evaluation of such interventions using the methods developed in this thesis would allow for more efficient research designs than those based on follow-up of fall incidence.

We identified fall history and depression as important factors contributing to fall risk. The relation between fall risk and depression is not yet understood. Depression might result from poor health or fear-of-falling, but may also reduce attention to environmental hazards or cause a decrease in daily activity and consequently affect balance capacity [195, 206-208]. Moreover, medication for depression might impair balance control [9, 208-210]. Future studies should clarify the relation between depression and fall risk, in order to identify cause-effect relations and targets for interventions.

Our results also suggest that the amount of gait is affected by fall history status (Chapter 6). A viable explanation is that older fallers restrict their activity because of for instance fear-of-falling [15, 18]. Such declines in activity after a fall may affect health negatively [70, 71, 195], and in turn decrease physical capacity and increase fall risk. There are indications that interventions to decrease fear-of-falling are effective [211], however more research is required to establish whether these
interventions also decrease fall incidence. We further identified gait quality, more specifically local dynamic stability, gait smoothness and gait intensity, as important factors contributing to fall risk. This raises the question if and how these gait quality characteristics can be improved. To our knowledge, the amount of literature on this aspect is limited. Experimental studies showed that local dynamic stability is sensitive to impairments of the vestibular and somatosensory system in healthy young participants (Chapter 2 & [212]). If possible, improvement of (processing of) this information might therefore be beneficial. In addition, the instruction to use a careful gait strategy counter-intuitively decreased local dynamic stability in healthy young adults [213], which may suggest that cautious walking, due to for instance fear-of-falling, might affect gait quality negatively. Moreover, fatigue has been shown to impair gait quality in older adults [214, 215], which suggests benefits of strength and endurance training. Physical exercise has already been shown to improve other gait quality indicators, such as the variability of stride time variability and a mediolateral balance composite score [216, 217], and a recent abstract suggests that exercise can improve local dynamic stability in older adults [218]. Future studies should evaluate the effects of interventions on local dynamic stability, gait smoothness and gait intensity, in order to pinpoint specific causes for impaired gait quality. Moreover, the methods developed in this thesis may allow for tailor-made interventions, which might increase their effectiveness.

Future research
As mentioned already above, more research is required to replicate the findings on the interaction between gait quality and quantity in larger and different populations. Other studies might pinpoint specific causes for impaired gait stability and explore the effects of intervening on these factors to gain additional insight in the mechanisms responsible for increased fall risk with ageing and disease. In addition, the prediction model should be externally validated and developed for individualizing interventions. The relation between misjudgment of one’s abilities and fall risk also deserves further investigation.
Besides these recommendations, further improvements in the assessment of gait quantity and quality and the prediction model can be made. The accuracy of the physical activity classification algorithm may benefit from the use of additional sensors, such as pressure sensors to detect height differences as occur during stair
negotiation and gyroscopes to detect trunk rotations during sit-to-stand movements and turning. Additional gyroscopes and pressure sensors might also aid in selecting only straight-lined gait episodes and allow for the assessment of extreme gait quality values, as was already argued in the discussion of Chapter 6. Moreover, complexity measures of daily activities, such as employed by others [219], might improve predictive value of physical activity for fall risk. Modern cell phones already incorporate accelerometers, gyroscopes and barometers and their application for gait recognition are promising ([220-223] and currently available applications for smart phones), hence future studies should explore their usefulness for fall risk assessment. Trunk accelerometry also allows for the detection of falls. Currently, these detection methods are not accurate enough to replace self-reported fall incidences, but they do hold promise for the future [115, 224-247]. Future research could focus on prediction of injurious falls and determine whether injurious falls have comparable predictors to non-injurious falls. In addition, predictive ability of a fall risk model including daily-life accelerometry might be further improved by using more advanced methods such as support vector machines or learning vector quantization, which do not assume linear relations between parameters and allow for complex interactions. Fall risk is a continuous scale and time until falling might provide valuable information on the severity of fall risk, hence models like Cox regression for recurrent events should be explored in future research. Finally, since gait quality is probably most predictive for falls during gait, developing methods to assess the quality of other activities, such as standing or sit-to-stand transitions, could enhance prediction of falls.

Conclusion
In this thesis, a method for ambulatory assessment of fall risk using a trunk accelerometer was developed. This work supports the use of gait quality measures to assess balance impairments, and provides ideas for standardization of the assessment of quality and quantity of daily-life activities to improve reliability. Moreover, it suggests that when physical activity is encouraged, improvement of quality of gait should not be overlooked to prevent an increase in fall risk. The insights obtained in this thesis contribute to a better understanding of the relation between gait quality, gait quantity and fall risk and provides opportunities to pinpoint and intervene on specific causes for increased fall risk to support the prevention of falls and fall-related injuries.