Summary

Muscle strength is an important indicator of physical function and independence in older people. Research on oldest-old people (>85 years) is limited. This thesis addresses some of the challenges that this population presents for research and clinical management, in relation to assessing muscle strength.

Chapter 1: Background

Sarcopenia is a progressive, generalized muscle disorder that not only affects the neuromuscular system but also other organ systems and leads to immense health problems when untreated. Characterized by excessive muscle wasting due to age, morbidity and inactivity, sarcopenia is an important geriatric syndrome. It has been recognized as an independent medical condition by the World Health Organization since 2016, which highlights its emerging importance in health-related adverse outcomes. The prevalence of sarcopenia is estimated to increase globally, as a consequence of the aging population. It is anticipated that approximately 20% of older people will be affected by 2045. Sarcopenia has been well studied in the so called young-old elderly (<75 years of age) and contributed to the improvement in health condition of this age group by implementation of the research findings into prevention strategies. However, rather little is known about health care needs specifically tailored to older and oldest-old age groups (>75 years), especially those that are institutionalized in nursing-homes.

The diagnosis of sarcopenia is defined by low muscle mass or decreased contraction quality in addition to low strength, and is commonly assessed by thickness and echotexture of ultrasound images in clinical research studies. Information about all three muscle characteristics, strength, thickness and quality, is important not only to diagnose sarcopenia but also to guide interventions aimed at improving strength. Although comprehensive geriatric assessment is necessary to evaluate the severity and potential causes of sarcopenia in detail, handgrip strength has been recommended as a conclusive, stand-alone measurement to screen older people at risk of poor health. According to the updated version of the European Working Group of Sarcopenia (EWGSOP2) the first stage of sarcopenia, called probable sarcopenia, is detected by low handgrip strength (<16 kg for women and <27 kg for men) or a slow performance on a repetitive chair-stand test (> 15 seconds on 5 sit-to-stands).

Aims of this thesis

The aims of the thesis were to; (1) complement existing reference values of strength measures of young-old people with those of the older age groups for clinical use, (2) apply recently published guidelines for detection of sarcopenia to update prevalence data of probable sarcopenia for public health monitoring, and (3) provide initial evidence of relationships between low muscle strength and functional performance as well as neuromuscular changes in nursing-home residents, which has not been studied before.
Chapter 2
Since handgrip strength declines with age, is lower in women than men and varies between living environments, country-specific reference values are required for men and women of all age groups to assess strength decline in clinical practice. Chapter 2 describes a cross-sectional study of 244 participants in which handgrip strength was measured in a Swiss community-living and institutionalised population aged 75 years and older. While the results of this study were consistent with previously reported strength values in people aged between 75-84 years, it provided, for the first time, handgrip strength reference values for men and women aged between 85 and 99 years. The oldest-old were found to have significantly (26-32%) lower handgrip strength than the young and older-old people. The reference values of handgrip strength presented in this thesis, collectively with previously reported normative values of Swiss elderly aged 75-84 years, are of direct clinical use. Handgrip measures are made clinically by physicians, and physical and occupational therapists to screen older people for overall strength and health condition.

Chapter 3
In 2019, the algorithm to detect sarcopenia changed from a loss of muscle mass as the key characteristic, to a loss of muscle strength. With the application of the new EWGSOP2 guideline, it is important to provide updated prevalence data for probable sarcopenia in the community for health monitoring purposes of this population. In Chapter 3, the point prevalence of probable sarcopenia was investigated in a representative sample (n=219) of community-living Swiss adults according to the new guidelines along with measures of physical activity. The results of this study demonstrated probable sarcopenia in 26% and 28% of oldest-old women and men living in the community. Although the prevalence of probable sarcopenia was lower than in previous research in which muscle mass was used for detection of pre-stage sarcopenia, almost one third of the older people still had an increased risk of health decline. Moreover, this research showed that people with low strength had 2.8 times higher risk of dependence in activities of daily living (ADL) than people with normal strength. The relation between strength and functional limitation highlighted the relevance of frequent strength assessments in clinical practice for timely initiation of counteracting interventions.

Chapter 4
Although Chapter 3 provided new data on the point prevalence of probable sarcopenia and its relation to dependence in ADL in community-living oldest-old, it is not clear whether strength testing for probable sarcopenia is feasible in nursing-home residents and indicative for health-related outcomes in that cohort. Consequently, Chapter 4 evaluated the feasibility and relevance of the handgrip strength test and the chair stand test in a cross-sectional study of institutionalized, older people (n=30). The findings showed that although measures of handgrip strength could be obtained from institutionalized older people, the chair-stand test could only be completed by about 50% of the participants; raising questions of the suitability of the chair-stand test to
screen for probable sarcopenia in institutionalized older people. Moreover, the point prevalence of probable sarcopenia was found to be 80% in this cohort; much higher than that for community living elderly people (26-28%) as shown in Chapter 3. It was also shown that probable sarcopenia detected by both tests was associated with diminished gait speed and more advanced frailty status in this cohort, while only low handgrip strength was related to lower overall muscle strength and ADL dependence. Hence, this research raises the possibility that handgrip strength might be suitable to estimate overall strength of old, frail nursing-home residents. Moreover, although further research is required, it also suggests that handgrip strength is a potentially simple clinical test that therapists could use to screen for physical function and ADL performance.

Chapter 5
Although low handgrip strength was related to ADL dependence in Chapter 4, quadriceps strength has been previously reported as key for specific daily activities, such as transfer activities from sit to stand and stable walking in community-living older people. ADL execution in institutionalized people with very low strength differs from that in community-living older people, as they use their hands and arms as support on standing up and for stabilizing body sway with walking aids. Therefore, assessment of isometric quadriceps muscle strength in this cohort merits special attention, particularly as only 50% of the institutionalized people were able to perform the chair-stand test, which provides an indirect estimate of quadriceps strength. Chapter 5 evaluated the relationship between quadriceps strength and ADL performance in 30 nursing-home residents. The results indicated that quadriceps strength is also crucial for ADL in nursing-home residents who use their hands for tasks that typically involve the use of the lower limbs. However, the strength required for independent performance was much lower than previously shown in the performance of community-living elderly people not using their hands (peak isometric torque normalized to body mass of 0.6 Nm/kg body mass versus 3-3.5 Nm/kg). The findings provide the first evidence that an isometric quadriceps strength of > 11kg (normalized peak torque of 0.52 Nm/kg) is 100% sensitive and 79% specific in predicting ADL-independence in this population. Therefore, isometric quadriceps strength measurement can be recommended as a specific screening test for ADL performance in nursing-home residents. Moreover, exercise programs can be guided by the target quadriceps strength of 11 kg (0.52 Nm/kg) for improvement of ADL independence.

Chapter 6
To specifically improve strength in older adults, age-related neuromuscular changes that contribute to loss of strength need to be evaluated and addressed by exercise interventions. Intramuscular adipose tissue accumulation has been shown to be one important component in decreasing muscle contraction quality and strength in community-living older people. Infiltration of adipose tissue changes the tissue composition within the muscle, which appears as increased echo intensity on ultrasound images. In oldest-old nursing-home residents, muscle changes might differ from young-old community-dwelling people, due to extremely low strength and different
percentage contributions of neural and muscular changes leading to low strength. The evaluation of sonographically measured muscle quality of the knee extensors and its relation with strength in institutionalized older adults was addressed in Chapter 6. The results added proof of concept that a relationship between an ultrasound-derived index of muscle quality and muscle strength also exists in the oldest-old, multi-morbid, frail nursing-home residents. However, the relationship is likely mediated by physical activity level, as the relationship could only be shown in people whose expanded energy per week was above the cut-off value for low physical activity, 383 kcal/week for men and 270 kcal/week for women. Changes in muscle quality were detected by a sonographic index of muscle heterogeneity, not previously established in age-related muscle evaluation. The results indicate the usefulness of ultrasound imaging in clinical sarcopenia assessment in nursing-home residents.

Conclusions
Overall, this thesis has produced several novel findings. The studies built upon research findings involving older-old people (75 to 84 years), to provide for the first time, reference values of handgrip strength in the oldest-old (85 to 99 years) for direct clinical use. Further, new specific point prevalence data for probable sarcopenia were established in the oldest-old Swiss population. Cut-off values of handgrip and quadriceps strength have been shown to specifically indicate dependence in ADL in nursing-home residents, potentially useful for screening institutionalized people at risk of functional decline. Furthermore, this thesis has provided the first insight into muscle characteristics of people most at risk of sarcopenia, the comorbid, nursing-home residents, highlighting a potentially new sonographic index of age-related changes in muscle quality.