Chapter 4

The Capability Approach in Epidemiological Studies

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4.1 Introduction

Population epidemiology is the science that deals with disorders and certain conditions at the population level, i.e. at the macro-level. In contrast to experimental studies, the scientist in epidemiology cannot manipulate conditions to make studies of associations as pure as possible. This might be seen as a disadvantage, but is actually an advantage because epidemiology studies conditions at the place where they are occurring, i.e. in real life. The science of epidemiological studies examines the occurrence of diseases, risk and protective factors for diseases and the prognosis of different disorders and conditions in different populations.

Population epidemiologists may also study the entire course of disorders, beginning with very mild symptoms occurring before the individual presents to the healthcare system. This contrasts with clinical studies, which can only study patients who have sought help from the healthcare system. The latter studies are thus

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influenced by the fact that individuals who seek help differ from those who do not regarding a number of factors. The occurrence of disorders is measured as prevalence and incidence. Prevalence is the number of individuals affected by a disease divided by the number of people living in the target population during a certain time period, while incidence is the number of new cases that occur during a certain time period. Prevalence is related to the burden of the disease for society, while incidence is related to the risk of developing the disease.

The capability approach is an ideal framework for epidemiological studies because it captures the dynamic and multiple processes involved in these types of studies, in relation to both time and space, as well as socioeconomic, psychological and biological factors. Determinants for common disorders and conditions include complex interactions among a multitude of factors acting between and within macro-, meso- and micro-levels during the life-course of an individual. Each of these may have a small positive or negative impact on the outcome (e.g. dementia, cognitive function, depression, well-being, functional ability), but may together have a large or substantial impact at the micro-, meso- and macro-levels depending on the individual or societal conversion factors. The latter may be related to factors such as cognitive, physical and social reserve at the individual level, or the effect of the welfare state and educational systems at the societal level.

The ultimate goal of population epidemiology is to prevent diseases and functional limitations, and to increase well-being, thus increasing capability at the individual and societal level. However, what may constitute a small risk at the individual micro-level may have a large impact on the burden of disease at the population level, i.e. at the macro-level, in both the short and long term. However, findings from observational studies do not always translate into results in randomised controlled trials (RCT), which are the gold standard for clinical trials. One reason could be time of follow-up. While observational population studies more or less have a

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lifetime perspective and act at the macro-level, RCTs could be regarded as acting at a meso- or micro-level, due to selection criteria for the individuals who participate, and they often have short follow-ups, not more than 5–6 years.

Primary prevention refers to interventions at the population level in individuals without symptoms or signs of a particular disorder (Skoog & Gustafson, 2006). This could be vaccination against a virus, or campaigns to increase physical activity, change to healthier diets or cessation of smoking. Primary prevention may have a large impact at the macro-level by decreasing prevalence and incidence, but the effect on capability at the micro- and meso-levels is not easy to measure, and not always appreciated by the individual. Secondary prevention acts on individuals who have a risk factor, but no diagnosis (Skoog, 1999). One example of secondary prevention is the treatment of hypertension to prevent stroke or myocardial infarction. Screening to detect disorders very early, before a diagnosis, is also part of secondary prevention, e.g. screening for breast cancer or prostate cancer. Secondary prevention is also related to macro-level effects, but also has a clearer effect at the micro- and meso-levels. Tertiary prevention refers to treatment when a disorder is already present. At this stage, treatment is mainly conducted at the micro-level, and its impact is mainly felt at the micro- and meso-levels. However, when treatment is introduced for a disorder that was previously lethal or resulted in long-term care, it may also have an impact at the macro-level. For example, if a treatment were introduced that slowed down the course of Alzheimer's disease or treated the disorder completely, it would have a huge effect on the costs of elderly care for society, i.e. for capability at the macro-level.

Population studies could thus be seen as acting at the macro-level, because they are supposed to study representative samples of populations. This is especially true in the study of prevalence, which is related to the burden of a disorder on society, i.e. with capability at the macro-level. Common chronic disorders, such as cardiovascular disorder, depression or dementia, lead to costs at the macro-level for the healthcare sector, for sick leave and for home care. The more severe a common disorder is, and the more widespread it is, the greater the costs for society and the greater the suffering for individuals and their families, i.e. the more it will affect capability at macro-, meso- and micro-levels. A severe rare disorder, on the other hand, leads to costs and suffering at the micro- and meso-levels, but may not have a large impact at the macro-level.

Risk and protective factors thus act at macro-, micro- or meso-levels. Some risk factors act on capability at more than one level. One example is education. A lower level of education is a risk factor for most of the common disorders in old age, e.g. dementia (Wang et al., 2012), depression (Skoog, 2011) and cardiovascular disorders (Chen et al., 2021), which all influence capability. At the macro-level, years of education, the quality of education, cost of education and the number of pupils in a school class are all dependent on political decisions taken at the macro-level. The effect of education is also dependent at the meso-level, for example the quality of teachers, the school, the influence of parents and family and the economic situation at home. At the micro-level, educational attainment is dependent on each individual's intellectual capacity and wishes. The impact of education is also strongly

dependent on socioeconomic circumstances, but these two conditions often have independent influences on the risk of dementia. Thus the simple finding of increased risk of dementia, depression and cardiovascular disorders with lower levels of education is dependent on a number of factors that act and interact at the macro-, meso- and micro-levels.

It needs to be emphasised that associations between risk factors and disease may not be stable between populations due to differences at the meso-levels between populations (e.g. differences in socioeconomic factors, educational level, climate, animal populations, political decisions, population density, access to healthcare and medication and a number of other factors). This is one obvious reason why findings from one population may be difficult to replicate in another.

Findings and risk factors may also differ between historical periods. In our H70 studies, which are representative population studies conducted among different birth cohorts of 70-year-olds born between 1901–1902 (first examined in 1971–1972) and 1944 (first examined in 2014) and followed until death (Rydberg Sterner et al., 2019a; Skoog, 2004), we have found a number of significant changes over time. For example, cognitive (Karlsson et al., 2015; Thorvaldsson et al., 2017) and physical function have improved, blood pressure has declined (Zhi et al., 2013; Joas et al., 2017), BMI has increased (Zhi et al., 2013), the prevalence of dementia (Skoog et al., 2017; Skoog, 2016; Wu et al., 2016, 2017), impairment in activities of daily living (Falk et al., 2014; Falk Erhag et al., 2021), depression (Rydberg Sterner et al., 2019b) and sleep problems (Skoog et al., 2019) has decreased, educational level, alcohol consumption (Ahlner et al., 2018) and sexual activity (Beckman et al., 2008) have increased, and even the overall personality of the population has changed considerably (Rydberg Sterner et al., 2019b; Billstedt et al., 2013, 2017). The greatest changes over time were observed in women. An interesting finding was that a restricted social network was a risk factor for depression in the 1970s, but not in the 2000s (Sjöberg et al., 2013). Thus, what is true in one time period may not be true in another. Reasons for the changes are to be found in macro-level changes in education, gender roles, socioeconomic circumstances, living and working conditions, healthcare and advances in medical science, such as the introduction of effective drugs against infections and hypertension (Skoog, 2016).

One of the most important aspects of epidemiology is to evaluate whether certain associations between risk factors and outcomes, or between disorders and consequences, are influenced by confounding factors. This is often achieved using statistical methods, such as regression analyses, where the independent effect of a particular factor is examined by controlling for other, associated factors. Age is one of the most important confounding factors for many associations, but the effect of age might also be confounded by age-related factors. One example is the reported association between age and death in individuals with Covid-19. When age was analysed in isolation, without taking other age-related factors into consideration, it became a very strong predictor for death. However, in Sweden, 75% of all deaths occurred in the small group (3%) receiving old-age care (home care and nursing homes) (www.socialstyrelsen.se/en/). Taking this into consideration, the age-related effect was considerably attenuated.

In the following, we will discuss certain concepts that are related to the epidemiology of capability in ageing, such as specific conditions that are important for capability, including cognitive function, mental health (mostly depression), multimorbidity and functional ability, and factors that may affect these conditions and affect capability in general, such as the non-modifiable factor of genetics (a trait) and the modifiable factor of nutrition (a state).

Cognitive function and mental health are among the most important determinants for capability in old age. Mental and cognitive health in older populations are positioned along a continuum, from complete wellbeing to defined disorders, such as dementia (e.g. Alzheimer's disease) and other mental disorders (e.g. depression). Even mild mental conditions have a profound impact on health, and how a person adapts to ageing and its related disorders, and thus to the individual's capability. Recently, we reported that pathological biomarkers for Alzheimer's disease are present in 45% of completely normal 70-year-olds (Kern et al., 2018), extending the continuum into symptom-free individuals, in whom the disorder has not yet had an impact on capability. The relevance of these subclinical conditions can only be studied in longitudinal, population-based samples.

4.2 Cognitive Function and Capability

Cognitive function in the population is positioned along a continuum from high to normal function, to subclinical stages (defined as having pathological biomarkers but normal cognitive function), to mild cognitive impairment (defined as decline in cognitive function without impairment in activities of daily life) to dementia (defined as cognitive impairment with impairment in social and functional abilities). The prevalence of dementia increases from 3% at ages 70–75 years to 52% in 95-year-olds (Börjesson Hansson et al., 2004). Mild cognitive impairment is even more common.

Dementia is the most important factor affecting capability in older people at the macro-, meso- and micro-levels, affecting the costs of care for society, the family of the person with dementia, and the individual who suffers from the disease, having an impact on all aspects of the individual person. The two most common forms of dementia are Alzheimer's disease (AD) and vascular dementia. Risk factors for AD at the macro-level include low educational level, and low socioeconomic status (Hasselgren et al. 2018; Wu et al., 2018). The prevalence of dementia is also related to time-trends and thus to historical periods at the macro-level. This is reflected in reports that the prevalence and incidence of dementia has declined during recent years, and is lower in later-born birth cohorts (Skoog, 2016; Wu et al., 2017).

The risk of dementia is also related to dietary patterns, which may be due to macro-, meso- and micro-level circumstances. At the meso-level, the risk of dementia is related to social networks and the type of work the individual has had. At the micro-level are genetic factors, such as possession of the *APOE* e4 allele, and risk factors, such as low educational level (Hasselgren et al., 2018), psychological stress

(Johansson et al., 2010), poor sleep, neuroticism (Johansson et al., 2014), poor lung function (Guo et al., 2007) and cardiovascular risk factors, such as hypertension (Skoog et al., 1996; Joas et al., 2012), being overweight (Gustafson et al., 2003), diabetes mellitus (Mehlig et al., 2014) and hypercholesterolemia, as well as protective factors, which could be regarded as conversion factors, such as midlife fitness (Hörder et al., 2018), and physical and cognitive activities (Najar et al., 2019). The importance of risk factors may also differ depending on the age at which they are measured. For example, stroke and Alzheimer encephalopathy are related to dementia, but the relative risk is lower in nonagenarians compared to septuagenarians and octogenarians (Andersson et al., 2012).

The different risk factors also interact in a complicated way. We recently reported that possession of the *APOE* $\epsilon 4$ allele and socioeconomic status interacted in the determination of time to dementia onset (Hasselgren et al., 2018). At the most fine-grained micro-level, the brain changes in Alzheimer's disease, as reflected by neurochemical changes in the cerebrospinal fluid, may influence cognitive change. For example, in a cooperation project with the Mayo Clinic, Rochester USA, higher levels of the protein neurofilament light, an unspecific biomarker for neurodegeneration, in cerebrospinal fluid was associated with higher risk of decline from normal cognition to mild cognitive impairment (Kern et al., 2019). This is important at the macro-, meso- and micro-levels because neurodegeneration leads to cognitive decline, which leads to societal costs for healthcare at the macro-level as patients with MCI and dementia may need more attention from professional caregivers at the meso-level. This, in turn, may lead to changes in political regulations at the macro-level and is related to less capability at the meso- and micro-levels.

4.3 Depression and Capability

Another common condition that negatively affects capability in older adults is depression, which is a syndrome characterised by low mood, loss of interest, loss of appetite, sleep problems, cognitive symptoms, motor retardation, guilt and suicidal feelings. Depression is one of the most common mental disorders in old age (Skoog, 2011), and is one of the leading causes of the global burden of disease among both men and women (Ferrari et al., 2010). During the past decade, depression has been ranked as the third-to-fifth most common cause of years lived with disability (YLD) (James et al., 2018). The prevalence among older populations is approximately 10%, including 1–5% with major depression (Fiske et al., 2009). From a lifetime perspective, approximately 40% of women have had major depression, rising to 70% if minor depression is included (Skoog et al., in manuscript). Depression is related to a number of consequences influencing capability at the macro-, meso- and micro-levels. At the macro-level, depression is related to an increased use of health services, a need for home care and, among younger ages, an increase in sick leave. At the meso-level, it affects the social network, family and workplace. At the micro-level, it is related to decreases in well-being, life satisfaction and cognitive function,

an increased risk of suicide and increased risk of somatic conditions, such as stroke and myocardial infarction, and an increased non-suicidal mortality rate (Skoog, 2011). Thus, depression is a major factor affecting capability, not only in old age, but also from a lifetime perspective.

Depression may thus affect, and be affected by, available resources at all societal levels. At the **macro-level**, risk factors for depression include poverty, discrimination, national pension systems, unemployment rates, disasters, other negative historical events and access to healthcare. Depression is related to increased use of healthcare and home-care services (Skoog, 2011), and is thus associated with higher direct and indirect costs for all age groups (König et al., 2019), especially older age groups, healthcare-related costs, lost productivity or premature death by suicide (Greenberg et al., 2015). Late-life depression is associated with early retirement (Zuelke et al., 2020), which may not only affect household finances, but will also generate productivity loss and lower income tax revenue at a societal level. Today, older adults are healthier than those of previous generations. Higher levels of depression in the population will prevent the potential societal benefits stemming from having older adults working beyond retirement age. Besides economic factors, another important macro-level issue related to late-life depression is the lack of access to mental healthcare. Globally, there is an unmet need for mental healthcare (Dakic, 2019). In a focus-group study from the H70 studies (Rydberg Sterner et al., 2020), participants expressed an awareness of the lack of access to specialised mental healthcare in Sweden, both from their own experiences and from media reporting. In addition, they were frustrated by the lack of psychotherapeutic options for the treatment of depression. It has been shown that antidepressants are prescribed to older adults by default, due to lack of time for discussion about other treatment options (Overend et al., 2015). The Swedish National Board of Health and Welfare acknowledges that depressed older adults have less access to specialised care and psychotherapeutic alternatives than their younger counterparts (Socialstyrelsen 2018; Socialstyrelsen 2019). Our participants did not trust that they would be prioritised by healthcare services if depression recurred. The lack of access to mental healthcare may have adverse effects on future help-seeking behaviour.

At the **meso-level**, risk factors for depression include poor social networks, lower socioeconomic status in relation to others, living in a poor environment, negative life events, an unhappy marriage or divorce and a family history of depression (Skoog, 2011). Among the core symptoms of depression are diminished interest in one's surroundings and lack of initiative. This may negatively affect one's ability to socialise with family and friends, which may generate a feeling of loneliness or lack of social support (Hsueh et al., 2019). Feeling lonely or experiencing a lack of social support may, in turn, increase the risk of depression (Bergdahl et al., 2007). Social support provided by a spouse, friends or family members is reported to be protective against late-life depression (Garipey et al., 2016; Tengku Mohd et al., 2019). The effects may include decreased levels of psychosocial stress due to emotional or economic support (Carr & Springer, 2010). The perception of social support is also suggested to act as a buffer by decreasing the risk of depression when exposed to negative life events (Hashimoto et al., 1999).

Having late-life depression may be accompanied by social stigma, generating a barrier towards reaching out to others (Rydberg Sterner et al., 2020). This barrier may entail the fear of not being understood, or being perceived as burdensome or weak (Rydberg Sterner et al., 2020; Black et al., 2007; Conner et al., 2010). Older adults with decreased capability due to depression may not be able to help others to the same extent as before. This may cause a great deal of frustration among those who are depressed, as they still have a strong need to be needed (Rydberg Sterner et al., 2020). However, having a social network per se is not necessarily beneficial in relation to late-life depression. As an example, social relationships may entail emotional, physical or financial abuse (Poole & Rietschlin, 2012; Roh et al., 2016), or marital dissatisfaction (Woods et al., 2019), which may contribute to an elevated risk of depression.

At the **micro-level**, risk factors for depression include genetic factors, somatic health, personality, smoking, a low level of education, cardiovascular disorders (Skoog, 2011) and several other somatic disorders (Skoog, 2011). Depression may be both a consequence and a cause of somatic disorders, for example in relation to stroke (Liebetrau et al., 2008; Bos et al., 2008). Risk factors for depression may already present during foetal development, perhaps due to early programming as a response to the intrauterine environment, indicating the role of epigenetics (Barker, 2003; Hodes, 2013). In addition, lower birth weight (Gudmundsson et al., 2011) has been related to depression. It has also been reported that old-age depression is related to lower levels of physical activity (Gudmundsson et al., 2015). Depression, including mild subsyndromal symptoms, may affect an older person's available resources at the micro-level in several ways. The consequences of depression include poor quality of life, disability, cognitive decline, suicide, increased mortality rate and increased risk of cardiovascular disease (CaD) (Skoog, 2011).

Mental health may also be considered a personal conversion factor within the framework of capability. Suffering from mental illness, such as depression, may reduce an older person's ability to utilise available resources, in order to reach goals of value. For example, a valued goal for an older person may be to spend every Sunday afternoon playing video games with his/her grandchildren. Even where all the available resources are present, such as access to public transport (macro-level), having positive relationships with the grandchildren (meso-level) and having sufficient economic resources to travel and to buy video games (micro-level), late-life depression may be a barrier to achieving this goal (lacking conversion factor). From a capability perspective, there is also a challenge in that individuals adapt their goals of value to their current life situation, meaning that expectations may affect the choice of goals. Older adults may perceive some goals as being out of reach due to having depression, compared to their life perceptions before having depression. It may also be questioned whether a person with mental illness has the same freedom of choice as those without. Depression may be perceived as a restraining factor because the person may feel as though he/she is no longer in control of his/her own body.

4.4 Multimorbidity and Capability

Multimorbidity can be defined as the co-occurrence of multiple chronic conditions within the same individual (Christensen et al., 2009; Fried et al., 2004). Studies show that multimorbidity increases the likelihood of death, functional disability and institutionalisation, over and above the risk attributable to individual diseases (Formiga et al., 2013). In Sweden, multimorbidity affects more than half of those aged 78 years and older (Marengoni et al., 2008), and in the USA more than two thirds of all older Medicaid beneficiaries have two or more chronic conditions (Fried et al., 2004). Thus, multimorbidity is an important determinant of capability in old age. In light of this, it is surprising that relatively little is known about how diseases are distributed and co-occur in the same individual, and how conversion factors, such as social ties and personal and situational antecedents, might affect functional disability, frailty and dependence in physically vulnerable older people (Marengoni et al., 2011; Fortin et al., 2012). By definition, older people with multimorbidity are heterogeneous in terms of severity of illness, functional status, prognosis and risk of adverse events, even when diagnosed with the same pattern of conditions. Studies show that there are gender differences in terms of clinical characteristics in patients with multimorbidity (Marengoni et al., 2008, 2011), and that there is a strong relationship between social ties and health (Ferlander & Mäkinen, 2009), as well as differences in symptoms experienced by different age groups (Zambroski et al., 2005).

Unlike single chronic conditions, for which strong epidemiological data is available, existing prevalence estimates of multimorbidity in older persons range from 55% to 98%, making it difficult to determine whether differences between studies are real or due to a wide variety of methodological issues (Marengoni et al., 2011). The operational definition of multimorbidity and the methods used for data collection are particularly critical issues that need consideration when studying prevalence estimates. Defining multimorbidity as two or more chronic conditions means that both individuals who may live relatively unaffected by multimorbidity, as well as those who face severe functional loss, are included in the definition (Fortin et al., 2005). Since multiple chronic conditions often represent the norm in older people, multimorbidity needs to be evaluated in relation to illness distress, disease severity and level of impairment at the macro-, meso- and micro-levels.

The lack of conceptual schemes guiding the terminology, measurements and hypotheses in the study of multimorbidity also makes it difficult to meaningfully compare findings from different studies. Relationships between pathology, impairment and illness distress can be as much a function of psychosocial characteristics at the meso- and macro-levels as it can be related to number of diagnoses or disease severity at the micro-level (Femia et al., 2001). Thus, how multimorbidity affects capability is dependent on all levels. At the macro-level, it is related to political decisions on the availability and quality of home care and aid devices, and how pharmacological research is able to find new drugs. At the meso-level, it is dependent on factors such as the condition of the home and access to help from relatives

and friends. At the micro-level, it is dependent on factors such as severity of diseases, personality and physical reserves.

4.5 Functional Ability and Capability

As the average expected lifespan increases, an important issue is whether the years added to life are characterised by good health and independence or by health problems and dependence, i.e. by high or low capability. Disability refers to the negative aspects of the interaction between a person and their environment (i.e. deficits), which leads to limitations in their activity and restrictions in their social participation (Üstün et al., 2010). Dependence, which severely affects all aspects of capability, arises when conversion factors, such as adaptation of the environment or the use of technical aids, can no longer compensate for the disability, which results in the need for help from a third person (Verbrugge & Jette, 1994).

At the micro-level, research on disability in old age has identified non-modifiable risk factors, such as age, gender and genetics, and modifiable factors, such as age-related diseases, impairments, functional limitations, poor coping skills, sedentary lifestyles and other unhealthy behaviours, and at the meso- and macro-levels, social and environmental obstacles (Vermeulen et al., 2011; Taş et al., 2007; Heikkinen, 2006; Stuck et al., 1999). It is common to distinguish between disabilities in the performance of the primary or basic activities of daily living (ADLs) on the one hand, and secondary or instrumental activities of daily living (IADLs) on the other. In comparison to disease prevalence, indicators such as ADL and IADL disability, which reflect the cumulative effects of morbidity, are more revealing in terms of describing health and capability in older populations because of the high rates of co-morbidity and the interaction between disease and the ageing process (Parker et al., 2008; Manton et al., 1993). Research shows that dependence in ADL is associated with increased risk of mortality (Millán-Calenti et al., 2010), and that those individuals who are dependent in ADL are also likely to be dependent in IADL (Wang et al., 2019).

At the macro-level, severe disability poses a significant financial burden on healthcare services since it often results in loss of independence, requiring the provision of round-the-clock assistance (Verropoulou & Tsimbos, 2017). Although disability rates increase with age, in particular among the oldest-old (Wang et al., 2019), there is much debate about whether later-born cohorts of older adults will face the same disability rates as earlier-born cohorts. Many studies have suggested a compression of morbidity, implying that the future care needs of older adults will not follow the demographic prognoses. Several recent studies have shown that later-born cohorts of older adults are healthier and more active than earlier-born cohorts, displaying great plasticity and variability between individuals in health status, quality of life and wellbeing in later life. For example, it has been shown that, between 2004 and 2013, there was a declining trend in ADL disability among adults older than 65 years in Europe (Verropoulou & Tsimbos, 2017). However, there is great

variability in prevalence between studies. Among older adults in Spain (mean age 75 years), 35% reported problems in at least one ADL activity, and 54% in at least one IADL activity (Millán-Calenti et al., 2009). In Ireland, among persons aged 75 to 79 years, 15% reported problems in at least one ADL activity, and 13% in at least one IADL activity (Connolly et al., 2017). Among Swedish 75-year-olds born in 1930, only 6% reported disability for at least one ADL activity and 13% with IADL, compared to 14% and 33%, respectively, in 75-year-olds born in 1901–1902 (Falk et al., 2014). However, in 90–94-year-olds, 71% reported ADL disability, and this figure rose to 89% in 95–99-year-olds, and 97% in centenarians (Berlau et al., 2009).

Sweden has had a large proportion of older adults in the population for many years and still leads the world regarding the proportion of very old people. Epidemiology has traditionally focused on the prevalence of specific diseases or conditions within a population, which affects society at the macro-level. While disease indicators reflect the need for medical care, indicators of disability and functioning are more helpful for capturing both living conditions and potential care needs. Estimating disability among community-dwelling older adults may help policymakers to plan and prepare for the needs of this population. At a time when society is faced with demographic transformations, an important public health issue at the macro-level is how to prevent or postpone the onset of disability in old age, since this is one of the central components fuelling cost increases at the macro-level (Verropoulou & Tsimbos, 2017; Parker et al., 2008) and low capability at the micro-level. Studying health in the older population of Swedish citizens is particularly relevant because the proportion of this age group is large compared to other western countries (Parker et al., 2008). In the context of increasing numbers of older adults, and conflicting findings among studies on disability trends, the comparison of levels of disability between birth cohorts can be of great significance.

4.6 Genetics and Capability

Genetics has a fundamental impact on older individuals' capability at the micro-level, since variations within the DNA constitute the molecular basis for our level of vulnerability to, or protection against, age-related disease, frailty and biological ageing. Although some disorders/traits are caused by a single genetic factor (i.e. they are monogenetic), the majority of disorders/traits, among both young and old individuals, are polygenic (also known as complex) and caused by variations in numerous genes in combination with environmental and lifestyle factors at the micro-, meso- and macro-levels. Genetic factors act at the micro-level of individuals' available resources, but findings in genetic research can have a great impact at all societal levels due to their importance for understanding disease pathogenesis, for the work with identifying potential drug targets, for identifying individuals who will benefit from preventative efforts, and for the inclusion of individuals in clinical trials. Within dementia research, it has been demonstrated that both the 'high effect' gene *APOE* (i.e. the *APOE ε4* allele) and combinations of genetic

variants into genetic risk scores (i.e. PRS = polygenic risk scores) are useful for identifying individuals at risk of disease (Altmann et al., 2020). Within the frame of the H70 studies, an increasing risk of developing dementia with an increasing PRS for Alzheimer's disease was seen among individuals who were *APOE* $\epsilon 4$ negatives (Najar et al., 2021). Furthermore, *APOE* was associated with the Alzheimer's disease biomarkers cerebrospinal fluid A β 42, t-tau, and p-tau, and PRS for Alzheimer's disease was associated with cerebrospinal fluid A β 42 and NfL, among cognitively healthy 70-year-olds (Kern et al., 2018; Skoog et al., 2021). Moreover, an association between the *APOE* $\epsilon 4$ allele and a larger decline in grip strength between the ages of 75 and 79 years (Skoog, 2016) was found. This association was independent of cognitive function, indicating either an association independent of dementia, or an association at a very early stage of the disease.

There is an overlap in genetic factors that is important for age-related disorders (i.e. one genetic factor can be associated with several different phenotypes = pleiotropy). Results from the H70 studies have shown associations between the genes *APOE* and *ACE* (angiotensin-converting enzyme) and both dementia and late-life major depression (Skoog et al., 2015; Zettergren et al., 2017). There are also genetic overlaps between different forms of dementia disorders, and between dementia and cardiovascular and metabolic disorders (Guerreiro et al., 2020). Moreover, genetic factors interact with environmental and lifestyle factors at the macro-, meso- and micro-levels. One example from the H70 studies is the discovery of interactions between genetic and social factors in relation to dementia risk among men, implying that socioeconomic status modifies the effect of *APOE* $\epsilon 4$, whereas, among women, high socioeconomic status does not seem to exhibit the same 'compensatory ability' (Hasselgren et al., 2019). Furthermore, a meso-level factor, such as control over one's work, was suggested to be the most influential work environment factor on the effect of *APOE* $\epsilon 4$, albeit in different ways among men and women (Hasselgren et al. 2018).

Genetics can also influence individuals' ability to cope with disease and ageing at an emotional level, since genetic factors are known to be associated with personality and behavioural traits (Sanchez-Roige et al., 2018). Twin studies of heritability have found that genetic factors account for a substantial part of the variance in individuals' self-rated health (Christensen et al., 1999; Leinonen et al., 2005). Self-rated health is a subjective, general indicator that strongly predicts mortality. Important domains known to influence self-rated health, and subsequent mortality, include individual and cultural beliefs and health behaviours, chronic illness, depression, cognitive function, socioeconomic status, functional impairment and physical activity (Leinonen et al., 2001; Leinonen et al., 2002; Stanojevic Jerkovic et al., 2015; Galenkamp et al., 2013). In a study of well-established longevity genes in relation to self-rated health, an association was found between the gene *FOXO3* and self-rated health in individuals aged 75–85 years from the H70 studies (Zettergren et al., 2018). Interestingly, the association between *FOXO3* and self-rated health was not influenced by cognitive or mental functioning. Thus, an

apparently micro-level factor, such as genetics, may influence capability at the macro-, meso- and micro-levels.

4.7 Diet and Capability

Diet may influence capability in a number of ways, such as our health in general or as a risk factor for certain diseases. Diet is affected by factors at the micro-, meso- and macro-levels. At the macro level, what we eat is affected by cultural and historical norms in society, by guidelines from the authorities and by the availability of certain foods. At the meso-level, it is affected by preferences among family and friends, and the socioeconomic situation of the family. At the micro-level it is affected by a number of factors, including personal preferences. Global and national dietary guidelines recommend dietary patterns containing nutrient-dense foods, such as vegetables, pulses, nuts, wholegrain cereals, low-fat dairy products and fish, as well as a limited intake of red and processed meat, refined cereals, high-fat dairy products, high-sugar foods/drinks and alcoholic beverages in order to promote health and reduce the risk of disease (Nordic Council of Ministers, 2012; Herforth et al., 2019). Obesity and chronic age-related non-communicable diseases, such as cardiovascular disease, diabetes and dementia, can in part be prevented or delayed by means of a healthy lifestyle and healthy dietary habits (Global burden of disease 2017 Diet collaborators, 2019, Samadi et al., 2019, Ley et al., 2014, Rodríguez-Monforte et al., 2015). In this case, diet acts as a conversion factor.

In Sweden, dietary habits among healthy older people are generally better than among younger adults (Swedish food agency, 2012). Results from the H70 birth cohort study show that dietary patterns among five birth cohorts of 70-year-olds have changed during the past five decades, with an increase in healthy foods and a higher nutrient density in later-born birth cohorts (Samuelsson et al., 2019). However, the intake of alcohol has increased and about 30% of the participants had an intake above the Swedish Food Agency's recommendation in 2014–2016 (Samuelsson et al., 2019; Nordic Council of Ministers, 2012).

There is an increased risk of malnutrition related to ageing and chronic illness (Cederholm et al., 2019), and malnutrition (both undernutrition and obesity) plays a key role in the pathogenesis of frailty, sarcopenia and cognitive decline (Volkert et al., 2019; Cruz-Jentoft et al., 2017; Cederholm et al., 2019; Ma & Chan, 2020; Gómez-Gómez & Zapico, 2019). Frailty and sarcopenia are associated with dependency, and preventive strategies could improve quality of life and well-being among older adults (Cruz-Jentoft et al., 2017; Govindaraju et al., 2018). In addition to chronic illness, there are several factors at the micro-level that could affect dietary intake among older adults. Sensory impairments (e.g., loss of taste and smell), gastrointestinal motility changes and diminished hunger and satiety control mechanisms are some of many physiological changes related to ageing that may affect appetite and lead to a decrease in food intake (Cox et al., 2019). Psychosocial and

environmental changes, such as isolation, loneliness, inadequate finances and depression may have a negative impact on food intake (Landi et al., 2016), and socioeconomic factors such as being unmarried, male sex, lower level of education, functional limitations and smoking have been associated with the risk of a poor-quality diet and malnutrition (Katsas et al., 2020; Nazri et al., 2020). Obesity, with its well-known negative health consequences, is an increasing problem among older people (von Berens et al., 2020; Bischoff et al., 2017). In the H70 birth cohort study (at 75 years), and the Uppsala Longitudinal Study of Adult Men (at 87 years), 4% of the women and 10–11% of the men were obese (von Berens et al., 2020). Globally, these numbers range between 18–30% (>65 years) (Gallus et al., 2015; Porter Starr et al., 2016). Effective dietary education, meal service and dietary interventions at macro to micro societal levels could reduce the risk of disease, improve health and increase quality of life and capability among older adults (Volkert et al., 2019, Global burden of disease 2017 Diet collaborators, 2019, Govindaraju et al., 2018, Zhou et al., 2018).

4.8 Conclusion

In this chapter, we have discussed how the capability approach can be used in epidemiology in general, and in old age in particular, using examples from specific conditions, such as cognitive function and dementia, depression, multimorbidity and functional ability, and non-modifiable and modifiable risk factors, such as genetics and nutrition. It can be seen that the capability approach is a valuable tool in epidemiological studies. In these types of studies, capability is the final outcome of the dynamic interactions between a multitude of factors at the micro-, meso- and macro-levels that lead to disorders and other conditions, which lead to restrictions in the individual's ability to perform actions in order to reach goals that he or she has reason to value.

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