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Epilogue
Thesis summary
To advance towards the goal of identifying older adults with a high fall risk, this thesis explored the feasibility of gait analysis in daily life and its potential for fall prediction. First, the algorithmic validity of gait characteristic estimators was addressed by the development of a general method for testing their accuracy and precision. Second, the feasibility of estimation of gait characteristics in daily life was investigated by the assessment of errors due to sensor positioning and potential added value of daily-life measurements and by determining the reliability of the gait characteristics over different weeks. Finally, the predictive value of the daily-life gait characteristics for falls was assessed.

Validity of gait characteristic estimators
For some characteristics, such as Lyapunov exponents and sample entropy, establishing validity of their estimators is complicated by the absence of gold standard reference values for physiological time series such as trunk accelerations during human gait. To overcome this problem, a benchmark method was introduced in Chapter 2, which compares estimates and semi-analytical values of a characteristic of interest, based on simulated data. This approach allows for determining accuracy and precision of any implemented estimation algorithm. The algorithms of Wolf et al. (1985) and Rosenstein et al. (1993) for estimation of Lyapunov exponents were submitted to this method. The results showed that Rosenstein’s method was more accurate for short time series, shorter than approximately 10 000 samples, whereas Wolf’s method was more accurate for longer time series. Precision was better using Rosenstein’s method. These results, combined with literature that favored Wolf’s method above Rosenstein’s (Cignetti et al., 2012a), led to a focus on Wolf’s method in the remainder of this thesis.

Estimation of gait characteristics in daily life
For taking gait analysis from the controlled laboratory setting to unpredictable daily life, some challenges were recognized and addressed in this thesis. The sensors used here, were worn with an elastic strap around the waist, and attached by participants themselves. This implies the risk of, at times, incorrect
positioning of the sensors due to accidental movement or improper mounting of the sensor with respect to the intended anatomical position. This might affect the estimation of gait characteristics. In Chapter 3, the agreement was tested between gait characteristics estimated from accelerations recorded during walking of 21 young adults, at two positions on the lumbar spine (L2 and L5) and at the right hip (ASIS). To improve agreement of the gait characteristics, an off-line realignment of the acceleration signals was applied, which was an adaptation of the vertical (VT) tilt correction method (Moe-Nilssen, 1998), to account for alignment errors in the horizontal plane, i.e., the medial-lateral (ML) and anterior-posterior (AP) directions. It was found that, in general, basic gait characteristics such as gait speed, stride time and their variability and regularity, showed excellent agreement between all three positions. For more advanced characteristics like symmetry, smoothness and local dynamic stability, agreement was generally good between the two lumbar positions L2 and L5, but poor when comparing with the ASIS position. This led to the recommendation to emphasize wearing the sensor at the lumbar spine in the wearing instructions.

Another challenge was related to agreements and differences between gait characteristics in the laboratory and daily life. It can be questioned whether information obtained in daily life actually has added value over and overlap with gait characteristics obtained in controlled settings. This topic was addressed in Chapter 4. Gait characteristics that had shown an association with falling, be it in the laboratory, in daily life, or both, were selected. Estimates of these characteristics were determined from accelerations recorded in 18 older adults during five minutes of walking on a treadmill and during walking over one week of daily life. Estimates from both settings were compared for systematic differences and correlations, which were assumed to indicate situational and personal fall risk factors, respectively. Characteristics typically displayed a systematic difference between the two settings, indicating their sensitivity to situational factors. Results of the correlations varied between characteristics. Several characteristics had a significant correlation, which agrees with the assumption that sensitivity to personal factors is shared by treadmill and daily-life settings. This suggests that gait analysis in daily life, compared to gait analysis in the laboratory, may add information about situational factors while preserving information about personal factors.
The sensitivity of gait characteristics to situational factors could have a negative impact on their reliability. In Chapter 5, gait characteristics estimated from acceleration data recorded during two different weeks were compared. To obtain one representative estimate of a gait characteristic over a whole week, the median value of estimates based on all gait episodes over the week was taken, and to avoid biases due to epoch duration, data were analyzed in non-overlapping epochs of 10 seconds. The results of this comparison showed that reliability of the characteristics was sufficient for comparisons between groups of people, such as fallers and non-fallers. Therefore, these representative estimates of gait characteristics could be used for further analysis to examine their potential for fall prediction.

**Gait analysis and fall risk**

The final part of this thesis focused on the potential of gait characteristics estimated in older adults’ daily life to predict falls. In Chapter 5, the daily-life gait characteristics’ potential for fall prediction was explored through their associations with fall history. Several characteristics were found to be associated with participants’ self-reported numbers of falls experienced in the year preceding the measurement: high- and low-frequency percentages in ML direction and AP and VT directions, respectively, and gait smoothness, local dynamic stability and amplitude and slope of the dominant frequency in VT direction. This indicated that daily-life gait analysis could contribute to the prediction of falls.

Within the overarching research project Fall Risk Assessment in Older Adults (FARAO), the added value of daily-life gait characteristics and amount of gait activity based on trunk accelerometry for fall prediction was confirmed in a prospective study (van Schooten et al., 2015). In Chapter 6, prospective fall risk prediction was further investigated. The associations of high- and low-frequency percentages and local dynamic stability with fall history that were found in Chapter 5 were confirmed by their associations with fall incidence during a six months follow-up period. Additional associations were found for gait speed and stride frequency, for the VT and AP directions of stride regularity (autocorrelation), movement intensity (signal RMS), and symmetry (harmonic ratio), and for the VT direction of sample entropy.
Furthermore, in Chapter 6, the added value of extreme values of gait characteristics over a week of recordings, with respect to median values was explored. For this purpose, associations of these extreme values of gait characteristics with future falls were compared with the associations of median values of the gait characteristics. In addition, fall prediction models were generated either by using questionnaires, activity durations, and median values of gait characteristics, or by replacing the median values by extremes if these had a stronger association. It was found that particularly the extremes at the low-risk end of some characteristics associated stronger with falling than the median values. These stronger associations were found for low variability, instability and entropy, and high regularity and symmetry. These low-risk values were suggested to reflect steady-state or ‘high-quality’ gait epochs, which may occur during situations that are more similar between participants than the situations reflecting the most representative value of a characteristic as expressed by the median value. This suggests that these characteristics express personal fall risk factors, since for personal fall risk factors one might expect that comparison under similar conditions would be optimal. Despite these promising findings, the use of extreme values of gait characteristics instead of their medians did not significantly improve the prediction models based on questionnaires, activity durations, and median values of gait characteristics.

**General discussion**

**Estimation of gait characteristics**

**Algorithmic validity**

The benchmark test described in Chapter 2 was applied to the algorithms of Wolf et al. (1985) and Rosenstein et al. (1993) for the estimation of Lyapunov exponents. The test design is generic, making it useful to test other algorithms and other characteristics, for example algorithms for estimating entropy or symmetry of gait. The use of this benchmark for other characteristics, however, does require corresponding reference values, the acquisition of which might be a challenge, depending on the characteristic at hand. Some characteristics may not be uniquely defined for dynamical systems (e.g., symmetry, variability,
intensity). When a definition is agreed upon, a (semi-)analytical or otherwise reliable method for obtaining the reference values needs to be selected.

**Lyapunov exponents**

In the course of the studies presented in this thesis, a choice was made to focus more on the use of Wolf’s algorithm for estimation of Lyapunov exponents than on Rosenstein’s method. Several reasons can be given in support of this choice. First, the findings of the benchmark test in Chapter 2 suggested using Wolf’s method, since they were more accurate for long enough epochs such as obtained during five minutes of treadmill walking. Second, Cignetti et al. (2012a) found that estimates based on Wolf’s algorithm, used for short time series, were better in distinguishing gait of young and old participants than the estimates based on Rosenstein’s algorithm. Third, in chapter 3, agreement between sensor locations was better for estimates by Wolf’s algorithm than those by Rosenstein’s algorithm. In Chapters 5 and 6, the potential of Wolf’s estimator to discriminate between groups was confirmed; it associated both with fall history and future falls. However, when processing daily-life data in 10-second epochs, support by the benchmark test in Chapter 2 is lost, since for these relatively short epochs the benchmark indicates a poor accuracy of Wolf’s method. In addition, further analysis of the data in Chapter 6 showed a strong negative correlation between stride regularity as assessed by the autocorrelation, and Lyapunov exponents by Wolf’s method; -0.95, -0.91, and -0.94 for VT, ML, and AP directions, respectively. These correlations were based on the medians of participants over all their 10-second epochs. The combination of all these observations suggests that for epochs of 10 seconds of gait, Wolf’s estimator does probably not provide a very accurate estimate of the Lyapunov exponent. Still, at least when taking the median over multiple of these 10-second epochs, it has a high potential to discriminate between groups, possibly caused by sensitivity to other aspects of gait such as its regularity.

The doubts on the validity of Wolf’s algorithm for the short epochs analyzed in daily life raise the question what the associations of Rosenstein’s algorithm with falls would have been. When applying Rosenstein’s algorithm instead of Wolf’s to the data in Chapter 6, the VT and AP directions did not have a significant association with falling (B = -0.12 and 0.12, $P = 0.42$ and 0.43, respectively),
but the ML direction showed a trend towards significance ($B = 0.29, P = 0.052$). This contrasts with the significant associations found with Wolf’s algorithm for VT and AP directions only. Correlations between the participants’ median estimates by Wolf’s and Rosenstein’s algorithms were 0.34, 0.00, and 0.08 for the VT, ML and AP directions, respectively. Apparently, the two algorithms estimate different aspects of gait when applied to short, 10-second epochs. Unexpectedly, when comparing the estimates by Wolf’s and Rosenstein’s algorithms after normalizing to stride time, the correlations increase to 0.68, 0.52 and 0.59, which may have happened because the estimates were then multiplied by identical stride times.

**High- or low-frequency percentage – what’s in a name?**

The low-frequency percentage estimator determines the percentage of spectral power below an adjustable threshold frequency. This estimator was designed as a generic characteristic for a range of frequencies. When used with relatively high cut-off frequencies, it may be a confusing term. After all, the low-frequency percentage below 10 Hz, for example, can be considered rather an estimator of the absence of high-frequency power than the presence of low-frequency power. Therefore, in this Epilogue, the term low-frequency percentage is avoided in favor of the term high-frequency percentage, in case of high cut-off frequencies.

**Gait analysis in daily life**

Although gait analysis in daily life was shown to provide reliable estimates for gait characteristics that have added value for fall prediction, some open issues need to be addressed.

**Validity of estimates of daily-life gait characteristics**

In addition to the algorithmic validity mentioned in the preceding, validity of gait characteristics’ estimates constitutes an issue in general, particularly when estimating them in daily life. Algorithms for estimation have typically been developed and tested based on data obtained in controlled settings, and differences between settings may affect their validity when applied to daily-life gait. For example, gait speed may be estimated from the vertical displacement of the trunk (Zijlstra and Hof, 2003). In daily life, walking on uneven terrain
might disturb the estimates obtained in this manner. Testing the validity of the estimates in daily life comes with the difficulty of obtaining reference values for comparison. One would need to obtain these reference values by additional measurements on a participant, preferably 24 hours a day. For some characteristics such as gait speed this might still be achievable by using additional information, e.g., GPS location in case of longer distances, or specialized sensing of in-house gait speed by other methods such as video or Microsoft Kinect (Pol et al., 2013; Rantz et al., 2013). However, for most of the characteristics tested in this thesis this seems not or at least not easily feasible. This means that one has to rely on the laboratory-based algorithmic validity and the other kinds of validity testing mentioned in the General Introduction: construct validity, predictive validity in a model, convergent validity in experimental studies and predictive validity in observational studies. Extensive work related to these validities has already been published, such as shown in the review by Bruijn et al. (2013), who stated that Lyapunov exponents and variability measures were supported best as viable stability measures. Stride regularity, low-frequency percentage, and the dominant frequency’s amplitude may be considered variability measures as well. The other characteristics that appeared in this thesis were not included in the review by Bruijn et al., although a very recent study on entropy measures provided support for the validity of sample entropy as a measure of gait stability (Leverick et al., 2014). The remaining characteristics, gait speed, frequency, intensity, smoothness and symmetry, may not be directly related to stability, but may be affected by underlying deficits that also affect fall risk.

The accelerometer and its positioning

The results in this thesis were obtained with the DynaPort MiniMod and DynaPort MoveMonitor accelerometers (McRoberts, The Hague, The Netherlands). These sensors provide continuously monitored raw acceleration data, which were needed to estimate the gait characteristics. Activities were categorized and hence gait episodes were selected with software provided by McRoberts. Although there is no specific reason to doubt portability of results to other accelerometers, one needs to keep in mind the instrument specifications, which were a range of -6g to 6g, a sampling rate of 100 samples per second and a resolution of 0.003g, as well as the availability of raw
acceleration data and effective activity categorization. The applied activity categorization software classified walking into the locomotion category (Dijkstra et al., 2010), which may also contain episodes of running, stair climbing and in some cases even cycling. Gait characteristics of participants who show many of these episodes may be somewhat biased, although the use of medians instead of means does prevent effects of outliers. In Chapter 6, where besides the median values also the extreme values of gait characteristics were used, the episodes suspected to be running were discarded. Despite the potential presence of these different ways of locomotion in the episodes used to determine daily-life gait characteristics, these characteristics appeared to contain valuable information for fall prediction.

Location and the manner of sensor mounting represent another factor in the generalizability of results. The results of Chapter 3 showed that the agreement between hip and lumbar spine was good for several of the characteristics, particularly speed, frequency and their variability, as well as regularity. However, several other sensor locations on or near the trunk have been mentioned in the literature, such as sternum, thoracic spine or thigh. Further investigations of effects of sensor location and manner of mounting are recommended. In addition to the agreement tests, these investigations might provide solutions if estimates do not agree between locations, i.e., directions to translate results (e.g., estimates of gait characteristics) from one location to another, or preprocessing steps to make characteristics more location independent. The realignment method described in Chapter 3 would be an example of such a preprocessing step. These solutions would be required to combine data sets obtained with sensors at different locations. Also the use of smartphones as monitoring instruments (Tacconi et al., 2011) would require similar solutions, because these devices are not bound to a fixed wearing location.

**Duration of gait epochs**

The daily-life data used in this thesis were divided into short, 10-second, epochs of walking. For some characteristics, such as variability and local dynamic stability, this is considered an insufficient period to obtain a reliable estimate (Bruijn et al., 2009b). However, a week of daily-life data consists of multiple
epochs, which enhances reliability. For variability and local dynamic stability, a study on agreement between estimates of longer epochs and averages of estimates of multiple shorter epochs, showed that variability did not correlate well between the longer and multiple shorter epochs, whereas local dynamic stability did (van Schooten et al., 2014).

As it can be questioned whether the 10-second duration of epochs is adequate, the effects of using longer epochs for daily-life gait analysis were further investigated in our data. When requiring a minimum summed duration of 500 seconds (e.g., 50 epochs of 10 seconds, or 25 epochs of 20 seconds) for estimating representative gait characteristics, it appeared that several participants did not produce a sufficient number of these longer epochs. Considering that this group of low-mobility participants can be of specific interest in fall prevention, the epoch length was kept at 10 seconds.

**Realignment**

Chapter 3 described a method for realignment of the sensor data to the VT-ML-AP reference frame. Application of the realignment improved the reliability of estimated gait characteristics and was applied in all subsequent chapters. This realignment method estimated one rotation for a complete time series. Changes in orientation of the sensor during the time series, which may occur due to movement of the sensor along or around the trunk, are thus not corrected for. In particular for longer periods of several minutes as used for the over-ground data in Chapter 3, these changes in orientation may occur. A time-dependent rotation should be considered for these longer epochs, which could be designed as an interpolation of rotations estimated from shorter time series. In our daily-life data, this was not an issue, since short epochs of 10 seconds were used. In addition to orientation changes due to movement of the sensor with respect to the trunk (lumbar spine), orientation changes occur within a stride, as would be measured by a gyroscope. Availability of gyroscope measurement may offer the possibility to refine the realignment in order to obtain accelerations in a global reference frame instead of the sensor (or lumbar spine) reference frame, which would likely further improve estimates of for example absolute ML excursions.
Fall risk prediction

Gait analysis in daily life can contribute to the prediction of fall risk. This was shown by different studies on the associations of gait characteristics with fall incidence (Chapter 5; Chapter 6; van Schooten et al., 2015), and by the added value of daily-life gait characteristics based on accelerometry for fall prediction models (Chapter 6; van Schooten et al., 2015; Weiss et al., 2013). Most of the participants in our previous study (van Schooten et al., 2015) also participated in Chapter 6. Some results differed slightly across these studies. The characteristics that had an association differed between studies both for fall history and future falls. Apart from significance issues due to different group sizes or random effects, adaptations in the estimators may have played a role for some characteristics. For low-frequency percentage in ML direction the threshold was set to 0.7 Hz in our previous study (van Schooten et al., 2015), following the settings used in Chapter 3 based on preliminary optimizations, while in Chapter 6 a threshold of 10 Hz (implying absence of high-frequency percentage) was used, following the settings found in Chapter 5 by optimization of separate directions for associations with fall history. Nevertheless, for the fall prediction models developed by van Schooten et al. (2015) and in Chapter 6, the predictive values as expressed by the area under the receiver operator curve were similar, 0.82 and 0.81, respectively. The higher value for the model by van Schooten et al. (2015) may be explained by allowing higher $p$-values for parameter addition, which resulted in more parameters in the model. As for the parameters that were selected for the resulting models, the questionnaire parameter for fall history and the sample entropy in ML direction were common in both models. Both models contained additional parameters on the quality of gait, although the selected gait-quality parameters were different. Apparently, with the availability of many fall-risk related parameters, the exact selection of parameters is sensitive to subtle differences.

Another interesting comparison is that of characteristics’ associations with past and future falls. This comparison was made by van Schooten et al. (2015) with the same participants for past and future falls. It turned out that the associations pointed in the same direction for past and future falls, although they were generally stronger for future falls than for past falls.
In Chapter 6, the associations of gait characteristics’ extremes with future falls were tested, expecting that this might provide more insight into high-risk situations. It appeared, however, that specifically the extremes of several gait characteristics indicating high gait quality had a more significant association with falling than the medians, indicating that the more regular, symmetric epochs of walking may be of specific interest for fall risk prediction. Possibly, the situations in these epochs of optimal performance are more similar between subjects, as would be the case in a controlled setting. This led to the question whether these high gait-quality extremes in daily life would have a higher correlation with the characteristics estimated on a treadmill than the medians. The same data and the same approach as in Chapter 4 were taken, except that now the extremes indicating high gait quality, instead of the medians were used. Generally, the high gait-quality extremes did indeed have higher correlations with the treadmill estimates. For ML high-frequency percentage, VT smoothness, and ML amplitude of the dominant frequency, the association with treadmill gait was not significant for the median estimates, but it was for the low-risk extremes.

Many measures depend on walking speed. If participants have sufficient episodes, it might be possible to extract the relations between speed and other characteristics for each participant and to compare the participants at ‘identical’ speeds, similarly to the controlling of walking speed that can be done for laboratory-based over-ground walking (Moe-Nilssen and Helbostad, 2004). In a similar way as the low-risk or ‘high gait quality’ extremes, this might be more predictive of falls for certain characteristics than the median over all walking epochs.

Future research

Gait characteristics

Algorithm updates using a next generation instrument

Ongoing development in sensor technology can be expected to create new opportunities for improvement of daily-life gait analysis and fall prediction. The studies described in this thesis were based solely on the use of a tri-axial
accelerometer, given the limitations in battery life when adding other sensors, such as a gyroscope, at the start of the project. Currently, technological improvements allow for measurements of at least one week of linear accelerations and angular velocity, as well as other quantities such as temperature, magnetic field and air pressure. This combination can be realized with a small device. For instance, the new version of the DynaPort MoveMonitor has the same casing as the previous version, but with added sensors and improved battery life. These added sensors may not only provide opportunities for further refinement of activity recognition algorithms, but also for improved estimation of gait characteristics. For instance, the low-frequency percentage below 0.7 Hz was suggested to represent slow postural changes affecting sensor orientation. The availability of angular velocity recordings would enable more accurate estimation of these changes in sensor orientation. As mentioned above, the method for realignment of sensor data to the VT-ML-AP reference frame may be refined in terms of a time-varying realignment to a global reference frame, which would pave the way for improvement of the estimation of VT and ML displacement and for gait speed, which is estimated from VT displacement.

**Underlying mechanisms of specific gait characteristics for fall risk**

It is not yet clear for all gait characteristics related to falling why they predict fall risk or which possible underlying impairments they quantify. For some of the newly found characteristics suggestions of underlying mechanisms were formulated, the validity of which needs to be examined. As mentioned above, whether low-frequency percentage below 0.7 Hz in VT and AP direction is related to slow forward-backward sway may be validated by simultaneously recorded gyroscope and accelerometer recordings. A mechanism underlying the association of this slow sway with fall risk may be a limited control of angular momentum. High-frequency percentage above 10 Hz in ML direction may be related to the ability to quickly generate forces, specifically in ML direction. This may be confirmed through measurement of maximal force generation by muscles that cause ML movement.

Also for other characteristics, the underlying mechanisms may require further investigation. However, one has to realize that it may not be a single, isolated
mechanism that causes changes in a certain characteristic. Low gait speed and
low stride regularity, both associated with falls, may be caused by a
combination of different deficits. The complexity of the sensory-motor system
that influences these characteristics will obscure effects of individual deficits or
abilities. Similar to gait speed, which could be considered a summary indicator
of vitality that predicts survival (Studenski et al., 2011), some of the gait
characteristics (including gait speed) might serve as a summary indicator of gait
quality, which is affected by impairments that determine fall risk.

**Daily-life gait analysis to select the right fall prevention intervention**
The fall-prediction models that were described in Chapter 6 and in our prior
paper (van Schooten et al., 2015) may be used to estimate fall risk. This would
help to identify individuals with a high fall risk, perhaps even before a first
injurious fall. As a next step, daily-life gait analysis could be used to help
therapists in deciding how to treat individuals with a high fall risk. The
prediction model by van Schooten et al. (2015) contained an interaction effect
between the amount and quality of gait that suggested that persons with poor
gait quality have an increased fall risk if they walk a lot, but persons with good
quality do not. Although this finding was not confirmed in the present thesis,
further research on this topic might, for example, indicate that persons with poor
gait quality should first improve their gait quality before increasing their
amount of gait. Other underlying information of the daily-life gait analysis may
also assist in such decisions. This would be the case if gait characteristics
obtained in daily life can be related to specific abilities or impairments, as
suggested above. For example, if future studies would confirm the high-
frequency percentage in ML direction to be related to the ability to quickly
generate force, this characteristic could be useful in predicting if a person would
benefit from an intervention specifically addressing the ability to quickly
generate forces.

**Analysis of non-gait activities in daily life**
The current thesis focused specifically on epochs of walking. This is an obvious
choice, since most falls are reported to occur during walking (Bergland et al.,
1998; Robinovitch et al., 2013). However, recordings of accelerations during other activities such as standing or sit-to-stand transitions may also provide information on stability or fall risk, since these tasks may be challenging and since falls occur during these activities as well (Bergland et al., 1998; Robinovitch et al., 2013). Characteristics of sit-to-stand transitions, such as peak power or sit-to-stand duration, may be relevant for fall risk, and the inclusion of gyroscopes may facilitate obtaining an accurate estimate of these characteristics (Regterschot et al., 2014).

**Conclusion**

Gait analysis in daily life is feasible and has added value for fall risk assessment. In other words, watching someone ‘walk on the wild side’ for a week, is enough to get a rough idea of how well they are able to find their way safely in this zone of ever-present danger and stay on their feet.

Validity and interpretation of certain estimators, such as Wolf’s estimator for Lyapunov exponents, are a matter of concern when applied to (short) time series obtained in daily life. Nevertheless, estimates of gait characteristics can be reliably obtained from a week of trunk accelerations recorded in daily life, and are generally robust against likely errors in sensor positioning. Moreover, estimates of many gait characteristics in daily life are associated with past and future falls, such as gait speed, regularity, symmetry, entropy, and also Wolf’s Lyapunov exponent. Finally, gait characteristics and amount of activities estimated in daily life can improve fall prediction models based solely on questionnaires.