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SUICIDAL BEHAVIOUR AND HEALTHCARE USE AMONG REFUGEES

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Suicidal behaviour and healthcare use among refugees
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"Whoever saves one life, saves the world entire."
Thomas Keneally, Schindler's List

POPULAR SCIENCE SUMMARY OF THE THESIS

According to the United Nations High Commissioner for Refugees (UNHCR), 91.9 million people were forcibly displaced globally "as a result of persecution, conflict, generalised violence or human rights violations" by the end of 2020. Among them, 30.5 million people were refugees and asylum seekers who commonly experience traumatic events such as torture and loss of their loved ones while migrating. Many, if not all, face difficult life circumstances even after reaching a safer place due to unknown language, financial troubles and discrimination. These vulnerabilities may negatively affect mental health, healthcare use, and the risk of suicidal behaviour (suicide attempt and death by suicide) among refugees. On the other hand, hopefulness for a brighter future and cultural norms and religious beliefs may deter suicidal behaviour. Despite the considerable increase in forced migration globally in recent years, research on suicidal behaviour and healthcare use among refugees is limited. The purpose of this thesis was to investigate the risk of suicidal behaviour and to examine patterns and determinants of healthcare use before and after a suicide attempt among resettled refugees compared to their host population. These inquiries were made using advanced statistical methods on data derived from high-quality nationwide registers in Sweden and Norway.

Contrary to common expectations, the results of this thesis suggested that resettled refugees with a residence permit in Sweden and Norway had a lower risk of suicide mortality relative to the respective host populations in both countries. In Sweden, refugees also had a lower risk of hospitalisation for suicide attempt. Inpatient and specialised outpatient healthcare use were slightly lower among refugees who attempted suicide than among the Swedish-born. The differences regarding antidepressants and other psychotropic medication use before and after a suicide attempt were marginal between refugees and the Swedish-born.

The results of this thesis suggest that resettled refugees are not substantially more vulnerable regarding suicidal behaviour than the host populations in Sweden and Norway, possibly owing to the protective nature of their inherent resiliency and negative attitude towards suicidal behaviour. It is, however, recommended to reduce the gap in treatment between refugees with a suicide attempt and their Swedish-born peers through the improvement of necessary skills and cultural competence among healthcare professionals.

ABSTRACT

Background: Despite higher rates of mental disorders among refugees, there is limited evidence on their risk of suicidal behaviour (suicide attempt and suicide) and how such risk is influenced by differences in country-level structural factors (e.g., the national healthcare and social services, national unemployment rates etc.) in the host countries. Moreover, research on any differences in patterns of healthcare use and trajectories of antidepressant use before and after a suicide attempt between refugees and the host population is lacking. Therefore, this thesis aimed to investigate the risk of suicidal behaviour in resettled refugees compared with the majority host populations in Sweden and Norway. A further aim was to investigate patterns of healthcare use, before and after a suicide attempt, among refugees who resettled in Sweden compared with the Swedish-born population.

Methods: In study I, three cohorts comprising the entire population of Sweden, 16-64 years of age on 31 December 1999, 2004, and 2009 (around 5 million each, of which 3.3-5.0% refugees) were followed for four years each through register linkage. Additionally, the 2004 cohort was followed for nine years to allow stratified analyses by refugees' country of birth. Multivariate-adjusted hazard ratios (aHRs) with 95% confidence intervals (CIs) were computed. In study IV, all cases who died by suicide when 18-64-years-old during 1998 and 2018 (17,572 and 9,443 cases in Sweden and Norway, respectively) were matched with 20 sex- and age-matched population controls. Multivariate-adjusted conditional logistic regression models yielding adjusted odds ratios (aORs) with 95% CIs were used to test the association between refugee status and suicide in study IV. The multivariate models in study I and IV were adjusted for socio-demographic, labour market marginalisation (LMM) such as unemployment, sickness absence and disability pension, and morbidity factors. Additionally, in study IV, analyses were stratified by sex and age groups, by refugees' region/country of birth and duration of residence in the host country. In study II, all refugees and Swedish-born individuals, 20-64 years of age, treated for suicide attempt in specialised healthcare during 2004-2013 (n = 85,771, of which 4.5% refugees) were followed three years before and after (Y-3 to Y+3) the index suicide attempt (t0) regarding their specialised healthcare use. With the same inclusion criteria and study design, another cohort of individuals with suicide attempt during 2009-2015 (n = 62,442, 5.6% refugees) was followed regarding their antidepressant use in study III. Annual adjusted prevalence estimates with 95% CIs of specialised healthcare use were assessed by generalised estimating equations (GEE) in study II. Trajectories of annual defined daily doses (DDDs) of antidepressants were analysed using group-based trajectory models in study III. Associations between the identified trajectory groups and different covariates related to socio-demographics, LMM, and healthcare use were estimated by chi^2-tests and multinomial logistic regression.

Results: The aHRs of suicide attempt and suicide among refugees vs the Swedish-born ranged from 0.38-1.25 and 0.16-1.20 according to country of birth, respectively, showing either non-significant or lower aHRs for refugees. Exceptions were refugees from Iran with a higher risk for suicide attempt - aHR 1.25; 95% CI 1.12-1.40, compared to individuals born

in Sweden. The risk for suicide attempt among refugees diminished slightly across the different cohorts (study I). In study IV, the aORs for suicide among refugees in Sweden and Norway were 0.5 (95% CI: 0.5-0.6) and 0.3 (95% CI: 0.3-0.4), compared with the respective host population. Stratification by region/country of birth showed similar statistically significant lower odds for most refugee groups in both host countries except for refugees from Eritrea (aOR 1.0, 95% CI: 0.7-1.6) in Sweden. The risk of suicide did not vary much across refugee groups by their duration of residence, sex and age except for younger refugees aged 18-24 who did not have a statistically significant relative difference in suicide risk than their respective host country peers. Factors related to socio-demographics, LMM and healthcare use had only a marginal influence on the studied associations in both countries in study IV as well as in study I in Sweden.

In study II, among individuals with a suicide attempt, refugees had somewhat lower prevalence rates of psychiatric and somatic healthcare use during the observation period than the Swedish-born. During Y+1, 25% (95% CI 23-28%) of refugees and 30% (95% CI 29-30%) of Swedish-born used inpatient psychiatric healthcare. Among refugees, a higher specialised healthcare use was observed in disability pension recipients than non-recipients. Among the four identified trajectory groups, antidepressant use was constantly low (≤15 DDDs) for 64.9% of refugees in study III. A 'low increasing' group comprised 5.9% of refugees (60-260 annual DDDs before and 510-685 DDDs after index attempt). Two other trajectory groups had constant use at medium (110-190 DDDs) and high (630-765 DDDs) levels (22.5% and 6.6% of refugees, respectively). Method of suicide attempt and any use of psychotropic drugs during the year before index attempt discriminated between refugees' trajectory groups. The patterns and composition of the trajectory groups, and the associations of the identified trajectory groups with the different covariates, were comparable among refugees and Swedish-born, except for previous sedative/hypnotic drug use, which explained the variability among the trajectory groups more for refugees than for the Swedish-born.

Conclusions: Resettled refugees had a lower risk of suicidal behaviour relative to the host population in Sweden and Norway. These findings may suggest that resiliency and culture/religion-bound attitudes towards suicidal behaviour among refugees could be more influential for their suicide risk after resettlement than other post-migration environmental and structural factors in the host country. Specialised healthcare use before and after a suicide attempt was somewhat lower among refugees than among the Swedish-born, and differences in antidepressant treatment were marginal between refugees and the Swedish-born.

SAMMANFATTNING

Bakgrund: Trots att en högre andel flyktingar har en psykisk sjukdom jämfört med infödda är forskningen begränsad med avseende på risken för självmordsbeteende (självmordsförsök och självmord) och hur denna risk påverkas av skillnader i strukturella faktorer (t.ex. sjukvård, socialtjänst, arbetslöshet etc.) bland länderna som tar emot flyktingar. Dessutom saknas forskning om skillnader i mönster för sjukvård och användning av antidepressiva läkemedel före och efter ett självmordsförsök. Denna avhandling syftar till att undersöka risk för självmordsbeteende hos flyktingar jämfört med den infödda befolkningen i Sverige och Norge. Ytterligare ett syfte var att undersöka de mönster av sjukvårdsanvändning, både före och efter ett självmordsförsök, hos flyktingar som bosatt sig i Sverige jämfört med personer födda i Sverige.

Metod: I studie I inkluderades tre kohorter bestående av alla flyktingar och personer födda i Sverige i åldern 16–64 år som var bosatta i Sverige år 1999, 2004 och 2009 (cirka 5 miljoner vardera, varav 3,3-5,0% flyktingar). Kohorterna definierades från rikstäckande register och alla kohorterna följdes i fyra år med avseende på sjukhusinläggning för självmordsförsök samt för självmord. Kohorten från 2004 följdes under nio år för att möjliggöra stratifierade analyser av flyktingarnas födelseland. Multivariatjusterade Hazardkvoter (aHRs) med 95% konfidensintervaller (CIs) beräknades i studie I. För studie IV matchades alla som dog av självmord (fall) när de var 18-64 år gamla under 1998 och 2018 (17 572 och 9 443 fall i Sverige respektive Norge) med 20 köns- och åldersmatchade kontroller från respektive befolkning. Multivariatjusterade villkorade logistiska regressionsmodeller, som gav justerade oddskvoter (aOR) med 95% CI, användes för att testa sambandet mellan flyktingstatus och självmord. De multivariata modellerna i studie I och IV justerades för viktiga bakgrundsfaktorer, däribland socio-demografi, arbetsmarknadsmarginalisering (LMM) såsom arbetslöshet, sjukfrånvaro, sjuk- och aktivitetsersättning och psykiatrisk eller somatisk samsjuklighet samt tidigare självmordsförsök. För studie IV stratifierades analyserna även för kön, åldersgrupper, flyktingarnas region/födelseland samt antal år i mottagarlandet.

I studie II följdes alla flyktingar och svenskfödda individer beträffande besök hos specialiserad sjukvård tre år före och efter (Y-3 till Y+3) index självmordsförsöket (t0). Dessa individer var 20-64 år gamla och hade specialiserad sjukvård för självmordsförsök under 2004-2013 (n = 85 771, varav 4,5% flyktingar). Med samma inklusionskriterier och studiedesign följdes ytterligare en kohort av personer med självmordsförsök under 2009-2015 (n = 62 442, 5,6% flyktingar) angående deras användning av antidepressiva läkemedel i studie III. Årligt justerad prevalens med 95% CI för specialiserad sjukvård beräknades med *Generalised Estimating Equations (GEE)* i studie II. Mönster för årliga definierade dagliga doser (DDD) av antidepressiva läkemedel analyserades med hjälp av så kallade *Group-Based Trajectory* modeller i studie III. Sambandet mellan de identifierade mönstren och olika bakgrundsfaktorer relaterade till socio-demografi, LMM och användning av sjukvård estimerades genom Chi2-tester och multinominala logistiska regressionsmodeller.

Resultat: Justerade Hazardkvoter (aHR) för självmordsförsök och självmord hos flyktingar vs svenskfödda varierade från 0,38-1,25 respektive 0,16-1,20 beroende på födelseland, vilket visar antingen icke-signifikanta eller lägre risker för flyktingar. Flyktingar från Iran uppvisade dock en något högre risk för självmordsförsök jämfört med personer födda i Sverige - aHR 1,25; 95% CI 1,12-1,40. Riskestimaten för självmordsförsök bland flyktingar i allmänhet verkade minska något över tid (studie I). I studie IV var aOR för självmord hos flyktingar i Sverige och Norge 0,5 (95% CI: 0,5-0,6) och 0,3 (95% CI: 0,3-0,4), jämfört med respektive infödd population. Stratifiering efter region/födelseland visade liknande signifikant lägre estimat för de flesta flyktinggrupper i båda mottagarländerna förutom hos flyktingar från Eritrea (aOR 1,0, 95% CI: 0,7-1,6) i Sverige. Risken för självmord varierade inte mycket mellan flyktinggrupperna med avseende på bosättningstiden, kön och ålder med ett undantag: yngre flyktingar i åldern 18-24 år hade ingen signifikant relativ skillnad i självmordsrisk jämfört med deras respektive infödda jämförelsegrupper. Faktorer relaterade till socio-demografi, LMM och vårdanvändning påverkade bara marginellt sambanden i båda länderna i studie IV, vilket också var fallet i Sverige i studie I.

I studie II hade flyktingar lägre prevalens av besök inom den specialiserade sjukvården, både psykiatrisk och somatisk vård, under observationsperioden jämfört med svenskfödda. Under Y+1 använde 25% (95% CI 23-28%) av flyktingarna och 30% (95% CI 29-30%) av svenskfödda psykiatrisk slutenvård. Bland flyktingar observerades en högre specialiserad vårdanvändning hos sjuk- och aktivitetsersättningsmottagare än icke-mottagare. Bland de fyra identifierade grupperna i studie III var användning av antidepressiva läkemedel konstant låg (≤15 DDD) för 64,9% av flyktingarna. En "svagt ökande" grupp utgjorde 5,9% av flyktingarna (60-260 årliga DDD före och 510-685 DDD efter indexförsöket). Två andra grupper hade mer konstanta användningsnivåer. I den ena av dessa grupper var nivån medelhög (110-190 DDD, 22,5% av flyktingarna), medan den var hög i den andra (630-765 DDD, 6,6% av flyktingarna). Metod för självmordsförsök och användning av psykotropa läkemedel under året innan indexförsök hade ett samband med grupptillhörighet bland flyktingar. Mönstren, sammansättning och sambanden mellan de identifierade grupperna och de olika kovariaterna, var nästan lika bland flyktingar och svenskfödda, förutom att tidigare användning av sedativa/hypnotiska läkemedel förklarade variationen bland de identifierade grupperna mer bland flyktingar än de svenskfödda.

Slutsatser: Flyktingar hade en lägre risk för självmordsbeteende i förhållande till infödda i både Sverige och Norge. Dessa resultat kan tyda på att motståndskraft och kultur/religions-bundna attityder mot självmordsbeteende hos flyktingar kan ha mer inflytande för deras självmordsrisk än andra miljömässiga och strukturella faktorer efter migration till mottagarlandet. Användning av specialiserad sjukvård var något lägre bland flyktingar, både före och efter ett självmordsförsök, än för de svenskfödda, men skillnaderna i användning av antidepressiva läkemedel mellan flyktingar och svenskfödda var endast marginella.

LIST OF SCIENTIFIC PAPERS

I. **Amin R**, Helgesson M, Runeson B, Tinghög P, Mehlum L, Qin P, Holmes EA, Mittendorfer-Rutz E. Suicide attempt and suicide in refugees in Sweden – a nationwide population-based cohort study. *Psychological Medicine* 2021;51(2):254–263

II. **Amin R**, Rahman S, Tinghög P, Helgesson M, Runeson B, Björkenstam E, Qin P, Mehlum L, Holmes EA, Mittendorfer-Rutz E. Healthcare use before and after suicide attempt in refugees and Swedish-born individuals. *Social Psychiatry and Psychiatric Epidemiology* 2021;56:325–338

III. **Amin R**, Rahman S, Helgesson M, Björkenstam E, Runeson B, Tinghög P, Mehlum L, Qin P, Mittendorfer-Rutz E. Trajectories of antidepressant use before and after a suicide attempt among refugees and Swedish-born individuals: a cohort study. *International Journal for Equity in Health* 2021;20(1):131

IV. **Amin R**, Mittendorfer-Rutz E, Mehlum L, Runeson B, Helgesson M, Tinghög P, Björkenstam E, Holmes EA, Qin P. Does country of resettlement influence the risk of suicide in refugees? A case-control study in Sweden and Norway. *Epidemiology and Psychiatric Sciences* 2021;30, e62, 1–10. doi:10.1017/S2045796021000512 (Epub ahead of print)

CONTENTS

LIST OF ABBREVIATIONS

ATC	Anatomical Therapeutic Chemical classification system
BIC	Bayesian Information Criterion
CI	Confidence Interval
DDD	Defined Daily Dose
DP	Disability Pension
GEE	Generalised Estimating Equation
HIC	High-Income Countries
HME	Healthy Migrant Effect
HR and aHR	Hazard Ratio and multivariate-adjusted Hazard Ratio
ICD-10	International Classification of Diseases version 10
LISA	Longitudinal Integration Database for Health Insurance and Labour Market Studies (Swedish acronym LISA)
LMIC	Low- and Middle-Income Countries
LMM	Labour Market Marginalisation
OR and aOR	Odds Ratio and multivariate-adjusted Odds Ratio
PTSD	Post-Traumatic Stress Disorder
SA	Sickness Absence
SMR	Standardised Mortality Ratio
STATIV	Longitudinal Database for Integration Studies (Swedish acronym STATIV)
WHO	World Health Organisation

1 INTRODUCTION

1.1 MIGRATION AND REFUGEE STATUS

Migration is one of the oldest phenomena in the history of mankind. People migrate from one place to another, both within and across countries, to settle either temporarily or permanently in their new destination. The number of migrants worldwide was estimated to be 281 million in 2020 (1). The multifaceted process of migration is tremendously heterogeneous and complex on many different levels. Migration occurring from one country of origin to another host country can be quite different compared to any other combination of origin and host countries, because of the socio-cultural differences between most countries and world regions. Moreover, differences in culture and ethnicity may exist between migrant groups from the same nationality and between different populations in the host country (2). Furthermore, the process of migration differs according to the reason. According to Everett Lee's "Push-Pull theory", some people migrate to seek better opportunities, e.g. education or employment, and are influenced by the pulling factors in the new country; some are pushed out of their origin country because of war, famine and political or religious persecution etc. (3). Apart from these factors, intervening obstacles such as the distance and means of conveyance between the destination and the origin as well as how migrants perceive such obstacles are also important elements in the process of migration (3). In this regard, distinctions are important between those who are forcibly displaced from their origin country and those who are not because pre- and post-migration conditions can be significantly different between these groups. Due to these differences in the migration process and the related heterogeneity between migrant groups, the following thesis focuses on a specific subgroup of migrants, namely refugees.

According to the United Nation's 1951 Refugee Convention (in article 1.A.2), a refugee is defined as any person who "owing to well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of such events, is unable or, owing to such fear, is unwilling to return to it" (4). At the end of 2020, there were 26.4 million refugees worldwide (5). A considerable proportion of them were received by European countries including Sweden, where, due to increasing migration in recent times, the demography is shifting towards a more multicultural society.

1.2 REFUGEES IN SWEDEN AND NORWAY

Due to several war and conflict situations that occurred over the last few decades, and for its relatively more generous stance on asylum before 2016, Sweden received historically high numbers of individuals seeking asylum during this period. In recent years, these numbers have become even larger. Among the nations in the European Union, Sweden granted the highest number of asylums per capita in 2016 (6). The surge in migration also brought considerable diversity to the population in Sweden. Moreover, as previously discussed, the heterogeneous nature of the process of migration also implies that the migrants and refugees in Sweden are diverse in terms of their ethnicity and culture. In this regard, it is essential to realize the history of migration in Sweden in order to try to comprehend the heterogeneity in migrants and refugees.

1.2.1 Historical perspectives

Emigration from Sweden, i.e. people migrating from Sweden to another country, dominated the history of migration in Sweden from the early 19th century until World War II (7). Nearly 1.3 million Swedes emigrated searching for a better life during a period that stretched around 100 years (7). However, the direction of migration, i.e. emigration vs immigration, in Sweden changed due to World War II, and because of it, Sweden then received about 200,000 refugees (7). Most of these refugees returned to their homeland at the end of the war except some people, mainly from the Baltic countries, who remained in Sweden (7). In the post-war period, up until the 1980s, predominantly labour immigrants, generally from Nordic and other European countries, came to Sweden in large numbers. During this period, refugees came intermittently, and the bulk of them originated from Chile, in relation to an armed conflict following a military coup in 1973 (7).

In the following decade, Sweden saw a predominance of migrants from outside Europe; the majority of them being refugees from war and conflict zones in Asia (Iran, Iraq and Syria) and Africa (Eritrea, Ethiopia and Somalia). Although the wave of refugees from these regions trickled down in the early 1990s, another wave originated from within Europe. Due to the breakdown of former Yugoslavia and subsequent conflicts and ethnic cleansing in that region, more than 100,000 refugees from former Yugoslavia (including today's Bosnia and Herzegovina, Croatia, Kosovo, North Macedonia, Montenegro, Serbia and Slovenia) were received by Sweden around that time (7). Since then, refugees came to Sweden sporadically without any distinguishable peak in the numbers until recently, when the escalation of war and human rights violations in several regions in Asia and Africa has led to yet another refugee crisis globally. A considerable proportion of these refugees came to Sweden. In 2015 alone, almost 163,000 persons applied for asylum in Sweden, of which nearly 1/3rd came from the war-ravaged Syria (7).

The history of refugee migration in Norway followed a somewhat similar pattern to Sweden mainly because the same international events and conflicts influenced the flow of refugee migration in Sweden's neighbouring countries (8). Notable differences were that more refugees from Vietnam and Sri Lanka in the 1970s and 1980s, respectively (9), migrated to Norway than to Sweden. Although in absolute numbers, Sweden has granted asylum to significantly more individuals than Norway over the years (10, 11), a per capita comparison

is more balanced. In 2019, refugees comprised 6.5% and 4.4% of the Swedish and Norwegian populations, respectively.

From the history of migration in Sweden and Norway, we get some idea about the diversity among refugees in terms of their country of origin. To disentangle more of these diversities in migrant and refugee populations, the following section includes some definitions of terms that will be used extensively throughout this thesis to refer to specific population groups.

1.2.2 Definitions of different migrant and comparison groups

Each individual who is not a citizen of Sweden or other Nordic countries requires a permit to reside in Sweden. Citizens, and their families, of the member states of the European Union, instead, have a right of residence (12). In both cases, the Swedish migration board records the most recent *reason for residence* for every individual. Since 1997 and up until 2010, these reasons were grouped under the following categories: employment, (family) ties, refugees, humanitarian grounds, in need of protection, pensioner /not economically active, studies, other extension, unknown and other (12). From 2011, three major categories were introduced for non-European immigrants: work and study, family ties and refugees (13).

Refugees are defined according to the 1951 Geneva convention definition of refugees (4) by the Swedish Migration Agency. In this thesis, individuals grouped in the categories related to the reason for residence named 'humanitarian grounds' and 'in need of protection' are also considered as refugees. Individuals from countries with armed or other severe conflict situations, as well as those who are persecuted in their home country, are considered to be in need of protection in Sweden (12). Refugee status for humanitarian grounds is applied to people whose health conditions do not allow them to return to their home country or if the condition in the home country is not safe enough for returning (13). The definitions for these categories varied over the years, and often overlapping definitions were used by the Swedish Migration Agency (13). Therefore, a more inclusive definition of refugees is used in this thesis.

Migrants are people who travel from their usual place of residence to a new destination which can be within the same country or across an international border to settle down either temporarily or permanently for various reasons (14). In this thesis, migrants refer to these overarching groups of people irrespective of their reason for residence and include refugees. Whenever a distinction with refugees is required, the term *other migrants* or *non-refugee migrants* is used interchangeably. Other migrants, in this case, refers to migrants whose reason for residence in Sweden was anything other than 'refugee' or 'humanitarian grounds' or 'in need of protection'.

Asylum seekers in Sweden are individuals who have applied for protection but have not yet got a decision on their asylum application (14). Therefore, their legal status as a refugee in the future awaits this decision. Not all asylum seekers are eventually granted a residence permit as a refugee in Sweden. In this thesis, asylum seekers are not included as refugees because it is administratively very difficult to gather information on this specific population. Studies in this thesis build on refugees with a residence permit, which is also the precondition to be included in the registers used for this work.

The Swedish-born population includes all people who were born in Sweden irrespective of their parents' country of birth. This population is used as a reference group throughout this thesis to draw comparisons with refugees residing in Sweden. Additionally, the Norwegian-born population is used as the reference group for comparison with refugees in Norway in one of the studies in this thesis. Both Swedish-born and Norwegian-born populations were considered to be the "host population" in their respective country.

1.3 REFUGEES' HEALTH

Before delving into the health conditions of refugees, it is important to discuss some related definitions and concepts to put things in a proper context. *Health* is defined by the World Health Organisation (WHO) as "a complete physical, mental and social wellbeing and not merely the absence of disease or infirmity" (15). A more recent definition considers health as "a state of balance, an equilibrium that an individual has established within himself and between himself and his social and physical environment" (16). *Mental health* is defined as "a state of wellbeing in which every individual realises his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community" (17). Ill-health or poor health, therefore, means loss of such equilibrium to some degree. On the other hand, mental disorders are defined as "health conditions that are characterised by alterations in thinking, mood, or behaviour (or some combination thereof) associated with distress and/or impaired functioning" (18). The definitions of ill-health and disorders can be overlapping and may complement each other when discussing the concepts of physical and mental ill-health or disorders among refugees. In this thesis, the terms mental ill-health or poor mental health were used interchangeably to suggest negative outcomes regarding mental health in a broader perspective. The terms psychiatric disorders or mental disorders were used to indicate diagnosed outcomes.

The complexities associated with the process of migration pose numerous challenges for those who undertake such a journey. Particularly for refugees, the various phases of migration include multiple stressors that can aggravate the risk of poor mental health (19). Here, several factors alone or by interacting with each other may affect the mental health of refugees both in the pre- and post-migration periods.

1.3.1 Pre-migration and post-migration factors and mental health

Traumatic experiences due to war, terrorism, natural disaster or persecution in the country of origin are common among refugees (20). Psychiatric symptoms were identified to be related to such pre-migration experiences of being lost and close to death, injuries, and sufferings in Somali refugees in the UK (21). These pre-migration stressors often come in combination (22), and in a meta-analysis, Bogic et al. (2015) found that the higher the number of war-related traumas, the higher the risk of mental disorders among refugees (23). While these pre-migration traumatic experiences push refugees out of their homeland to seek asylum elsewhere, the journey itself can be equally, if not more, harrowing. The peri-migration experience of torture, sexual violence, separation or loss of family members and being abused by smugglers are, among others, frequently reported by refugees (23, 24). A traumatic past can be strongly associated with future psychiatric problems among refugees. In their systematic review with meta-regression, Steel and colleagues (2009) included 181 surveys comprising 81,866 forcibly displaced persons across 40 countries (25). They found torture as the most influential predictor of post-traumatic stress disorder (PTSD) and the experience of any potential traumatic event as the strongest predictor of depression. In a more recent critical review of 40 articles that were published after the meta-analysis by Steel et al. (2009), older age, female sex, type and severity of torture, time until contact with healthcare services, residency status, social support, being married and following Islam (compared to Christianity or Buddhism) were found to be predicting psychological distress among individuals who

experienced potential traumatic events (26). Finally, life in the new country can be full of stressors due to problems with communication, uncertainty about the future, financial constraints, inadequate social identity, marginalisation etc. (27, 28). Lack of social support in the post-migration environment can additionally lead to psychological stress among refugees (23).

As refugees face a wide range of harshness and difficulties during the different phases of migration, quite expectedly, refugee studies have reported a high prevalence of depression, anxiety and PTSD in this population (28-31). Apart from these common mental disorders, a higher risk of psychotic disorders was reported among refugees when compared with both the host population (32) and non-refugee migrants (33). A recent meta-analytical synthesis of 26 studies across Asia, Africa, Europe and North America, including 5,143 refugees and asylum-seeking populations, revealed a much higher prevalence of depression and PTSD than in the general population (31.5% vs 12% and 31% vs 3.9%, respectively) (34). However, the authors found comparable prevalence estimates of anxiety disorders and psychosis among these vulnerable populations as in the general population (11% vs 16% and 1.5% vs 3%, respectively). The prevalence of anxiety disorders was influenced by duration of residence, favouring those who stayed longer in the host country. In another systematic review and meta-analysis, similar prevalence estimates for diagnosed depression, anxiety disorders and PTSD were found among resettled refugees in high-income countries (HIC) (35).

On the other hand, resilience, defined as "an interactive concept that refers to relative resistance to environmental risks or overcoming stress or adversity" (36), can be a coping mechanism that protects against poor mental health outcomes among refugees. A systematic review (37), including both quantitative and qualitative studies on refugee/asylum-seeking populations, found a strong association between positive mental health outcomes and resilience factors such as community support (38-42), bonds with family and friends (40-42), and religion (40-42).

1.3.2 Mental health and post-migration difficulties when seeking asylum

In the post-migration stage, several factors, among others, specific to the asylum-seeking phase, may have a negative effect on asylum seekers' mental health. Uncertainty about the future concerning a negative decision or a decision of temporary residence instead of a permanent one (43-46), accommodation at asylum centres lacking adequate personnel or scope for activity (47), frequent change of asylum centres (48), and violence or sexual harassment mostly in detained asylum seekers (49-51) are all detrimental to the mental health of asylum-seeking individuals. Moreover, several studies in Denmark (52-54), the Netherlands (55, 56), Switzerland (57), Australia (58) and the USA (59) found an association between a longer waiting time for asylum decisions and mental ill-health among asylum seekers.

Between 2010-2020 in Sweden, the average time to a decision on one's asylum application ranged from six months to 16 months, with the peak in 2017-2018. Primarily, an unusually large number of applications led to longer waiting times from 2015 and onwards, which was still dragging (302 days on average) in 2020 (60). Proportions with a positive decision varied from 23% in 2020 to 60% in 2016 (60). The directorate of immigration in Norway reported

six months as the average time to a decision for asylum with variations between cases (61). According to the available data, the acceptance rate in Norway, 49%-62%, was more stable than in Sweden between 2014-2020 (62).

In Sweden, persons seeking asylum may choose to stay with family or friends or arrange their own accommodation if possible (63). Otherwise, the Swedish migration agency offers temporary accommodation. Adults awaiting a decision are entitled to emergency healthcare and dental care, and healthcare that cannot wait (63). They have the right to work under certain conditions, e.g. if they have identity papers. Adult asylum seekers are offered language training, but do not have the right to formal education while waiting for an asylum decision. On the other hand, the right to education and healthcare for asylum-seeking children is the same as that for the host population in Sweden (63). The rights for asylum seekers are similar in Norway as in Sweden, with a few exceptions. Asylum seekers in Norway are first placed in asylum centres until their initial interview with the directorate of immigration. Later, they may decide to leave the asylum centre and live independently or with family/friends (64, 65). All asylum seekers are entitled to healthcare in Norway (65).

1.3.3 Migration and somatic health

The various phases of refugees' migration not only affect their mental health but also give rise to a wide variety of somatic problems. Pre-migration harsh conditions in the country of birth, during the flight and in refugee camps often lead to accidental injuries, hypothermia, skin problems and disorders of the cardiovascular, respiratory, gastrointestinal and metabolic systems (66). Refugees are more likely to migrate from countries with higher incidence of infectious diseases, e.g. hepatitis A, typhoid fever, and tuberculosis (67). Not only communicable diseases but also the burden of some non-communicable disorders can be higher among different refugee populations, for example, refugees in Canada had much higher rates of increased blood pressure than the host population (68). However, there are also contradictory findings showing mortality and morbidity advantage in migrant and refugee populations compared to their host populations, from which several explanatory hypotheses emerged. Among these, the "healthy migrant effect (HME)" is the most discussed hypothesis in the literature.

1.3.4 Predominant theories regarding migrants' health

According to the HME, migrants may appear to be healthier than the host populations in their new country because they undergo several health selection processes and can handle the harsh process of migration because of their health advantage (69, 70). The health selection may emerge from either self-selection, e.g., labour migrants, or from policies adopted by the host country, e.g., generous vs restrictive, or as a combination of both. An extension of the HME is the convergence theory which suggests that the health advantage that migrants have in the early years after migration fades away over time and 'regresses to the mean' of their host population because of acculturation (70). The evidence for the HME is, however, not consistent in the literature. In Belgium, an investigation on all-cause and cause-specific mortality from census data during 2001-2011 revealed support for both the HME and convergence theory; the mortality advantage diminished with increasing length of stay among migrants, and it was more marked among non-western immigrants than western immigrants

(71). Helgesson et al. (2019) reported a similar mortality advantage for both western and non-western migrants in Sweden than the Swedish-born host population. However, their results regarding cardiovascular and psychiatric disorders did not support the HME because the risks for these disorders were the same in western migrants vs the Swedish-born. For non-western migrants, the risks were higher (72).

The evidence for HME and convergence theories regarding mental health is mixed. While a survey during 2011-2012 in Spain showed that a longer duration of residence among migrants was associated with higher symptoms of mental ill-health (73), another survey in Australia measuring mental component summary scores (74) found no mental health advantage among first-generation migrants over the host population (75). These mixed findings regarding HME for mortality, somatic disorders and mental health suggest that the HME is not universal. Therefore, one should be cautious before considering the HME as a potential explanation for findings in studies on migrant populations. This is probably even more so for studies on refugees because the health selection process can be much stronger for those who migrate for work or education vs those who are forcibly displaced. However, there is limited evidence on to which extent these hypotheses apply to refugees. One of the few studies found on these topics for refugees investigated several health outcomes among refugees in Denmark: cardiovascular disorders, diabetes mellitus, tuberculosis, breast and lung cancer. Apart from a lower risk of stroke among recently resettled refugees (0-5 years) and a lower risk of breast cancer irrespective of the duration of residence, the authors did not find any support for the HME in refugees (76). They also concluded that their study provided weak evidence for the convergence theory among refugees for the studied outcomes. On the contrary, in a study from Canada, refugees had an all-cause and cause-specific mortality advantage over the host population, which did not wear off with a longer duration of residence (77). In their recent study in Sweden, Helgesson et al. (2021) found lower risk of all-cause and cause-specific mortality advantage among refugees across all somatic and mental disorder categories (78).

Any evidence for or against the HME and the convergence hypothesis regarding suicidal behaviour is lacking in the literature. Therefore, it is essential to investigate to what extent these theories are applicable among refugees regarding their suicidal behaviour. Moreover, the study of suicidal behaviour among refugees becomes particularly interesting because identifying at-risk populations for suicidal behaviour is both a local and global public health challenge of the highest priority. Considering the consistent evidence of psychiatric disorders as risk factors of suicidal behaviour (79-82) (please also see section 1.4.3 on risk factors for suicidal behaviour) and a higher burden of such disorders among them, refugees can be prone to such vulnerability regarding suicidal behaviour.

1.4 SUICIDAL BEHAVIOUR

1.4.1 Definition

Several definitions of suicidal behaviour are in use. Most often, the term suicidal behaviour encompasses a range of behaviour with suicidal intent; attempted suicide and death due to suicide (83). In this thesis, suicidal behaviour is used as an umbrella term and includes suicide attempt and suicide. *Suicide attempt* is often defined as any self-injurious behaviour with a non-fatal outcome where death was intended (83). Silverman et al. (2007a, b) emphasised that only behaviour intended to end life should be considered suicidal behaviour, and one should distinguish such behaviour from self-harming behaviour with unclear intent (84, 85). However, determination of the suicidal intent is challenging in practice for both fatal and non-fatal outcomes of this behaviour. In the case of suicide, one must rely on other sources to establish intentions because the person is no longer among us. On the other hand, for non-fatal outcomes, intents can be refused or hidden as a psychological defence mechanism or due to the fear of future stigmatisation or hospitalisation (83). Therefore, a more inclusive term, 'deliberate self-harm', defined as any self-injurious non-fatal behaviour with or without suicidal intent, was proposed (86). Parasuicide is another term that comprises suicide attempts as well as other self-harm behaviour (87, 88). The WHO/EURO Multicentre study (88) initially adopted the term *parasuicide* but later changed the terminology to *attempted suicide* (89). Both terms were used interchangeably with a broader definition of suicidal behaviour that did not take an individual's intentions into account (89). In this thesis, the term suicide attempt is used throughout except in study IV, where deliberate self-harm was used to ensure comparability between the measurements in different host countries, i.e. Sweden and Norway.

Differences in the interpretation of the definitions of suicidal behaviour may introduce differential practices regarding postmortem examination, classification of death and legislations related to these practices, which subsequently affect the statistics on suicidal behaviour (90, 91). Determining intent is often difficult, and events where intent was classified as 'undetermined' were claimed to be 'hidden' suicidal behaviour (92). However, when determining the cause of death, there could be misclassification involved not only between countries but also among different groups within a country. Regarding across country differences, Tøllefsen et al., 2017 reported that when reclassifying 1800 deaths during 2008 from Denmark, Norway and Sweden, experts in the field of psychiatry, pathology and public health reclassified 9% of accidental or natural deaths in Norway and 21% of events of undetermined intent in Sweden as suicides (93). Moreover, underreporting due to cultural taboo was considered to be the reason behind the overrepresentation of migrants in undetermined manner of deaths in Sweden (94). The reasons for using or not using events of undetermined intent in the different studies in this thesis are explained in detail in section 3.4.1.

1.4.2 Epidemiology

Suicidal behaviour is one of the major public health concerns of our times. Globally, around 800,000 people die by suicide every year (95). The suicide rates among different regions and countries vary quite extensively (96). In 2019, the age-standardised suicide rate per 100,000

was 9 globally (96) (all rates are reported in this thesis as per 100,000 people, unless it is specifically mentioned otherwise). A higher average rate than this global average was found in Africa, south-east Asia and Europe (11.2, 10.2 and 10.5 respectively) (96). Generally, countries with Muslim-majority populations and some central Asian countries have lower suicide rates (96). In Sweden and Norway, the age-standardised suicide rates for all ages were 12.4 and 9.9 in 2019, respectively, which were, on average, higher than both the European and the global average (96). Among the major refugee-generating countries to Sweden and Norway, suicide rates vary between 2.1 in Syria and 17.3 in Eritrea (96).

Globally, the number of people attempting suicide is staggeringly much higher than those who die by suicide – up to 20 times more (97). Compared to the available data on suicide mortality, few countries in the world have surveillance systems for nationwide data collection on suicide attempts which makes it difficult to make international comparisons regarding the incidence and prevalence of suicide attempts. Nock and co-authors (2008) compared data on lifetime prevalence of suicide attempt in seven low- and middle-income countries (LMIC) and ten HIC, which was collected under the World Mental Health Survey Initiative (98). They reported an overall prevalence of 2.7% across these countries. However, large variations existed among both the HIC (0.5% in Italy vs 5% in the USA) and the LMIC (0.7% in Nigeria vs 4.7% in Columbia). In the WHO/EURO Multicentre study, similar variations in rates of suicide attempt were observed across the different European centres. The lowest rates were 69 and 45 per 100,000 population for females and males, respectively, in Spain. The highest rate for females was 462 in France and for males, 314 in Finland (88). In 2019, the age-standardised rate of hospitalisation for suicide attempt among individuals 15-years or older in Sweden was 74.1 per 100,000 population (55.8 for men; 92.2 for women) (99). During 2008-2013, among individuals 10-years or older in Norway, the incidence rates of receiving inpatient or specialised outpatient healthcare for deliberate self-harm were 108.6 and 133.4 among men and women, respectively (100).

1.4.3 Risk and protective factors

As a general trend all over the world, suicide rates increase with increasing age (101), with some exceptions between HIC and LMIC (96, 102). Suicide in men is almost twice as likely as in women (96), and hanging, firearms, self-poisoning and jumping from heights are common methods of suicide (95). Past history of suicide attempts and present major depression are the strongest determinants of death by suicide (103). However, the different factors contributing to suicide risk and their strength may vary during different stages of life (104). Several risk factors of fatal and non-fatal suicidal behaviour are overlapping (101, 105), although subtle differences in demography and common choice of methods are distinguishable.

Compared to death by suicide, suicide attempt is more common in the young than in older ages, more common in women than in men (106) and most often done by self-poisoning by a wide range of medications and other substances (107). Suicide attempt is also around 10-30 times more common than suicide (101).

Apart from sex and age, other socio-demographic risk factors of suicidal behaviour were reported as being single (88, 108-110), having a low educational level and being unemployed

(88, 98, 110, 111). While two to four times higher risk of suicide was identified among the unemployed (112-114), some authors argued that the association between unemployment and suicidal behaviour is possibly mediated by individual risk factors (115) such as alcohol consumption (116) and poor mental health (113). Additionally, several psychiatric, psychological, cultural and biological risk factors of suicidal behaviour were identified (101). A meta-review reported that, among psychiatric determinants, depression and bipolar disorders increase the risk by 20 and 17 fold, respectively, compared with the general population (117). In this review, borderline personality disorder was reported to be associated with the highest risk for suicide – 45 times higher. However, the authors mentioned that the study population of individuals with personality disorder comprised the most severe patients who required hospitalisation (117). For PTSD, anxiety disorders (any) and schizophrenia, the risk of death by suicide was 3.3, 2.5 and 13 times higher. The same risk was 9 and 16 times higher for alcohol use disorder among men and women, respectively (117). Not only psychiatric disorders but also somatic disorders are associated with suicidal behaviour. Among individuals who attempted suicide, the proportion with any somatic disorders was estimated to be 27-50% (118). Suicide risk is higher among cancer patients, especially for head and neck, gastrointestinal and prostate cancer (118). For certain neurological disorders, suicide risk is two-fold higher in those with multiple sclerosis (118) or epilepsy (119), irrespective of comorbid psychiatric disorders. For patients with stroke (120) or traumatic brain injury (121), this risk is 1.8 and 2.4 times higher. Two review articles concluded that any chronic pain (122) or chronic abdominal pain (123) increases the risk of suicide, even after controlling for psychiatric disorders.

1.4.3.1 Factors associated with culture

Culture as a concept is very broad and is defined in numerous ways without much agreement among these definitions. Marsella defined *culture* as "shared acquired patterns of behaviour and meanings that are constructed and transmitted within social-life contexts for the purposes of promoting individual and groups survival, adaptation and adjustment" (124). Both internal factors, e.g., world views, identities, values, etc., and external factors, e.g. artefacts and roles interact with each other to constitute culture and norms (124). Based on this view on culture, *ethnicity* can be regarded as the identity of a group of people who share characteristic cultural features. Although ethnicity and country of birth are often used interchangeably in the literature, ethnic variations may exist within a country, and using country of birth data does not capture the within-country diversity adequately. *Country of birth* is defined as the geographically and politically demarcated place where an individual was born. Compared to culture or ethnicity, it is less challenging to measure country of birth and therefore, it is commonly used as a proxy of these concepts in epidemiological studies. Specifically, for research on suicidology, this method is a viable alternative in two aspects. First, registration of ethnicity on death certificates will have to depend on information from someone other than the deceased, which will be less accurate. Second, the comparative rarity of suicidal behaviour may introduce statistical power problems when stratifying by ethnicity in very diverse study populations. The aspects of culture, ethnicity and country of birth are important in the context of migration because differences in the culture of the country of birth can influence the suicidal behaviour among refugees in the host country (125).

Based on cultural views and stigma towards mental ill-health, refugees may experience and express mental health problems differently, reflect on their mental healthcare needs differently, and cope with past traumas in different ways than the host populations in the new country (125-127). Higher levels of stigma towards mental ill-health was reported among Bhutanese refugees in the USA (128), and among Iraqi and Sudanese refugees in Australia (129), compared with the host population. A more recent study in 2019 reported that among 103 Arabic-, Farsi-, or Tamil-speaking refugee men in Australia, higher severity of PTSD was associated with self-stigma for seeking mental healthcare and stigma for PTSD (130). Moreover, negative attitudes and stigma associated with suicidal behaviour in the origin culture and religion may influence whether a person will ultimately act on suicidal ideation (19, 126, 131). Furthermore, risk factors for suicide attempt and suicide may differ across cultures, even though there are shared features of suicidal behaviour that exist in nearly all cultures (127, 132). For example, in the case of suicidal behaviour, Asian women were reported to have higher impulsivity to stressful life events even though they had lower rates of mental ill-health compared with West-European women (127). A higher degree of regret among Asian women also corroborates the higher impulsivity of their self-harm behaviour in the absence of any current mental disorder and shows support for cultural influences in suicidal behaviour between these groups (127). Moreover, as death registration is often carried out by a collaboration between medical and legal entities, cultural dimensions may affect the classifications of suicide mortality across and within countries (133). The level of stigma and legality of suicidal behaviour are important in this context as cultural influence may bias the determination of death by suicide vs homicide or suicide vs accidental or undetermined cause of death (133). For example, suicide by burning at home among women in several LMIC could be, in reality, homicides related to family conflicts and dowry disputes where the medical and legal systems responsible for determining the cause of death could also be intertwined in the process of making this error, along with the family (134-138).

Culture-influenced differences in help-seeking behaviour, expression of symptoms of mental illness, idioms of distress and attitudes towards suicidal behaviour also highlight the importance of transcultural psychiatry and cultural competence among health professionals. Such *cultural competence* can be defined as the awareness of the influence of culture on mental health when treating individuals, and to contemplate how the health professional's own cultural identity and preconceptions about other cultures may have an impact on the treated individual and the treatment process (139). Lack of cultural competence at the individual as well as institutional level may affect access to healthcare and the therapeutic process in multiple ways (please see section 1.5.1 for details on barriers to healthcare), and subsequently, may negatively affect the identification of suicidal individuals or follow-up care for those who attempted suicide. Therefore, transcultural psychiatry and its appropriate implementation to improve the quality and access to mental healthcare among migrants and refugees are ever more critical in this era of fast globalisation and unprecedented forced migration.

1.4.3.2 Factors associated with religion

In close proximity with cultural views, religion-bound attitudes may also influence suicidal behaviour. Religion, specifically participation in religious activities rather than religiosity (140, 141), provides better coping strategies with stress, reduces depressive symptoms and

substance abuse, gives meaning and purpose in life and helps maintaining social support networks (142). However, it will be too simplistic to assume that religion is a sole protective factor of suicidal behaviour because neither it is static nor separable from larger socio-political and cultural contexts that play diverse roles in the complexity of suicidal behaviour (143). Even then, it is important to note that suicidal behaviour is generally condemned in the Muslim world and among Catholic and Orthodox Christianity but not among protestants (143). Rates of suicide mortality are generally lower in countries deemed less secular (144), particularly in countries with a higher proportion of Muslims (145, 146). Suicide rates are often lower in Catholic countries in the Mediterranean than Protestant countries in northern Europe (147). Among hospitalised individuals for depression, those with lower religious affiliation had a more positive attitude towards suicidality, and they were more likely to have a history of lifetime suicide attempt (148). In their systematic review, Lawrence et al. (2016) concluded that affiliation with religion and attending religious services have a protective role in preventing suicide attempt and possibly death by suicide (126). They also acknowledged the complexity of the relationship between religion and suicidal behaviour and suggested that, through social support networks and by providing hope in times of distress, religion may hinder acting on suicidal thoughts.

1.4.3.3 Risk and precipitating factors among migrants and refugees

In a review of the literature on precipitating and risk factors of suicidal behaviour among migrant groups, the author argued that the available evidence suggests a less important role of psychiatric disorders or past history of suicidal behaviour for migrants than the host population and interpersonal problems such as family conflicts were more highlighted (149). In this review, a similar role of age and sex was found for suicidal behaviour among migrants as in the general population. However, the literature was either contradictory or insufficient to be conclusive regarding the role of marital status, socio-economic position, education and employment (149). Several studies reported that perceived discrimination by migrants and stereotypical attitudes towards migrants' ethnicity and religion by the host population negatively influenced suicidal behaviour among migrant groups (150-152). Lack of social support networks and social isolation were also predictors of suicide (94) and self-harm (151) among migrants. In this regard, increasing neighbourhood ethnic density was found to be associated with decreasing suicide (153) and self-harm (154) rates among migrants in the UK and suicide rates among migrant groups in the Netherlands (155). Social support networks through religious activities and the connectedness religion may create with the community are also found to be working protectively for suicidal behaviour in migrants (156). Finally, cultural factors require special attention in case of the risk of suicidal behaviour in migrants and refugees because these groups usually hold on to their cultural values and religious beliefs when they migrate (157).

To understand how the risk and protective factors may play a role in refugees' suicidal behaviour, the stress-diathesis model (158) is perhaps the most relevant among other explanatory models of suicidal behaviour. Earlier models of suicidal behaviour have recognised stressful life events as key triggering factors. According to the stress model, individuals may become suicidal in the presence of severe adverse life events even when specific predispositions to psychological or biological risk factors are absent (131, 158). However, this stress model lacks an explanation of the fact that severe stress does not always

lead to suicidal behaviour. Therefore, a possible interaction of any distal vulnerability or diathesis with stressful life events was proposed in the stress-diathesis model. This model implies that biological, cognitive and social predispositions are the diathesis for suicidal behaviour, which upon interaction with stressful life events, increases the risk of suicidal behaviour (131, 158). For refugees, the different phases of migration, accompanied by war- and torture-related trauma, perils during the flight, difficult conditions in refugee camps and loss of or separation from family members, can be contemplated as adverse and stressful life events that may affect their risk of suicidal behaviour (19, 159). Moreover, the model also acknowledges that through individual coping mechanisms and preventive interventions, suicidal processes can be abated. The resilience factors discussed in section 1.3.1 may work in a protective way for suicidal behaviour among refugees.

1.4.4 Suicidal behaviour among migrants and refugees

1.4.4.1 *Suicidal behaviour among migrants*

The literature on suicidal behaviour among migrants is much more extensive than on suicidal behaviour among refugees – a sub-population of migrants. In a recent meta-analysis, Amiri (2020) synthesised 51 articles on this topic and reported lower odds of suicide mortality among migrants than their host population (Odds ratio/OR: 0.91, 95% Confidence Interval/CI: 0.90-0.93) (160). Based on the risk of bias analysis, most studies in this review were deemed high quality. However, a high degree of heterogeneity existed among these studies in terms of age groups, generations of migrants, reason for residence, outcome measure (suicidal ideation and suicide plan were additionally included in some studies as suicidal behaviour) (160). In this regard, studies that had detailed information on first-generation migrants from outside Europe, North America and Oceania are more comparable, assuming that a considerable proportion of these migrants come from refugee generating countries. Lower risk of death by suicide for first-generation migrants from non-western regions/countries was found in several longitudinal studies in the Netherlands (Risk Ratio: 0.62, 95% CI: 0.55 - 0.70) (155), Norway (range of ORs: 0.34 - 0.56) (161) and Sweden (Hazard Ratio/HR: 0.44, 95% CI: 0.33 - 0.49) (162). Both male and female migrants from the Middle-East in California, the USA, also had 0.5 times lower odds of suicide mortality than their host population (163). Westman et al. (2006) also reported a lower risk for suicide among migrants from the Middle-East and other non-western counties (HR 0.53 and 0.66, respectively) than the Swedish-born population (164).

On the contrary, the review by Amiri (2020) estimated a higher odds of suicide attempt for migrants than their host country peers (OR: 1.15, 95% CI: 1.10-1.20) (160). In a study of all hospital admissions during 1993-1998 in Sweden, Westman and colleagues (2003) found a higher risk of suicide attempt in migrant women from Iran, Iraq and the other countries from the Middle East, other Asian countries, and Latin America (range of HR: 1.4 - 2.2) whereas migrant men from non-western countries generally had a lower risk (165). In the WHO/EURO Multicentre Study on Suicidal Behaviour across 25 centres in 20 countries, migrants from former Yugoslavia had consistently higher suicide attempt rates than the host population in Germany, Sweden and Switzerland (166). In this study, migrants from Iran had lower rates in three centres in Israel and Sweden, and migrants from Chile had higher rates in two centres in Sweden. In a study on younger individuals (18-29 years) in Sweden, non-

European migrant women had a significantly higher risk of lifetime suicide attempts (OR: 3.52, 95% CI: 2.61 - 4.74) than Swedish-born women, but the risk for migrant men did not differ from that among men in the host population (167).

From an international perspective, rates of death by suicide in Sweden and Norway are medium-high (96). When comparing suicidal behaviour among refugees vs the host population, the differences in suicide rates in the host country and the country of birth may influence the direction and the strength of the association. Therefore, comparison with rates of suicidal behaviour in the country of birth may add further perspective. However, most often, refugees come from countries that lack adequate registration systems, so direct comparisons become difficult. Even then, comparing the suicide rates in the most refugee-generating countries, and the rates in Sweden and Norway as host countries show much variations. While age-standardised suicide rates were nearly half in Afghanistan, Iran and Iraq (6.0, 5.1 and 4.7 per 100,000 population, respectively) than in Sweden and Norway (12.4 and 10.0, respectively) in 2019, the rates were comparatively much higher in Eritrea and Somalia (17.3 and 14.7, respectively) (168). Regarding suicide attempt, Shirazi et al. (2012) estimated a weighted mean rate of 26.5 per 100,000 population in Iran, based on results from studies during 1981-2007 (169). This rate was much lower than the rates of suicide attempt in Sweden (123.8) in 2007 (99).

As previously mentioned, the migration process varies a lot by the different phases of migration and the reasons for migration, the following sections focus on the available evidence for suicidal behaviour among refugees and asylum seekers in LMIC and HIC.

1.4.4.2   Suicidal behaviour among refugees in low- and middle-income countries

A consequence of HIC adopting more restrictive migration policies is that more refugees are shifted towards LMIC (170). Refugees migrating to these settings face some unique challenges. Mental health professionals are usually inadequate in camps. Moreover, socio-political situations in these countries are often unstable, which escalates tension between the host population and those seeking asylum (170). Few studies investigated suicidal behaviour among refugees living in LMIC, and even fewer reported comparable quantitative figures. Rates of suicide and suicide attempt were 198 and 667 per 100,000 population, respectively, at a camp in India hosting refugees from Sri Lanka (171). In 2019, suicide rates in India and Sri Lanka were the same - 12.9 per 100,000 (168). In a camp for refugees from Myanmar in Thailand during 2014-2016, the suicide rate was reported to be 24.8 per 100,000 per year, which was four times higher than the population rate in Thailand during the same period (172). In Nepalese refugee camps in Bhutan, the age-adjusted suicide rate was much higher than the rate in Bhutan (20.8 vs 13.9 per 100,000 population) (173).

1.4.4.3   Suicidal behaviour among asylum seekers in high-income countries

While the average suicide rate in the UK was 9 per 100,000 population, among asylum seekers in detention centres, the rate was staggeringly high during two follow-up periods; 112 during 1997–2005 and 222 during 2002–2004 (174). Among asylum seekers in South Korea, the one-year prevalence of self-reported suicide attempt was higher (0.8%) than South Korean nationals (0.2%) (175). In the Netherlands, male asylum seekers in reception centres had a higher rate ratio for suicide mortality (rate ratio: 2.00, 95% CI: 1.37 – 2.83) and

hospitalisation for self-harm (rate ratio: 1.42, 95% CI: 1.20 – 1.66) than men in the host population. These risks did not differ between female asylum seekers and their Dutch counterparts (176). Similar findings of higher standardised mortality ratio (SMR) for male asylum seekers in the Netherlands was also reported by van Oostrum and co-authors (2011) (177). Among asylum seekers in Denmark, the number of suicide attempts were 3.4 times higher in 2001 than among the Danish-born host population (178).

1.4.4.4 Suicidal behaviour among resettled refugees in high-income countries

Despite the finding of a high prevalence of mental disorders and other stressors (23, 28) that may heighten the risk of suicidal behaviour (131, 179), studies investigating the risk of suicidal behaviour among resettled refugees are limited. Norredam et al. (2013) reported that male refugees in Denmark had a significantly lower risk of suicide than the Danish-born population (180). For female refugees, no statistically significant difference regarding suicide mortality was found compared with their Danish-born counterparts. However, this study did not investigate differences in the risk of suicide attempt among refugees. In a recent population-based cohort study in Ontario, Canada, the crude rates of suicide and self-harm were lower among refugees than in the host population (125). Another study following a national cohort in Canada during 1980-1998 reported lower SMR for suicide among refugees than the host population; SMR: 0.43, 95% CI 0.34–0.51 among males and SMR: 0.58, 95% CI: 0.35–0.81 among females (77). Contrary to these findings, Bhutanese refugees in the USA had higher suicide rates than the rates in the general population (181). Nevertheless, these studies lacked detailed information on the risk of suicide among refugees by their country of birth. The heterogeneity among refugees, therefore, highlights the importance of such stratified analyses. Within these heterogeneities, attitudes towards suicidal behaviour can differ among different groups based on their cultural and religious views towards suicidal behaviour (19, 126). The current evidence on the risk of suicidal behaviour also lacks information on how structural factors, apart from the individual differences, may influence the risk of suicide attempt and suicide among refugees.

1.4.5 Structural factors

Not only individual factors, as described above, but also structural factors might influence the rates of suicidal behaviour. Such structural factors include but are not restricted to the structure of the national healthcare and social services, migration policies, social insurance regulations (19) and national unemployment rates (182) (more details on post-migration factors related to healthcare use and labour market marginalisation (LMM) that may affect suicidal behaviour among refugees are provided in section 1.5 and 1.6, respectively). Health and social inequalities among refugees vs the host population can be shaped according to such structural factors, and these factors might also change over time, potentially leading to time period effects. During the last two decades, several temporal changes have occurred in Sweden, e.g. the mental healthcare reforms in the 1990s. This reform aimed to deinstitutionalise the treatment and management of severe mental disorders and promote more community support and outpatient care (183). Given that multiple barriers exist for refugees to access healthcare (please see section 1.5.1 for details), such reform should have minimised the disparities in psychiatric healthcare use for refugees. Another important change between different time periods was the implementation of stricter regulations of the

social insurance system in 2008 in Sweden, which might have had differential labour market consequences for refugees than for the Swedish-born population (184). Furthermore, according to their country of birth, the structure of the refugee population differed during different times in Sweden (11), which could potentially contribute to time period effects. Additionally, the rates of LMM over time were not constant, and compared with the host population, migrant groups were found to be marginalised on the labour market (185). This differential LMM may also lead to possible time period effects in the risk of suicidal behaviour among refugees.

Not only time period effects but also differences regarding several country-level structural factors in the host countries may influence the risk of suicidal behaviour among refugees. Differences regarding the healthcare and social insurance systems may exist between host countries, and integration policies in the post-resettlement period may also differ (19). Such differences in structural factors might be associated with differential processes regarding acculturation, post-traumatic stress and other mental health problems, social marginalisation and healthcare utilisation, which might be reflected in differences in risk of suicidal behaviour in different countries of resettlement (19, 159). Differences in migration policies between host countries may also affect suicidal behaviour among migrants and refugees. The influx of many forcibly displaced individuals in different host countries in recent years has led to a global rise in anti-migrant and anti-refugee sentiments (186, 187). Therefore, more restrictive changes in migration policies may not reflect pro-migration sentiments in the host population, rather the opposite. If the host society is less welcoming, refugees will likely face more discrimination and distress in the post-migration phase, which are detrimental to their mental well-being (28). On the other hand, restrictive migration policies can be employed to ensure a high level of integration among migrants and refugees. Such policies, if implemented correctly, may have a positive impact on migrants' mental health and suicidal behaviour. In light of these differences in structural factors, whether inter-country differences in determinants of suicide can explain, to some extent, the association between refugee status and subsequent risk of suicide is a critical inquiry.

Comparing two countries in Scandinavia, i.e. Sweden and Norway, regarding such inter-country differences is uniquely advantageous. Firstly, international comparisons of suicide mortality among refugees are lacking in the literature and given the comparative rarity of suicidal behaviour in minority populations like refugees, nationwide data is required to investigate these associations. Sweden and Norway are two of the very few countries that register such information. Secondly, there exists a long tradition of collaborative research on suicidal behaviour between Sweden and Norway, which aids further collaborations in data sharing. Moreover, age-adjusted suicide rates in both countries were almost similar since 2000 (168). Furthermore, governance and structural institution-building are also quite similar in these countries. However, regarding migration and integration of refugees, Sweden and Norway differ to some extent. More refugees have migrated to Sweden than Norway in the past decades (10, 11). Migrants and refugees often live in ethnically dense environments in their host country. As previously mentioned in the section on risk and precipitating factors among migrants and refugees, ethnic density may have a protective effect on suicidal behaviour among migrants (154, 155). On the other hand, the probability of culture conflicts becomes higher when living in areas of high ethnic density (188). Such conflicts, arising from

"disparity between traditional and modern attitudes in oneself as well as social and gender role expectations from individuals' significant others" (188), appear to be important interpersonal determinants of suicidal behaviour among migrants and refugees, specifically among women (149).

Moreover, even though both countries have nearly similar integration policies for refugees (189), newly arrived refugees experience somewhat better integration in the labour market in Norway than in Sweden (190). Also, annual unemployment rates have consistently been lower in Norway than in Sweden over the years (191). In addition, social insurance regulations are stricter in Sweden than in Norway (in a subsequent section on LMM, details on these differences are described) (185, 192, 193).

Furthermore, refugees in Sweden (194) may face differential access to psychiatric healthcare than refugees in Norway (69), compared with their respective host country peers, even though healthcare systems in these neighbouring countries have more similarities than differences (195, 196). Health expenditure per capita is generally higher in Norway than in Sweden (4505 vs 3919 Euro in 2019 in Norway and Sweden, respectively), but health expenditures as a percentage of the gross domestic product are rather similar in these countries (197). However, the coverage of psychiatric healthcare is much better in Norway than Sweden, in terms of the number of psychiatrists (30 vs 17 in Norway and Sweden, respectively in 2015), psychologists (103 vs 63) and the number of hospital beds in psychiatry (115 vs 44) per 100,000 inhabitants (198). These discrepancies may have a differential impact on the psychiatric healthcare use among marginalised groups such as migrants and refugees in these host countries. In Sweden, all refugee groups by their country of birth except refugees from Afghanistan were underrepresented regarding dispensed psychotropic drug use in 2009 compared with the Swedish-born host population (194). On the other hand, refugees in Norway had consistently higher use of specialised mental healthcare than Norwegian-born individuals during 2008-2011 (69).

Based on these comparisons regarding country-level structural factors, the risk of suicide might be hypothesised to be comparatively lower among refugees who resettled in Norway than among refugees resettling in Sweden. This hypothesis anticipates a relatively strong influence of structural factors on the risk of suicidal behaviour. In contrast, if not structural factors but resiliency and culture/religion-bound attitudes toward suicidal behaviour are more influential for the risk of suicide among refugees, then one may expect similar suicide risk for refugee groups from the same country/region who resettled in different host countries (Sweden and Norway).

1.5 SUICIDAL BEHAVIOUR AND HEALTHCARE USE

Healthcare contacts are essential elements of all strategic models of the prevention of suicidal behaviour (199). A secondary or selected prevention can be achieved by identifying individuals with a higher risk for suicidal behaviour, e.g. those with a mental disorder or substance use disorder. Healthcare contacts before a suicide attempt are, therefore, an opportunity for healthcare professionals to intervene. Moreover, once someone attempts suicide, as part of tertiary prevention, future healthcare contacts and psychosocial follow-ups are mandatory to prevent recurrence and deterioration (199).

In general, higher use of primary (200-202), emergency (202, 203), inpatient (202-204) and outpatient (202, 205) healthcare during the last year before suicide was reported among suicide decedents compared with the healthcare use among non-decedents. In a study on 1198 persons who attempted suicide, the majority had at least some healthcare contact during the one year before and after the index suicide attempt, i.e. only 12% and 8% did not use healthcare before and after a suicide attempt, respectively (206). However, such consistency in higher healthcare use around the time point of suicidal behaviour in the general population does not always hold when healthcare use is stratified by migration background. Immigrants were reported to be less likely to contact primary healthcare prior to suicide compared with the majority population in Norway (207). Given that migrants generally use healthcare less than the host population (208, 209), it can be speculated that healthcare use before and after a suicide attempt is also lower among migrants and refugees compared with the majority host population.

1.5.1 Healthcare use before and after suicide attempt

Research on potential differences in healthcare use before and after a suicide attempt between refugees and the host population is scarce in the literature. A study in Sweden reported that asylum seekers received less specialised mental healthcare, in comparison with the population control group, after a suicide attempt (210). However, the comparability of healthcare use between asylum seekers and refugees is limited because adult asylum seekers can only avail "treatment that cannot wait" in Sweden (210), while refugees have similar access to healthcare as any other Swedish-born individual. Therefore, healthcare use among refugees could be quite different from asylum seekers in Sweden. In studies not distinguishing between refugees and non-refugee migrants, a lower recommended healthcare use, i.e., follow-up care after hospitalisation and referral to outpatient, was found among migrants vs the host populations. Non-European immigrants were found to be 1.3 times more likely to be recommended no care at all or non-psychiatric care after a suicide attempt in Europe, compared with general populations in their respective host country (211). In the UK, compared with the majority host population, South Asian migrants were underrepresented regarding psychiatric healthcare use following self-harm (212).

Discrepancies in healthcare needs and utilisation before and after a suicide attempt between refugees and the host population can be influenced by cultural differences between these groups. Cultural perceptions of somatic and mental ill-health may influence how refugees seek healthcare and how they express their health problems to the healthcare professionals (19, 132). Language barriers and missing information may also lead to inadequate healthcare

use among refugees (213). Several of these barriers and their impact on healthcare use among refugees can also be related to health literacy. Among 513 Arabic-, Dari- and Somali-speaking refugees attending civic orientation courses in Sweden, 67% had inadequate or problematic health literacy measured by the short European health literacy questionnaire (214). The corresponding proportion was 28% among the Swedish-born, using the same instrument in another study (215). A consequence of such limitations can be refugees lacking confidence in the healthcare system in the host country. Moreover, discrepancies in healthcare use between the refugees and the host population may arise from the lack of transcultural competence among healthcare professionals in the host country (19, 132). Furthermore, consideration should also be given to the HME hypothesis mentioned in section 1.3.4 when discussing the healthcare use by refugees before and after a suicide attempt.

1.5.2 Antidepressant use before and after suicide attempt

Assessment of mental health using validated tools or self-reported questionnaires often requires a lot of time and resources (216, 217). An alternative, therefore, can be the use of administrative registers with good coverage. In Sweden, such secondary data on prescribed drug use also offers a different perspective on healthcare use as it is more comprehensive and covers healthcare visits to both specialised and primary healthcare. Although previous studies acknowledged this method to be less than optimal as indications for drug use might vary, medication use was effectively used as a viable proxy measure of psychiatric morbidity (218, 219). As individuals with a suicide attempt are often diagnosed with affective and anxiety disorders for which antidepressants are commonly prescribed (220), information on antidepressant use is specifically advantageous in this population. Therefore, investigating the patterns of antidepressant use during the years before and after a suicide attempt should provide important insights on healthcare use and treatment for affective and anxiety disorders among refugees. However, such crucial information on refugees who attempted suicide is lacking in previous literature.

In a population-based cross-sectional study in Sweden, female refugees aged 18-64 years, compared with non-refugee women, had 1.3 times higher odds of using psychotropic drugs (including antidepressants) (218). A higher risk of antidepressant prescriptions during 2008-2014 was reported among working-age female migrants from North Africa and the Middle East - a group of migrants mainly composed of refugees, compared with the majority of the Finnish-born population in Finland (220). On the other hand, compared with their Swedish-born counterparts, lower rates of antidepressant drug use in 2009 were found among refugees in Sweden (194). These contrasting findings can be due to the heterogeneity in refugee groups across different countries, and according to their socio-demographics, LMM and migration-related factors as well as clinical characteristics.

It is likely that the patterns of antidepressant use before and after a suicide attempt among refugees are influenced by different characteristics. The use of psychotropic drugs (including antidepressants) among migrants to Sweden from refugee-generating countries such as Iran and Chile was reported to be influenced by socio-demographic factors (sex, marital status

etc.) (221). Rates of antidepressant use among refugees also varied according to their duration of residence and country of birth (194). Similar heterogeneity may exist concerning LMM and clinical characteristics among refugees. The risk of LMM [as a composite measure of long-term unemployment, long-term sickness absence (SA) and disability pension (DP)] among refugees varied according to their region or country of birth and was higher than that in the host population (222). Furthermore, great heterogeneity exists among people who attempted suicide concerning their socio-demographic and clinical characteristics such as underlying mental disorders (87) and the method of suicide attempt (87, 125). Therefore, it is important to identify the potential individual variabilities in patterns of antidepressant use before and after a suicide attempt and link such distinct trajectories to subgroups of individuals with possible inherent characteristics related to socio-demographics, LMM, migration-related and clinical factors.

1.6 LABOUR MARKET MARGINALISATION

In the post-migration period, LMM leading to social marginalisation is well known to be detrimental to mental health and may increase the risk of suicidal behaviour (19, 132, 159). Such marginalisation can be differential between the refugees and the host population. The discrepancies in LMM can get even more widened by the fact that refugees usually have a lower socio-economic status in the new country, in comparison with the host population (5, 19).

Despite the differences in the definitions of LMM in the scientific literature, one common theme in these definitions is the individual's distance from the labour market, which can be temporary or permanent. Although unemployment is frequently used as a measure of LMM (223, 224), from a social insurance perspective, a broader definition of LMM, including SA and DP, is adopted in this thesis. This is analogous with previous studies (185, 225, 226), where LMM was conceptualised as the receipt of social security benefits as compensation for lost income due to temporary or permanent detachment from the labour market. Such a composite measure of LMM is required to avoid over or underestimation of LMM among refugees (185). Compensations as unemployment benefit and SA benefit may indicate temporary marginalisation from the labour market, and on the other hand, DP may indicate permanent LMM.

1.6.1 The social insurance systems in Sweden and Norway

Both the Swedish and Norwegian social insurance systems are public and aim at providing financial security to the country's residents. In both countries, unemployment insurance comprises basic insurance and income-related optional insurance. All individuals aged 20-64 years in Sweden who are not covered by the voluntary income-related insurance are entitled to basic unemployment benefit provided that certain preconditions are met, i.e. they are registered at the National Public Employment Service to seek jobs and ready to enter the labour market if suitable jobs are offered (227). Unemployment benefits in Sweden cover 80% of an individual's lost income (with an upper limit of 910 SEK per day) for the first 200 days of unemployment and then, 70% until day 300 (227).

Through publicly-financed health insurance that does not condition on baseline health status, from the age of 16, all individuals in Sweden are allowed SA benefits if their work capacity is reduced at least 25% due to disease or injury (227). These benefits amount up to 80% of lost income from work or unemployment benefits. The first 14 days, excluding one qualifying day of SA benefit, is paid by the employer. A physician's certificate is required from day 8. Sick leave periods extending more than 14 days are compensated by the Social Insurance Agency (227). According to the reduction of work capacity, SA benefits can be claimed full- or part-time (e.g. 25%, 50% or 75%). All individuals 30-64 years of age with permanent impairment of work capacity due to disease or injury are compensated by a permanent DP in Sweden (227). On the other hand, individuals 19-29 years of age are granted temporary DP where work disability is expected to last a minimum of one year or if they cannot complete their education due to health issues (226, 227).

After fulfilling similar criteria for unemployment insurance as in Sweden, individuals aged 18-67 years in Norway may get unemployment benefits for 26 weeks up to 2 years based on

previous income from work. The benefits can be a maximum of 1532 NOK per day (0.24% of 6 times the basic amount of 106,399 NOK in 2021) (192, 228). This benefit covers 80% of lost income when previous income was under three times the basic amount (62.4% when previous income was 3-6 times the basic amount) (192, 228). The basic amount is calculated each year by Statistics Sweden and Statistics Norway for the respective country. This calculation reflects the price development in the society and the government then decides on the level of pensions and other insurances for that particular year based on this calculation (192, 229).

In Norway, the employer pays for the first 16 days (without any qualifying day) of SA benefit, and thereafter payments are received from the Norwegian Labour and Welfare Administration (192). SA benefits equal 100% of the previous income and are paid for one year. Individuals who were employed for ten months or more may self-certify the first three days of their sick leave four times per year (192). Otherwise, medical certification from a physician is required. Individuals aged 18-67 years who had a permanent reduction of at least 50% of their work capacity due to disease or injury are entitled to disability benefit in Norway (192).

1.6.2 Labour market marginalisation and suicidal behaviour among refugees

A higher risk of LMM among refugees than among the Swedish-born individuals in Sweden was reported (222). This study also reported a higher risk of unemployment, SA and DP among refugees according to their region/country of birth in comparison with the host population in Sweden (222). In studies where a distinction between refugee and non-refugee migrants was not drawn, a higher risk of unemployment was found among migrants than among the Swedish-born (230, 231). Moreover, unemployment at an earlier age was associated with future unemployment, SA and DP among both migrants and the host population (232). Furthermore, SA (233) and DP (234-238) were found to be more common among migrants than among the host population, and the higher risk of DP was shown to be due to discrepancies in socio-demographic and work-related factors between migrants and the host population (239). Previous studies reported that SA/DP, specifically SA due to any mental disorder (240-242), predicted death by suicide (240, 243), suicide attempt (240, 242) and deliberate self-harm (241). It is, therefore, necessary to investigate how LMM factors influence suicidal behaviour and healthcare use before and after a suicide attempt among refugees.

2 RESEARCH AIMS

2.1 OVERALL AIMS

This PhD thesis aimed to investigate the risk of suicidal behaviour (suicide attempt and suicide) among resettled refugees compared with the majority host population. A further aim was to investigate patterns of healthcare use, before and after a suicide attempt, among refugees who resettled in Sweden compared with the Swedish-born population.

2.2 SPECIFIC AIMS

Study I

To investigate 1) the risk of suicide attempt and suicide among refugees in Sweden, according to their country of birth, compared with that of the Swedish-born population and 2) to what extent time period effects, socio-demographics, previous LMM and morbidity explain these associations.

Study II

To investigate 1) if the patterns of specialised psychiatric and somatic healthcare use, within an observation window of three years before and three years after a suicide attempt, differ between the Swedish-born population and refugees in Sweden and, 2) to explore if patterns of specialised healthcare use differ among refugees who attempted suicide according to their sex, age, education or receipt of DP.

Study III

To investigate 1) the patterns (trajectories) of antidepressant use among refugees and the Swedish-born population, during an observation window of three years before and three years after a suicide attempt and, 2) to elucidate if the identified trajectory groups of antidepressant use are associated with socio-demographic, LMM, migration-related and clinical factors among refugees in Sweden, compared with the Swedish-born.

Study IV

To investigate 1) the risk of suicide among refugees in Sweden and Norway, in general, and according to their sex, age, region/country of birth and duration of residence, compared with the risk of suicide in the population born in the respective host country and 2) if factors related to socio-demographics, LMM and healthcare use explain the risk of suicide among refugees differently in different host countries (Sweden and Norway).

3 MATERIALS AND METHODS

3.1 DESIGN AND STUDY POPULATION

Using nationwide register data in Sweden (Study I-IV) and Norway (Study IV), four population-based longitudinal studies were conducted. An overview of these studies is presented in table 1. The selection steps to reach the final study population for all studies is shown in table 2.

In study I, *three cohorts* were formed according to the inclusion criteria (table 1), and each cohort was followed prospectively regarding inpatient healthcare for suicide attempt as well as death due to suicide for four years. *Cohort 2* (table 2) was also followed for a total of nine years (until 31 December 2013) to improve statistical power in the subgroup analyses for refugees from specific countries of birth.

An open cohort of all individuals, 20–64 years of age with at least one hospitalisation or visit in specialised outpatient healthcare for suicide attempt (index attempt) between 1 January 2004 and 31 December 2013 (n = 99,050 individuals) in Sweden comprised the initial study population in study II. After applying the inclusion criteria (table 1-2), the final study population included 85,771 individuals, of which 81,916 were Swedish-born, and 3855 (4.5%) were refugees. These individuals were followed three years before and after the index attempt regarding healthcare use.

In study III, an open cohort of all individuals treated for suicide attempt in inpatient or specialised outpatient healthcare in Sweden from 1 January 2009 – 31 December 2015 and 20–64 years of age at the date of the index attempt was identified (n = 72,306 individuals). The final study population was selected based on the inclusion criteria (table 1-2), and it comprised 3492 (5.6%) refugees and 58,950 (94.4%) Swedish-born individuals.

A nested case-control study design was conceived in study IV. All individuals aged 18-64 years who died by suicide during 1998-2018 in Sweden and Norway were included as cases. For each case, up to 20 controls were randomly selected from the general population of the respective host country who were alive, and of the same sex and age as the case at the time of suicide. Matching was done to ensure statistical power in subgroup analysis regarding the matching factors. This method yielded 17,572/351,440 and 9443/188,860 cases/controls in Sweden and Norway, respectively.

In the subsequent sections in this thesis, baseline year indicates the one-year period before cohort entry (Study I), or year of index suicide attempt (study II-III), or selection as case or control (study IV), if not otherwise specified.

Table 1: Overview of the four studies in the thesis

	Study I	Study II	Study III	Study IV
Design	A cohort study with baseline data on 31 Dec 1999 (cohort 1), 2004 (cohort 2) and 2009 (cohort 3), and four years of follow-up for each cohort. Cohort 2 was additionally followed up for nine years in total.	A cohort study with baseline data on the date (t_0) of specialised healthcare for suicide attempt (index attempt) or 31 Dec of the year before index attempt. Follow-up period was three years before and after t_0.	A cohort study with baseline data on the date (t_0) of specialised healthcare for suicide attempt (index attempt) or 31 Dec of the year before index attempt. Follow-up period was three years before and after t_0.	A nested case-control study during 1998-2018.
Inclusion criteria	Refugees and Swedish-born individuals; aged 16-64 years; alive and resident in Sweden at baseline.	Refugees and Swedish-born individuals; aged 20-64 years at index suicide attempt; alive and resident in Sweden during the three years before index attempt; use of specialised healthcare for at least one suicide attempt in between 1 Jan 2004 and 31 Dec 2013.	Refugees and Swedish-born individuals; aged 20-64 years at index attempt; alive and resident in Sweden during the three years before index attempt; use of specialised healthcare for at least one suicide attempt in between 1 Jan 2009 and 31 Dec 2015.	All suicide cases during 1998-2018 with ICD-10[a] codes X60-X84 from the cause of death registers in Sweden and Norway; up to 20 controls, randomly selected from the general population who were alive and of the same sex and age as the case at the time of suicide.
Population (n)	4,993,691, 5,083,618 and 5,171,135 individuals in cohort 1-3, respectively (of which 3.3%, 3.9% and 5% were refugees, respectively)	85,771 individuals who attempted suicide (of which 4.5% were refugees)	62,442 individuals who attempted suicide (of which 5.6% were refugees)	17,572/351,440 and 9,443/188,860 cases/controls in Sweden and Norway, respectively
Data sources	LISA[b], STATIV[c], NPR[d], Cause of death register	LISA, STATIV, NPR, Cause of death register	LISA, STATIV, NPR, Cause of death register, Prescribed drug register	Cause of death register and NPR in Sweden and Norway, LISA, STATIV, central population register in Norway, Statistics Norway´s events database

Table 1: Overview of the four studies in the thesis (continued)

	Study I	Study II	Study III	Study IV
Outcome	(Inpatient healthcare due to) Suicide attempt and suicide	Inpatient and specialised outpatient healthcare use for psychiatric and somatic diagnoses (annual crude and adjusted prevalence, mean number of visits and, mean duration of hospitalisation)	Annual use (DDD[e]) of antidepressants	Suicide
Factors included in the analyses	Socio-demographic factors: Age, sex, educational level, type of residential area, family situation; LMM[f] factors: Unemployment, SA[g], DP[h]; Healthcare factors: History of specialised healthcare use for i) suicide attempt ii) any psychiatric or somatic disorder	Socio-demographic factors: Age, sex, educational level, type of residential area, family situation; LMM factors: Unemployment, SA, DP	Socio-demographic factors: Age, sex, educational level, type of residential area, family situation; LMM factors: Unemployment, SA, DP; Clinical factors: History of specialised healthcare use for i) any suicide attempt ii) any somatic disorder, history of neuroleptic, anxiolytic or sedative drug use, method of index attempt, diagnosis of specific mental disorder at index attempt	Socio-demographic factors: Age, sex, educational level, type of residential area, family situation; LMM factors: Unemployment, SA, DP; Healthcare factors: History of specialised healthcare use for i) any deliberate self-harm ii) any psychiatric disorder
Statistical methods	Descriptive, chi^2 (χ^2) tests, cox proportional hazard regression models	Descriptive, χ^2 tests, independent sample t tests, repeated measure logistic regression with generalized estimating equations and an autoregressive correlation structure	Descriptive, χ^2 tests, group-based trajectory models, multinomial logistic regression, log likelihood χ^2 tests	Descriptive, χ^2 tests, conditional logistic regression models

[a]ICD-10: International Classification of Diseases version 10, [b]LISA: longitudinal integration database for health insurance and labour market studies (Swedish acronym), [c]STATIV: longitudinal database for integration studies (Swedish acronym), [d]NPR: National Patient Register, [e]DDD: Defined Daily Dose, [f]LMM: Labour Market Marginalisation, [g]SA: Sickness Absence, [h]DP: Disability Pension

Table 2: Selection steps of the study populations of the four studies in the thesis

	Study I			Study II	Study III	Study IV	
	Cohort 1	Cohort 2	Cohort 3			Sweden	Norway
n=Initial study population	5,587,931 individuals alive and resident in Sweden on 31 Dec 1999	5,750,669 individuals alive and resident in Sweden on 31 Dec 2004	5,982,221 individuals alive and resident in Sweden on 31 Dec 2009	99,050 individuals who had specialised healthcare for suicide attempt during 2004-2013	72,306 individuals who had specialised healthcare for suicide attempt during 2009-2015	17,572 cases who died by suicide and their 1:20 age and sex matched population controls (n=351,440)	9,443 cases who died by suicide and their 1:20 age and sex matched population controls (n=188,860)
n=Individuals with uncertain reason for residence in Sweden were excluded (% of initial study population)	206,753 (3.7)	224,276 (3.9)	221,342 (3.7)	3,547 (3.6)	2,495 (3.4)	Not applicable	Not applicable
n=Non-refugee immigrants were excluded (% of initial study population)	387,487 (6.9)	442,775 (7.7)	589,744 (9.8)	7,670 (7.7)	5,563 (7.7)	Not applicable	Not applicable
n=Non-residents in Sweden during three years before index suicide attempt were excluded (% of initial study population)	Not applicable	Not applicable	Not applicable	2,062 (2.1)	1,806 (2.5)	Not applicable	Not applicable
n=Final study population	4,993,691 (of which 3.3% refugees)	5,083,618 (of which 3.9% refugees)	5,171,135 (of which 5.0% refugees)	85,771 (of which 4.5% refugees)	62,442 (of which 5.6% refugees)	Not applicable	Not applicable

3.2 DATA SOURCES

Pseudonymised individual data from Swedish (study I-IV) and Norwegian (Study IV) nationwide registers were used in this thesis. Register linkages were done by unique 10-digit or 11-digit personal identity numbers in Sweden (study I-IV) and Norway (study IV), respectively. Details of the registers used in this thesis are given below.

3.2.1 Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) in Sweden

This database is maintained by Statistics Sweden and contains annual data on factors related to socio-demographics and labour market since 1990, covering the entire adult population aged ≥16 years in Sweden (227). In this thesis, data on sex, age, educational level, type of residential area, family situation, immigration, emigration, country/region of birth, as well as unemployment, SA and DP were obtained from LISA. Exceptions were data on age and sex, which were acquired from the national patient register in Sweden in study II and study III, and from the respective cause of death registers for individuals who died by suicide in Sweden and Norway in study IV. The completeness and validity of LISA are generally excellent regarding most variables. However, data on educational level is missing for 1.7% of individuals (mostly among those born outside Sweden). The correctness of educational level was evaluated in 2006, and it was estimated to be 85% correct (99% correct for those with higher educational level).

3.2.2 The Prescribed Drug Register in Sweden

The National Board of Health and Welfare holds this register in Sweden, and it contains information on all prescribed and dispensed medications for all residents in Sweden since 1 July 2005 (244). The register, however, does not have information on purchases of over-the-counter drugs or medication use during hospitalisations (the register is, therefore, estimated to cover 84% of all drug purchases in Sweden) (244). From this register, information on date of prescription and dispensing of medication, anatomical therapeutic chemical (ATC) classification system codes, and defined daily dose (DDD) per package was used in study III of this thesis.

3.2.3 Longitudinal Database for Integration Studies (STATIV) in Sweden

Statistics Sweden, along with the Swedish Integration Board, developed this database to provide a basis for describing and analysing data related to integration, segregation, and migration (12). Data is available since 1997 in this register for all residents in Sweden. In all the studies of this thesis, information on reason for residence in Sweden was obtained from this database. Across the study populations in this thesis, 3.4-3.9% individuals had incomplete information regarding their reason for residence (table 2).

3.2.4   The National Patient Registers in Sweden and Norway

In Sweden, this register is maintained by the National Board of Health and Welfare, and it contains information on inpatient (nearly 99% of all hospitalisations since 1987) and specialised outpatient (around 80% of all visits since 2001) healthcare (245). Data on primary healthcare is not included in this register. According to the International Classification of Diseases version 10 (ICD-10), diagnostic codes from primary and secondary diagnoses from this register were used in all four studies to construct different variables (please see the sections on outcome and covariates for details on the diagnostic codes). Information on external cause of injury was used to create the outcome variable and covariates regarding suicidal behaviour. Data on external cause of injury was 95.7% complete during 1987-2007 for the inpatient register and 81.7% complete during 2001-2007 for the specialised outpatient register (245).

The Directorate of Health holds the National Patient Register in Norway with availability of data on all public specialised healthcare since 2008. In study IV, data from this register was used to create variables related to healthcare use among refugees in Norway and the Norwegian-born population. The Norwegian Registry for Primary Healthcare was established at the end of 2017 (246), and data from that register was not used in this thesis. Comparison with other quality registers in Norway had revealed that the completeness of the National Patient Register was generally very good (completeness ranged from 85.5% to 99.8% for national quality register for children, and for chronic obstructive pulmonary disease, respectively) (247).

3.2.5   The Cause of Death Registers in Sweden and Norway

The Cause of Death Register in Sweden is currently maintained by the National Board of Health and Welfare, and data is available from 1952 (248). Since 2012, it also includes all deaths in Sweden irrespective of residence status (99% completeness). Moreover, it covers the residents of Sweden who died abroad. From 1997 onwards, the causes of death are coded according to ICD-10 (248). In all four studies, data on the date of death was used to measure the follow-up period, and data on cause of death was used to identify individuals who died by suicide or due to other causes.

The Norwegian Institute of Public Health currently maintains the Cause of Death Register in Norway, which is 98% complete (249). It includes all individuals who died in Norway (including non-residents since 2012). Additionally, Norwegian residents who died abroad are also included. From 1996, the causes of death in this register are coded according to ICD-10 (250). Data on date and cause of death from this register was used in study IV to identify individuals who died by suicide and to match population controls who were alive until the selection into the study population.

3.2.6 Central Population Register and Statistics Norway's events database in Norway

Both databases are maintained by Statistics Norway and were used in study IV of this thesis to get information on factors related to socio-demographics and labour market attachment for refugees in Norway and the Norwegian-born individuals. Information on sex, age, region and country of birth, and reason for residence (for refugees only) was obtained from the Central Population Register (251) with national coverage since 1964 (reason for residence is available since 1990). Data on type of residential area, family situation, educational level, number of annual days with unemployment benefits, number of annual days with SA and DP was obtained from Statistics Norway´s Events Database with data availability since 1992 (252). Although both databases cover the entire population in Norway from the given year, completeness may vary for specific variables, e.g. educational level. This variable only indicates education obtained in Norway and, therefore, has a higher degree of missingness for migrants than Norwegian-born individuals. In study IV of this thesis, 7.4% of the controls (as the representative population sample) had missing data regarding this variable.

3.3   EXPOSURE AND COVARIATES

3.3.1   Migration-related factors

In all four studies, individuals with a refugee background were considered as the exposed group, and the Swedish-born (Study I-IV) and Norwegian born (Study IV) populations were considered as the comparison group. In Sweden and Norway, the respective migration agencies are responsible for granting residence permits to refugees and mainly defines refugee status according to the Geneva Convention definition (5). The Migration Agency in Sweden also considers refugee status for the following reasons for residence: 'in need of protection' or 'humanitarian grounds' (11). Likewise, the Directorate of Immigration in Norway permits residence to convention refugees, resettlement refugees and refugees with 'other/unspecified' reason for residence (10). In this thesis, an individual with a refugee background was identified if that person had received a residence permit in the respective host country (Sweden for study I-IV or Norway for study IV) as a refugee according to the abovementioned definitions/categories. For subgroup analyses, refugees were further categorised according to their region and country of birth in Study I and IV (according to the categories presented in table 2 in study I and IV). Swedish-born (Study I-IV) and Norwegian-born (Study IV) individuals were considered as the host population in the respective host country. All other individuals who did not have a refugee background or belonged to the host population were categorised as non-refugee immigrants. In study I-III, these individuals were excluded when selecting the final study population (table 2). As study IV was a matched case-control study, excluding non-refugee immigrants would have distorted these matched strata. Therefore, they were included in all analyses as a separate single category. In a sensitivity analysis in study III, country of birth was also considered as a covariate in the analytical model for refugees.

Based on the information on latest year of immigration to the host country, another migration-related variable on duration of residence was used as a covariate in study III (0-5, 6-10 and >10 years) in a multivariate-adjusted analytical model for refugees. This variable was also used for stratification in study IV (0-5, 6-10, 11-15 and >15 years) to investigate if any significant difference regarding the risk of suicide exists within the subgroups.

3.3.2   Socio-demographic factors

In all four studies, age, sex, educational level, type of residential area, and family situation were considered as socio-demographic covariates (categories are presented in table 1 in Study I-IV). All these factors were controlled in the multivariate-adjusted analytical models in all four studies except in study II where type of residential area and family situation were not adjusted to avoid the risk of over-adjustment in the GEE models. Additionally, analytical models were stratified by age and sex in study I and IV to identify any significant differences between the subgroups regarding the risk of hospitalisation for suicide attempt (study I) and death by suicide (study I and IV). In study II, the estimated annual adjusted prevalence of specialised healthcare use among refugees was also stratified by age, sex, and educational level. Additionally, in study IV, age and sex were used as the matching factors in the matched case-control design. Individuals with missing data on educational level (study I-IV) and family situation (study I) were categorised as a separate category.

3.3.3 Labour market marginalisation factors

The following LMM factors were considered as covariates in all four studies: unemployment (0, 1-180 and >180 annual days), SA (0, 1-90 and >90 annual net days) and DP (yes, no). These factors were measured for the one-year period before selection in the cohorts in Study I, the year before index suicide attempt in study II-III, and the year before selection as case or control in study IV. These factors were adjusted for in all multivariate-adjusted models in all four studies except in study II; these were not controlled for to avoid the risk of over-adjustment in the GEE models. Instead, a sensitivity analysis was done to overcome this limitation. The details of that analysis are provided in section 4.5.4. Additionally, DP was considered as a stratification variable in GEE models in study II to analyse if the estimated annual adjusted prevalence of specialised healthcare use differs between the subgroups of refugees with or without DP at baseline.

3.3.4 Factors related to morbidity, healthcare use and medication

Morbidity represents ill-health or showing symptoms for a particular disease or health condition and is generally measured as prevalence or incidence in epidemiological studies (253). In this thesis, the covariates related to morbidity were measured as prevalence estimates, i.e. the proportion of the study population who had a health condition during a defined period, for example, any mental disorder during the three years before the start of the study. In study I, history of any hospitalisation for suicide attempt and history of any inpatient healthcare use (any diagnosis) were considered as covariates, and these factors were adjusted for in the regression models. These morbidity factors were measured for a five-year period before the start of the follow-up in all three cohorts with four years of follow-up. For the 2004 cohort with nine years of follow-up, specialised outpatient healthcare was also included to improve the coverage of the morbidity factors, and both inpatient and specialised outpatient healthcare were measured for four years preceding the start of the follow-up. As data on specialised outpatient healthcare was not available before 2001, to ensure comparability, this information was not used to construct the morbidity factors in the 4-year-follow-up cohorts. History of specialised healthcare for suicide attempt (study II-III) or deliberate self-harm (study IV) was measured for a three-year period before index suicide attempt in study II-III or before selection as case or control in study IV. In study IV, any specialised healthcare due to mental disorders during a three-year period before selection as case or control was also measured as a covariate.

Several other factors related to the index suicide attempt were considered as covariates in study II and study III: year of index suicide attempt (study II), method of suicide attempt (study II-III), history of any specialised healthcare due to somatic diagnoses during three years before index attempt (study III) and mental disorder as main or secondary diagnosis in specialised healthcare at index suicide attempt (study II-III). Moreover, in study III, any use of neuroleptics, anxiolytics and hypnotics/sedatives drugs (yes, no) during the year before index suicide attempt were considered as covariates. Diagnostic information to construct the factors related to morbidity, healthcare, and medication-related variables are presented in table 3. Similar variables were constructed with the same codes in all four studies except in study IV, where the history of healthcare use for deliberate self-harm was

coded differently in Sweden and Norway to be analogous with the local coding practices and recommendations in the respective countries (100, 254, 255).

Table 3: Diagnostic information on the outcome, healthcare, and morbidity-related variables

Variables	ICD-10[a] codes	Note
Healthcare use for any mental disorder	F00-F99	Outcome in study II and covariate in study I, IV
Healthcare use for any somatic disorder	All ICD-10 codes except F00-F99, O00-O99, P00-P96, Q00-Q99	Outcome in study II and covariate in study I
Diagnosis of specific mental disorder at index suicide attempt		Covariate in study III
Depressive disorders	F32-F34	
Bipolar disorders	F30-F31	
Anxiety disorders	F38-F48 except F43.1	
Post-traumatic stress disorder	F43.1	
Schizophrenia, schizotypal and delusional disorder	F20-F29	
Other mental disorders	F00-F19, F50-F99	
Healthcare use for suicide attempt (study I-III)/deliberate self-harm (study IV)	X60-X84, Y10-Y34 in study I-IV in Sweden and a devised coding system in Norway in study IV (100)	Covariate in study I-IV
Method of index suicide attempt		Covariate in study III
Self-poisoning	X60–69, Y10–19	
Self-injury	X70–84, Y20–34	
	ATC[b] codes	
Use of medication		
Antidepressant drug(s)	N06A	Outcome in study III
Neuroleptic drug(s)	N05A	Covariate in study III
Anxiolytic drug(s)	N05B	Covariate in study III
Hypnotic and sedative drug(s)	N05C	Covariate in study III
[a]ICD-10: International Classification of Diseases version 10; [b]ATC: Anatomical Therapeutic Chemical classification system		

3.4 OUTCOME MEASURES

3.4.1 Suicide attempt and suicide

In study I and study IV, the outcome of interest was suicidal behaviour defined as hospitalisation for suicide attempt in study I and death by suicide in study I and IV. The inpatient register in Sweden was used to identify suicide attempts according to ICD-10 codes X60-X84 and Y10-Y34. Death by suicide was identified from the cause of death register in Sweden (study I and IV) and Norway (study IV). In study I, events of undetermined intent (ICD-10 codes: Y10-Y34) were included to limit the potential effects of underreporting and regional and temporal variations in case ascertainment (254, 256). However, because such codes are rarely used in Norway, these were not included in study IV to ensure comparability between results from Sweden and Norway.

3.4.2 Healthcare use

In study II, outcome measures comprised psychiatric and somatic healthcare use, measured separately from inpatient and specialised outpatient healthcare. The crude prevalence rate was defined as the proportion of individuals having had such healthcare (yes, no) during each observation year (three years before and after the index suicide attempt). An annual time scale was used, with t0 indicating the date of index attempt, Y-1 to Y-3 referring to the three respective years before t0, and Y+1 to Y+3 referring to the three respective years after t0. Additionally, the estimated prevalence of healthcare use was calculated after adjusting for several covariates. Finally, healthcare use was also conceptualised as the mean annual number of visits to inpatient or specialised outpatient healthcare and the mean annual duration (days) of hospitalisation among those who had such healthcare during each of the observation years. The total duration of hospitalisation was calculated by deducting the overlapping days when spells of inpatient healthcare overlapped in the register data (257). Diagnostic information to construct these outcome variables is presented in table 3.

3.4.3 Antidepressant use

Prescribed antidepressants vary a lot by drug class, mode of action, recommended dose, price, pack size etc. making it difficult to compare drug consumption among different groups. In this regard, DDD allows a standardised measure for comparison purposes. "The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults" (258). In study III of this thesis, the outcome of interest was antidepressant use which was measured as the annual DDDs of antidepressants (identified by ATC code N06A) during the three years before and after the index attempt. The same annual time scale as in study II was used in this study. The sum of the DDDs of all antidepressants prescribed to an individual during a given year indicated the total amount of DDDs for that individual for that specific observation year. Any annual DDD >1500 was considered unusual (e.g. error in data or large purchase before travel), and truncation was done for DDDs that exceeded that level. Due to unavailability, it was not possible to include data on antidepressant use for 0.02% of refugees and 0.02% of Swedish-born individuals for the last two months during Y+3.

3.5 STATISTICAL ANALYSES

3.5.1 Descriptive statistics

In study I, sex- and age-standardised (259) rates of suicide attempt and suicide for refugees were calculated using Swedish-born as the reference population. Differences between refugees and the Swedish-born population (Study I-III) and between cases and controls (study IV) in the distributions of factors related to baseline socio-demographics, LMM and healthcare use were tested using the Chi-square ($\chi2$) tests. In study II, group differences between refugees and the Swedish-born individuals regarding annual crude prevalence rates of healthcare use were also tested using the $\chi2$ tests. In the same study, mean differences between refugees and the Swedish-born host population concerning the number of visits to specialised outpatient healthcare and duration and number of hospitalisations for a particular observation year were evaluated by independent sample *t*-tests.

3.5.2 Cox proportional hazard regression

Cox proportional hazard regression models yielding crude and multivariate HRs and aHRs, respectively with 95% confidence intervals (CIs) were applied in study I to compare refugees, in general, and from different countries, with the Swedish-born population regarding subsequent suicide attempt and suicide. Regression models were also stratified by age and sex (online supplementary tables S2 and S3 in study I). To calculate person-time, data was censored in the event of emigration, death due to any cause (for regression models where suicide attempt was the outcome), death due to a cause other than suicide (for regression models where suicide was the outcome) and, end of follow-up, whichever occurred first. The multivariate-adjusted cox models were controlled for specific covariates in the following manner: Model 1 – socio-demographic factors; Model 2 – additionally for LMM factors, and Model 3 – additionally for morbidity/healthcare factors (table 2-4 in study I). The assumption of the proportional hazard was confirmed by plotting log-minus-log Kaplan–Meier survival curves.

3.5.3 Generalised estimating equations

This regression method is robust for several reasons when analysing repeated measurements in longitudinal studies (260). First, it does not require the outcome to be normally distributed. Moreover, by assigning correlations between measurements, it minimises the bias from the interdependence between the repeated intra-individual measurements. Furthermore, it can incorporate subjects in the models even if they have missing values on some repeated measurements regarding the dependent variable (260). Therefore, in study II, annual adjusted prevalence rates of specialised healthcare use with 95% CIs were assessed using repeated measure logistic regression analysis with the generalised estimating equations (GEE) method. For the working correlation matrix, an autoregressive correlation structure was used, assuming that the correlation of healthcare use should be stronger between adjacent time points of measurements (260). All GEE models were adjusted for sex, age, educational level and year of the index suicide attempt. Additionally, GEE models were used to analyse the estimated annual adjusted prevalence of specialised healthcare use among the refugees, stratified by sex, age, educational level and receipt of DP at baseline (with mutual adjustment of these covariates in the respective

models). Healthcare use in the subsequent follow-up years was considered as missing for those who died or emigrated during Y+1 and Y+2 ($n = 2917$ individuals, of which 80 refugees).

3.5.4 Group-based trajectory analysis and multinomial logistic regression

Group-based trajectory models (261, 262) were used separately among refugees and Swedish-born individuals in study III to identify potential differences in patterns (trajectories) of antidepressant use during three years before and after a suicide attempt. This method aims to identify clusters of individuals who follow a similar trajectory over time on a specific outcome of interest. These clusters are named trajectory groups (263). First, Bayesian information criterion (BIC) was used to identify the best-fitted model. The size of the estimated trajectory groups was considered when selecting the final model to ensure adequate statistical power in the subsequent multinomial logistic regression analysis. Therefore, four trajectory groups with at least 4% of the study population in each group were preferred to a five-group model with higher BIC values. The probability of an individual belonging to a specific trajectory group was calculated, and the highest estimated probability was considered for group belonging. According to Coté and co-authors, an average probability of ≥0.70 for individuals of a trajectory group indicates a good fit (262). In study III, these probabilities were 0.92 and 0.90 for the models for refugees and Swedish-born, respectively.

Subsequent to the group-based trajectory analyses, multinomial logistic regression was used to identify potential associations among the trajectory groups and the covariates. First, Log likelihood χ^2 tests were applied to estimate if a covariate was associated with a specific trajectory group. Then, Nagelkerke pseudo R^2 values were applied to evaluate the strength of such potential associations by comparing between a full model (with all covariates) and a model without the specific covariate. Moreover, separate models with or without migration-related factors were analysed to draw valid comparisons between refugees and the Swedish-born. In case of death or emigration during a specific year of follow-up, outcome data for an individual was considered as missing for that year and the subsequent follow-up years.

3.5.5 Conditional logistic regression

For matched case-control data, conditional logistic regression is a more robust method than unconditional regression, and it reduces bias from sparse data problems and matching distortions (264). Therefore, in study IV, the association between refugee status and suicide was tested using conditional logistic regression models yielding multivariate-adjusted odds ratios (aORs) with 95% CIs. Moreover, these analyses were stratified by subgroups of refugees with specific region/country of birth and duration of residence in the host country (categories are presented in table 2-4 in study IV). By applying three different analytic models, first, Model 1 was adjusted for the matching factors (age, sex). Although matching reduces statistical uncertainty within strata of confounders, the matching factors were still adjusted for in the analysis to reduce confounding bias according to a method proposed by Sjölander and Greenland (2013) (265). Model 2 was additionally adjusted for educational level, type of residential area and family situation, and Model 3 was further adjusted for LMM factors. To ensure comparability of the measurements between the host countries,

healthcare factors were adjusted in separate analytical models where only cases and controls during 2011-2018 were included because this method guaranteed three years of information for these variables according to the coverage years in the registers. These analyses were also stratified by sex (women and men) and age-groups (18-24, 25-44 and 45-64 years) and included 6,561/131,220 and 3819/76,380 cases/controls in Sweden and Norway, respectively.

All analyses in this thesis were performed using Statistical Analysis System (SAS) v. 9.4 except for the log-minus-log Kaplan–Meier survival curves in study I and GEE analyses in study II which were carried out in Statistical Package for the Social Sciences (SPSS) v. 25. For all statistical analyses, a p-value less than 0.05 was considered statistically significant.

3.6 ETHICAL CONSIDERATIONS

All studies in this thesis are based on analyses of pseudonymised individual-level data obtained by linking several nationwide registers in Sweden and Norway. The Regional Ethical Review Board of Stockholm, Statistics Sweden, the National Board of Health and Welfare in Sweden, and the Social Insurance Agency in Sweden have approved the use of these databases in Sweden. Similarly, the use of register data in Norway was approved by the Regional Committees for Medical Research Ethics – South-East Norway, Statistics Norway, the Directorate of Health, and the Norwegian Institute of Public Health. Only eligible researchers in the project group were allowed to access this sensitive data for research purposes. Strict procedures guided by the Swedish Ethical Review Act, the Personal Data Act, and the Administrative Procedure Act are followed in this process of data acquisition and usage. Because the data is derived directly from the registers, there is no chance of personal contact and associated risks to the participants. The integrity and anonymity of the persons are secured through the de-identification of the individuals. Any possibility of backward identification is eliminated by presenting results on a group level. In all four studies, low cell values in the tables (<10 in study I-III and <9 in study IV) were not reported for this purpose. Furthermore, high standards of data safety were maintained when handling the data. Taking these rigorous safety measures into account, the benefits of generating crucial knowledge regarding suicidal behaviour and healthcare use of vulnerable groups such as refugees exceed the potential risks for individuals in the study population that may arise due to loss of integrity.

4   RESULTS

4.1   BASELINE DIFFERENCES REGARDING COVARIATES

In study I-III, refugees from the general population (study I) and refugees who were treated in specialised healthcare for suicide attempt (study II-III) had higher proportions of men and younger individuals compared with their Swedish-born peers (table 1 in study I-III). Refugee groups in these studies also had lower educational level, a higher proportion of individuals living in urban areas, and a lower proportion of people who lived alone than the Swedish-born host population (table 1 in study I-III). In study IV, for both host countries, controls from the general population had higher educational level and were almost twice more likely to be married than those who died by suicide (table 1 in study IV).

Regarding LMM factors at baseline, more refugees were unemployed, and fewer refugees had SA benefit or DP than the Swedish-born population in study I-III except for the 2009 cohort in study I, where the proportion of DP recipients was slightly higher among refugees (table 1 in study I-III). In study IV, in both Sweden and Norway, population controls had a lower proportion of unemployed individuals, and SA/DP recipients than the cases (table 1 in study IV).

During the three (study II-III) to five-years (study I) period before baseline, a higher proportion of refugees had a history of hospitalisation for any psychiatric or somatic disorders (study I), but a lower proportion of refugees had a history of hospitalisation for suicide attempt than the Swedish-born (study I-III) (table 1 in study I and III, and table 5 in this thesis). In study II-III, higher proportion of refugees had a diagnosis of depressive disorder, anxiety disorder or PTSD than the Swedish-born during the three baseline years (table 5) or at index suicide attempt (table 1 in study III). Generally, any psychotropic drug use was lower among refugees compared with their Swedish-born peers in study III (table 1 in study III). Any contact with specialised healthcare for mental disorders during the three baseline years was almost seven times higher among the cases than the controls in study IV.

4.2 SUICIDAL BEHAVIOUR AMONG REFUGEES

4.2.1 Suicide attempt

During a nine-year follow-up period, the aHR of hospitalisation for suicide attempt among refugees was 0.82 (95% CI 0.78–0.86) in comparison with the Swedish-born. While sex- and age-stratified analyses for this association showed somewhat similar estimates (supplementary table S2 in study I), stratification by refugees' country of birth revealed some variations (Model 3, table 2 in study I). Compared with the Swedish-born, for some refugee groups by their country of birth, the risk of hospitalisation for suicide attempt did not vary (Afghanistan, Syria, Chile). On the other hand, some refugee groups showed statistically significant lower (Eritrea, Ethiopia, Somalia and Iraq) or higher (Iran) risk. Figure 1 (panel a) shows a comparison of these aHRs for the refugee groups in total and by their specific country of birth. Comparison of the different analytic models (Model 1-3 in study I) showed that socio-demographic factors marginally explained the association between refugee status and suicide attempt (table 2 in study I). The influence of LMM and morbidity factors on this association was close to none (table 2 in study I).
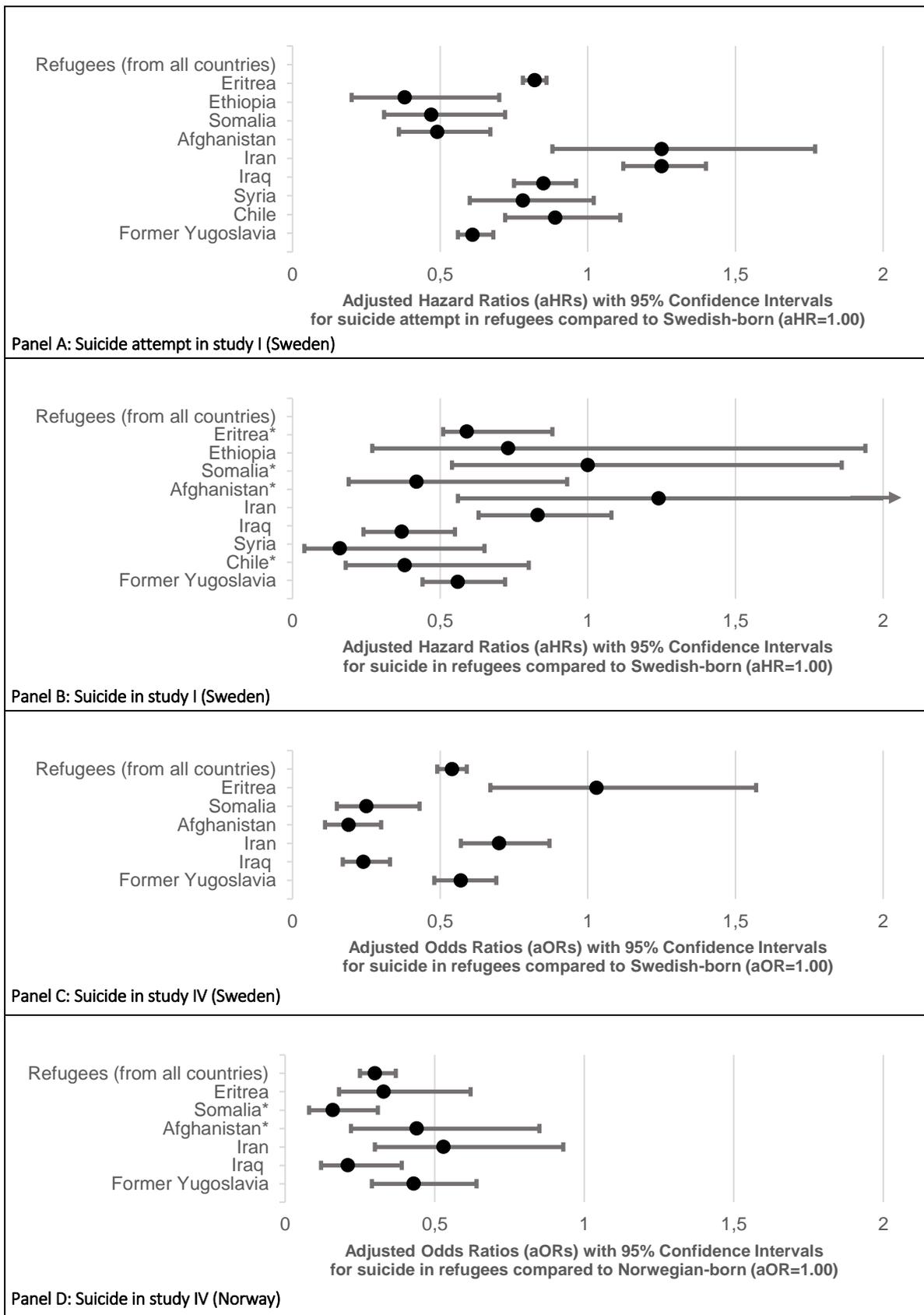
4.2.2 Suicide

In both study I and IV with nine and 21 years of follow-up, respectively, refugees had lower aHR (study I) or aOR (study IV) for suicide compared with their respective host country peers. The analyses stratified by sex and age also revealed similar risk estimates in both studies except for younger refugees (supplementary table 3 in study I and table 5 in study I). The number of deaths by suicide in refugee groups from Eritrea, Somalia, Afghanistan and Chile were relatively low in study I (table 3 in study I). Apart from these countries, refugees from Iraq, Syria and former Yugoslavian countries had a statistically significant lower aHR of suicide (figure 1, panel B). On the other hand, the risk for suicide among refugees from Iran and Ethiopia did not vary from their Swedish-born comparison group (figure 1, panel B). In study IV, due to a low number of deaths by suicide in Norway, refugee groups from Ethiopia, Syria and Chile were combined with the category 'other countries'. Otherwise, all country-specific refugee groups in Sweden and Norway had statistically significant lower aOR of suicide (figure 1, panel C-D) except refugees from Eritrea in Sweden (aOR 1.0, 95% CI 0.7-1.6). In both study I and IV, adjusting for the different covariates only marginally affected the risk estimates for suicide among refugees. Refugee groups by their duration of residence (years) had similar aHRs (supplementary table in study I) and aORs (table 4) for suicide in Sweden and Norway compared with their respective host populations.

4.2.3 Time period effects

In study I, incidence rates (per 100,000 person-years) of hospitalisation for suicide attempt and death by suicide among refugees decreased somewhat from the 1999 cohort to the 2009 cohort (table 4 in study I). The aHRs for suicide attempt among refugees showed a marginal decline chronologically (aHR 1.1, 0.9, 0.8 in the 1999, 2004 and 2009 cohorts, respectively), but it was somewhat stable across the three cohorts in case of suicide as the outcome of interest (table 4 in study I).

Figure 1 (from study I and IV): Risk of suicidal behaviour (suicide attempt and suicide) among refugees in Sweden and Norway

Panel A: Suicide attempt in study I (Sweden)

Panel B: Suicide in study I (Sweden)

Panel C: Suicide in study IV (Sweden)

Panel D: Suicide in study IV (Norway)

*The number of deaths by suicide was <10

4.2.4 Host country of resettlement

Compared to the host population, refugees in both host countries had almost similar lower aORs of suicide in study IV (aOR 0.5, 95% CI 0.5-0.6 in Sweden and aOR 0.3, 95% CI 0.3-0.4 in Norway). In the country-specific analyses, most refugee groups in Norway had comparatively lower point estimates of aORs of suicide than the same groups in Sweden (figure 1). However, the CIs were generally overlapping for most refugee groups (table 2 and 3 in study IV).

Table 4 (from study IV): Multivariate-adjusted odds ratios (aORs) with 95% confidence intervals (CIs) for suicide during 1998-2018 among refugees in Sweden and Norway, stratified by duration of residence in the respective host country, in comparison with the Swedish-born and Norwegian-born population, respectively

Duration of residence (years)	Number of cases/controls	Model 1[a] OR (CI)	Model 2[b] OR (CI)	Model 3[c] OR (CI)
Swedish-born	15,253/291,170	1	1	1
Refugees in Sweden	517/17,049	**0.57 (0.53-0.63)**	**0.59 (0.54-0.65)**	**0.54 (0.49-0.59)**
0-5	72/3,175	**0.43 (0.34-0.54)**	**0.47 (0.37-0.59)**	**0.48 (0.38-0.60)**
6-10	94/3,571	**0.50 (0.41-0.61)**	**0.55 (0.45-0.68)**	**0.52 (0.42-0.64)**
11-15	129/3,829	**0.64 (0.53-0.76)**	**0.69 (0.58-0.83)**	**0.60 (0.51-0.72)**
>15	222/6,474	**0.65 (0.57-0.74)**	**0.68 (0.60-0.78)**	**0.57 (0.49-0.65)**
Norwegian-born	8,537/152,125	1	1	1
Refugees in Norway	104/5,217	**0.34 (0.28-0.41)**	**0.38 (0.31-0.46)**	**0.30 (0.25-0.37)**
0-5	31/1,608	**0.33 (0.23-0.47)**	**0.38 (0.26-0.54)**	**0.28 (0.19-0.40)**
6-10	25/1,376	**0.31 (0.21-0.47)**	**0.34 (0.23-0.51)**	**0.28 (0.19-0.42)**
11-15	18/1,059	**0.29 (0.18-0.46)**	**0.31 (0.20-0.50)**	**0.26 (0.16-0.42)**
>15	30/1,174	**0.43 (0.30-0.62)**	**0.47 (0.33-0.68)**	**0.39 (0.27-0.56)**

aORs with 95% CIs in bold indicate statistically significant associations (p-Value <0.05).
Non-refugee immigrants were included as a separate category in all the models (data not shown)
[a] Model 1: Adjusted for the matching factors: sex and age.
[b] Model 2: Adjusted for Model 1 and other socio-demographic factors: educational level, family situation and type of residential area.
[c] Model 3: Adjusted for Model 2 and labour market marginalisation factors: unemployment, sickness absence and disability pension.

4.3 HEALTHCARE USE BEFORE AND AFTER A SUICIDE ATTEMPT

4.3.1 Healthcare use for psychiatric disorders

Patterns of inpatient and specialised outpatient healthcare use for psychiatric disorders were quite similar among refugees and the Swedish-born (figure 2). Both crude and adjusted prevalence rates increased until the year after the index suicide attempt (Y+1) and then decreased in both groups (table 2 in study II and figure 2). However, the proportion of refugees having such healthcare was significantly lower than the Swedish-born during the six years of follow-up (table 2 in study II and figure 2, $p < 0.05$). Regarding the mean number of visits to specialised healthcare and the mean duration of hospitalisations among those treated in specialised healthcare, the differences in psychiatric healthcare use between refugees and the Swedish-born population were less prominent (table 2 in study II).

4.3.2 Healthcare use for somatic disorders

Considering the crude and adjusted prevalence, hospitalisations for somatic disorders were significantly lower among the refugees than their Swedish-born counterparts during the entire follow-up period (table 3 in study II and figure 2, $p < 0.05$). The patterns of hospitalisations, however, were similar in both groups. In contrast, specialised outpatient healthcare use for somatic disorders showed a slightly different pattern among refugees. Specifically, a somewhat higher proportion of refugees (adjusted prevalence) had such healthcare during Y+2 and Y+3 than the Swedish-born because of a sharper decline in specialised outpatient healthcare use in the Swedish-born following Y+1 (figure 2). Regarding mean number of visits and mean duration of hospitalisations for somatic disorders, refugees generally were slightly undertreated than the Swedish-born during the six observation years (table 3 in study II).

4.3.3 Determinants of specialised healthcare use among refugees

Although the crude models showed that specialised healthcare use differed by refugees' sex, age and by receipt of DP (yes, no) (data not shown), mutual adjustment for these covariates explained these associations except for receipt of DP at the baseline year (figure 2 in study II). Among refugees who were non-recipients of DP, the adjusted prevalence of all-cause specialised healthcare showed a sharp increase until Y+1 and a sharp decrease afterwards (from 45% in Y-3 to 74% in Y+1 and then 60% in Y+3). On the contrary, among refugees who were DP recipients at baseline, the pattern of specialised healthcare use was relatively stable across the whole observation period with only a significant peak during Y+1 (figure 2 in study II).

Table 5 (from study II): Descriptive statistics of factors related to an index suicide attempt among 81,916 Swedish-born and 3,855 refugees[a], aged 20-64 years and residing in Sweden in the baseline year[b] who sought inpatient or specialised outpatient healthcare for the index attempt in between 2004 and 2013

Characteristics	All n (%)	Swedish-born n (%)	Refugees n (%)
	85,771 (100.0)	81,916 (95.5)	3,855 (4.5)
History of suicide attempt[c]			
No	73,641 (85.9)	70,143 (85.6)	3,498 (90.7)
Yes	12,130 (14.1)	11,773 (14.4)	357 (9.3)
Method of index suicide attempt			
Poisoning (X60-69, Y10-19)[d]	42,579 (49.6)	40,433 (49.4)	2,146 (55.7)
Hanging, strangulation and suffocation (X70, Y20)[d]	1,052 (1.2)	992 (1.2)	60 (1.6)
Firearm or explosives (X72-75, Y22-25)[d]	328 (0.4)	293 (0.4)	35 (0.9)
Cutting or piercing (X78, Y28)[d]	8,462 (9.9)	8,065 (9.8)	397 (10.3)
Jumping from a height (X80, Y30)[d]	1,079 (1.3)	1,021 (1.2)	58 (1.5)
Other (X71, X76-77, X79, X81-84, Y21, Y26-27, Y29, Y31-34)[d]	32,271 (37.6)	31,112 (38.0)	1,159 (30.1)
Mental disorder[e] at index suicide attempt			
No diagnosed mental disorder	66,315 (77.3)	63,268 (77.2)	3,047 (79.0)
Depressive disorders (F32-F34)[d]	4,708 (5.5)	4,423 (5.4)	285 (7.4)
Bipolar disorders (F30-F31)[d]	720 (0.8)	709 (0.9)	11 (0.3)
Anxiety disorders (F38-F48 except F43.1)[d]	3,153 (3.7)	2,961 (3.6)	192 (5.0)
Post-traumatic stress disorder (F43.1)[d]	97 (0.1)	62 (0.1)	35 (0.9)
Other mental disorders (F00-F29, F50-F99)[d]	10,778 (12.6)	10,493 (12.8)	285 (7.4)

Differences between the Swedish-born individuals and the refugees regarding all factors related to the index suicide attempt were statistically significant based on Chi-square tests ($p < 0.05$).
[a]Individuals who settled in Sweden as 'refugee' or 'in need of protection' or 'humanitarian grounds'.
[b]The year prior to the index suicide attempt.
[c]Measured as any inpatient or specialised outpatient healthcare due to suicide attempt during 1987-2003 and 2001-2003, respectively
[d]International Classification of Diseases version 10 code(s)
[e]As main or side diagnosis in specialised healthcare.

Figure. 2 (from study II): Estimated annual prevalence of specialised psychiatric and somatic healthcare use, adjusted for sex, age, educational level and year of index suicide attempt, at different time points three years before and after an index attempt in between 2004 and 2013 (error bars indicate 95% Confidence Intervals; Y-3: 3 years before; Y-2: 2 years before; Y-1: 1 year before; Y+1: 1 year after; Y+2: 2 years after; Y+3: 3 years after index attempt.)
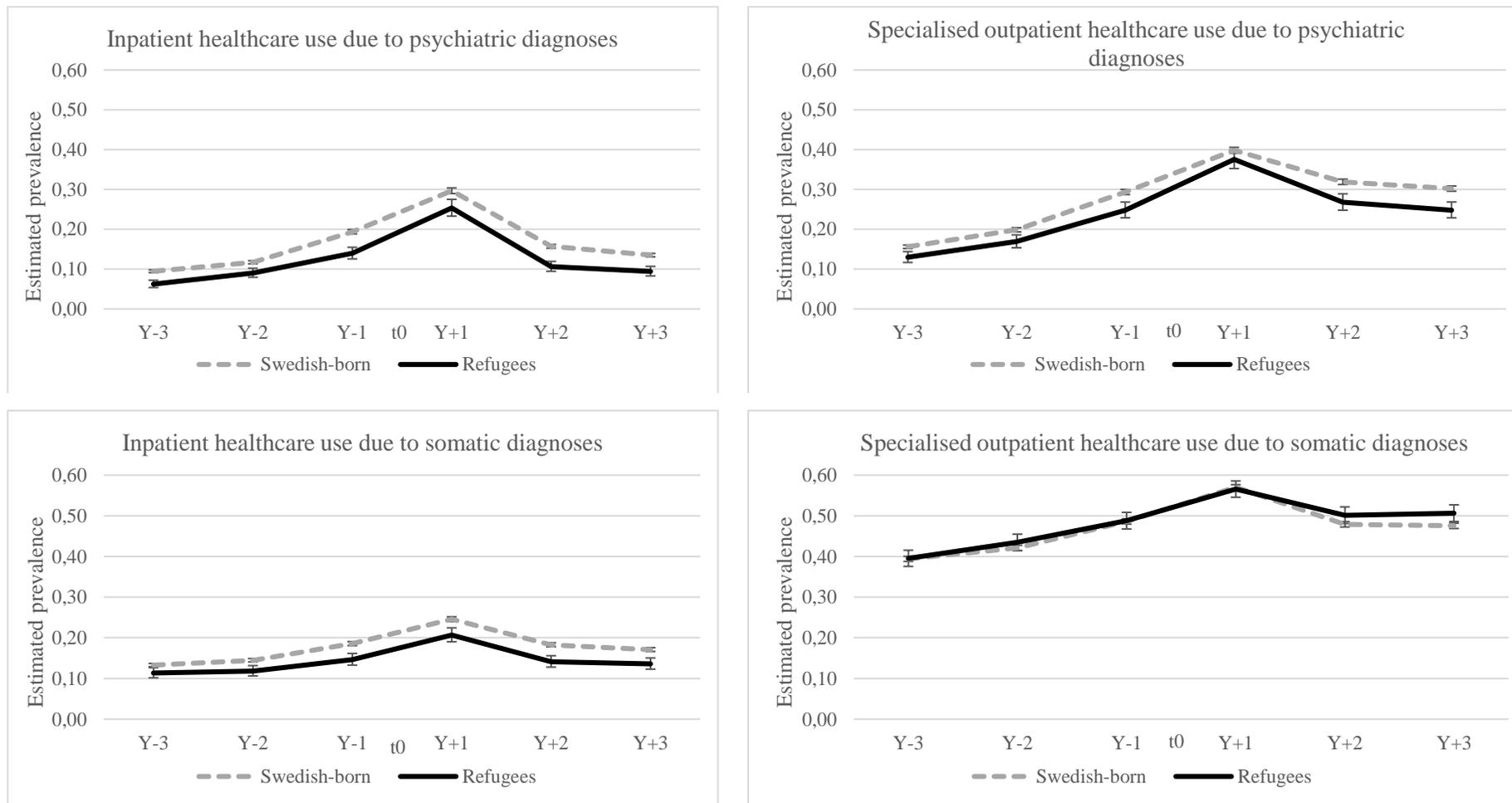
4.4 TRAJECTORIES OF ANTIDEPRESSANT USE

Among both refugees and the Swedish-born, four distinct trajectory groups of antidepressant use were identified. These groups were named as 'Low constant' (in both groups), 'Low increasing' (in both groups), 'Medium constant' (among refugees)/ 'Medium decreasing' (among Swedish-born), and 'High constant' (among refugees)/ 'High increasing' (among Swedish-born) (figure 3). A higher proportion of refugees (64.9%) than the Swedish-born (59.7%) belonged to the 'Low constant' group. Regarding the 'Low increasing' group, the increase of annual DDDs was much sharper among refugees (5.9%) than the Swedish-born (10.8%). Annual antidepressant use at medium and high levels were constant throughout the six observation years for refugees (22.5% and 6.6% of refugees, respectively) but not for the Swedish-born (19.1% and 10.4% of the Swedish-born, respectively) (figure 3).

The covariates included in study III (table 2 and 3 in study III) explained 43.9% and 38.9% of the variance across the trajectory groups in refugees and the Swedish-born, respectively (according to the Nagelkerke pseudo R^2 values in respective trajectory models). As individual factors, use of other psychotropic drugs than antidepressants during the year before suicide attempt (Y-1), as well as the method of index suicide attempt were more influential in explaining the variance than other socio-demographic, LMM and clinical factors in both groups (according to the difference in Nagelkerke pseudo R^2 values between a full model and a model excluding the specific covariate, summary results shown in table 6). However, these factors explained the variance across the trajectory groups to a lesser extent among the Swedish-born than among refugees.

Among the trajectory groups in refugees, the 'Low constant' group stood out in terms of a higher proportion of men and younger people as well as a lower proportion of individuals with SA/DP, those who used self-poisoning as the method of index attempt or people who used psychotropic drugs during Y-1 (table 2 in study III). Other trajectory groups were almost on par regarding the different covariates (table 2 in study III).

Figure. 3 (from study III): Trajectory groups of antidepressant use according to annual defined daily doses (DDDs) during 3 years before and 3 years after the date of seeking inpatient or specialised outpatient healthcare due to a suicide attempt (t_0) in between 2009 and 2015 in Sweden among 3,492 refugees and 58,950 Swedish-born, aged 20-64 (The dotted lines represent 95% confidence intervals)
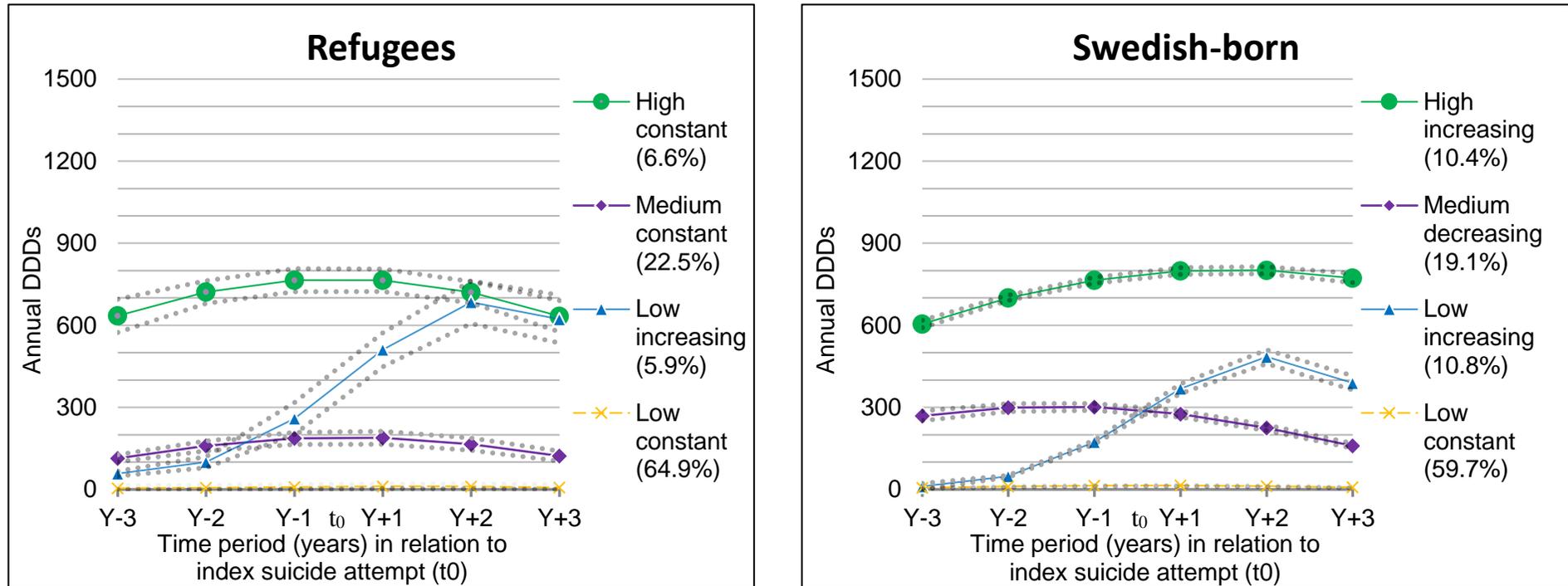
Table 6 (from study III): Distributions and associations of method of index attempt and use of psychotropic drug(s) except antidepressants in each trajectory group of antidepressant use among refugees and the Swedish-born who attempted suicide[a]

Characteristics	Low constant n (column %)	Low increasing n (column %)	Medium constant n (column %)	High constant n (column %)	p-value of log-likelihood χ^2 test	Difference[b] in Nagelkerke pseudo R^2
Refugees						
All (row percentage)	2 267 (64.9%)	207 (5.9%)	786 (22.5%)	232 (6.6%)		
Method of index attempt (ICD-10 code[c])						
Self-poisoning (X60-69, Y10-19)	894 (39.4)	162 (78.3)	554 (70.5)	183 (78.9)	<0.0001	0.020
Self-injury (X70-84, Y20-34)	1 373 (60.6)	45 (21.7)	232 (29.5)	49 (21.1)		
Use of psychotropic drug(s)[d] except antidepressants (ATC code[e])						
Neuroleptic drug(s) (N05A)	92 (4.1)	73 (35.3)	211 (26.8)	90 (38.8)	<0.0001	0.019
Anxiolytic drug(s) (N05B)	205 (9.0)	100 (48.3)	307 (39.1)	139 (59.9)	<0.0001	0.019
Hypnotic and sedative drug(s) (N05C)	262 (11.6)	145 (70.0)	417 (53.1)	173 (74.6)	<0.0001	0.039

	Low constant n (column %)	Low increasing n (column %)	Medium decreasing n (column %)	High increasing n (column %)		
Swedish-born						
All (row percentage)	35 205 (59.7)	6 340 (10.8)	11 265 (19.1)	6 140 (10.4)		
Method of index attempt (ICD-10 codec)						
Self-poisoning (X60-69, Y10-19)	11 782 (33.5)	4 339 (68.4)	7 779 (69.1)	4 465 (72.7)	<0.0001	0.024
Self-injury (X70-84, Y20-34)	23 423 (66.5)	2 001 (31.6)	3 486 (30.9)	1 675 (27.3)		
Use of psychotropic drug(s)[d] except antidepressants (ATC code[e])						
Neuroleptic drug(s) (N05A)	1 982 (5.6)	1 040 (16.4)	3 285 (29.2)	2 327 (37.9)	<0.0001	0.010
Anxiolytic drug(s) (N05B)	4 899 (13.9)	3 023 (47.7)	6 088 (54.0)	4 095 (66.7)	<0.0001	0.023
Hypnotic and sedative drug(s) (N05C)	5 897 (16.8)	3 112 (49.1)	6 832 (60.6)	4 342 (70.7)	<0.0001	0.019

[a]Trajectory group of antidepressant use according to annual defined daily doses (DDDs) among 3 492 refugees and 58 950 Swedish-born, aged 20-64 years and residing in Sweden who sought inpatient or specialised outpatient healthcare for the index attempt in between 2009 and 2015; [b]Difference in Nagelkerke pseudo R^2 between model including tested variable and model without tested variable. Nagelkerke pseudo R^2 for full model including all socio-demographic, labour market marginalisation and clinical factors was 0.433 for refugees and 0.389 for the Swedish-born; [c]International Classification of Diseases version 10 code; [d]Measured during the year before index attempt. 'No neuroleptic drug use', 'No anxiolytic drug use' and 'No hypnotic and sedative drug use' categories are not presented; [e]Anatomical Therapeutic Chemical classification system code

4.5 SENSITIVITY ANALYSES

In the following sections, both the methods and the results for specific sensitivity analyses are described. It is difficult to interpret the results from these analyses without knowing the specific methods and therefore, the description of these methods, and key results are combined in one section to avoid repetition. It is also important to note that most sensitivity analyses were performed for the main research questions involving the whole study population in a particular study. It was not possible to perform the same sensitivity analyses for the different subgroups of refugees in respective studies due to a lack of statistical power.

4.5.1 Events of undetermined intent

In study I-III, sensitivity analyses were performed to check if the inclusion of cases with undetermined intent (ICD-10 codes: Y10-Y34) had introduced bias. Analyses with and without these cases yielded similar results for the main analyses in all three studies (data not shown). To ensure comparability between Sweden and Norway in study IV, cases with undetermined intent were not selected in the study population because these codes are rarely used in Norway.

4.5.2 Reason for residence

Sensitivity analyses were performed by excluding 'non-convention' refugees ('in need of protection', and on 'humanitarian grounds') from study I-III and these findings showed similarity with the main results (data not shown). These analyses were not relevant for study IV as the sub-categories for reason for residence is slightly differently coded in the registers in Sweden and Norway.

4.5.3 Specialised outpatient healthcare use for suicide attempt

In study II-III, individuals treated in the specialised outpatient healthcare for suicide attempt were included in the study population. However, this measure distorted the sex distribution (fewer women than men) in the study cohorts than the expected sex distribution in this research field; that is suicide attempt is more common among women than men (106). So, in both studies, sensitivity analyses were carried out by excluding individuals who sought healthcare in the specialised outpatient for suicide attempt. These analyses showed similar results to the main analyses in study II-III (data not shown).

4.5.4 Differences in labour market marginalisation factors at baseline

Due to risk of over-adjustment, differences in baseline LMM between the Swedish-born and the refugees were not adjusted in the GEE models in study II. Therefore, a sensitivity analysis was done in a cohort of suicide attempters without any unemployment, SA or DP in the baseline year. The results in this selected cohort showed no difference between refugees and the Swedish-born (supplementary figure 1 in study II), which was slightly different than the finding of 'marginal difference' in the main analyses in study II. However, this sensitivity analysis was underpowered. Therefore, the scope for adequate comparability with the main results was limited.

4.5.5 Missing data

In study III, attrition-related bias was checked by doing a sensitivity analysis where annual DDDs of antidepressants was imputed from the latest available follow-up year. The trajectory groups for refugees and the Swedish-born population identified by this method were the same as the groups identified in the main analyses (data not shown).

4.5.6 Miscellaneous

In study III, a sensitivity analysis was carried out, including only the persons who attempted suicide and had a diagnosis of depressive disorders at baseline (n = 249 refugees, 3164 Swedish-born). This analysis showed similar trajectory groups to our main analysis (data not shown). In another sensitivity analysis in study III, antidepressant use was measured at 6-monthly intervals (instead of yearly intervals) (supplementary figure 1 in study III). Moreover, instead of separate trajectory models for refugees and the Swedish-born, all individuals in the cohort were included in a single analytical model. In this model, the variable on refugee status ('Swedish-born' = 0 and 'Refugee' = 1) was entered in addition to the covariates used in previous separate models. The trajectory groups from this single model were nearly identical to those from the model for the Swedish-born (supplementary figure 1 in study III). The variable on refugee status did not seem to explain any major part of the variance across the trajectory groups in this model (difference in Nagelkerke pseudo R^2 0.001, data not shown).

5   DISCUSSION

5.1   MAIN FINDINGS

In general, the risk of suicidal behaviour was lower in refugee groups than their host country peers in Sweden and Norway. Among individuals who attempted suicide, refugees were slightly underrepresented than the Swedish-born regarding specialised healthcare use and antidepressant use during the period of three years before and after a suicide attempt.

Following a nationwide cohort of refugees and Swedish-born individuals for nine years regarding suicidal behaviour (hospitalisation for suicide attempt and death by suicide) revealed a lower risk in refugee groups by their region/country of birth. An exception was refugees from Iran with a higher risk of suicide attempt. Across three cohorts with 4-year-follow-up periods, a slight decrease in the risk estimates for suicide attempt over time was observed. The risk of suicidal behaviour for refugees was marginally affected by the factors related to baseline socio-demographics, LMM, and morbidity.

During three years before and after an index suicide attempt, the crude and adjusted prevalence of healthcare use for psychiatric and somatic diagnoses among refugees was somewhat lower than among the Swedish-born. Among refugees who attempted suicide, specialised healthcare use did not vary much by their age, sex, or educational level. However, refugees who were recipients of DP before index suicide attempt had higher specialised healthcare use than non-recipients.

During three years before and after a suicide attempt, four trajectories of antidepressant use among refugees were identified. These trajectories revealed that 64.9%, 22.5% and 6.6% of refugees had a constant use at low, medium, and high levels (≤15, 110-190 and 630-765 DDDs, respectively). A sharp increase after the index attempt was observed among 5.9% of refugees (from <100 to around 650 DDDs). The method of suicide attempt and history of psychotropic drug use explained the variability among the trajectory groups in refugees better than other covariates. In general, though, the trajectory groups identified among the refugees were relatively similar in pattern, composition, and regarding their association with the covariates, compared with the trajectory groups identified among the Swedish-born.

Compared with their host country peers, refugee groups (by region/country of birth) in Sweden and Norway had lower odds of suicide during 1998-2018. An exception was resettled refugees from Eritrea in Sweden who had higher odds. A relative comparison of the aORs showed a somewhat similar suicide risk in refugee groups in Sweden and the same region/country of birth groups in Norway. Several covariates measuring socio-demographics, LMM and healthcare use marginally affected the suicide risk in both host countries. Sex or duration of residence did not reveal any modifying effect on the association between refugee status and death by suicide. However, some modifying effect of age was observed. Contrary to the generally observed lower risk of suicide in almost all refugee groups, the youngest age group (18-24 years) did not show a statistically significant difference between refugees and the respective host populations in Sweden and Norway.

5.2 DISCUSSION OF THE RESULTS

5.2.1 Suicidal behaviour among refugees

The risk of suicide attempt and suicide was lower, compared with the Swedish-born population, in most of the refugee groups in our study. Several factors may underlie these results. First, a positive health selection could be in play, suggesting that refugees are more likely to be physically and mentally healthier than their origin population. Therefore, they were able to withstand the challenges and hardships associated with migration. Inherent resiliency and hopefulness are, therefore, likely to be protective of suicidal behaviour among refugees. Second, refugee populations included in the studies of this thesis comprise resettled refugees with permanent residence in their respective host country. In previous studies, higher rates of suicidal behaviour were found in detained asylum seekers in the UK (174) and those in the community in the Netherlands (176). The difference in the study populations could partly explain such contradictory findings, i.e. some stressors associated with the asylum application process (176) are probably no longer present among refugees with residence permit in the post-resettlement period. Finally, differences in the acceptability of suicidal behaviour according to culture and religion plays a role in how people view suicidal behaviour and act upon suicidal thoughts (266). Compared with the host populations in Sweden and Norway, such factors may have contributed as a deterrent for the risk of suicidal behaviour among refugees.

5.2.1.1 Risk of suicide attempt

The risk of hospitalisation for suicide attempt was significantly lower among refugees than among the Swedish-born population in study I. A similar lower risk was observed for most refugee groups from specific region/country of birth, specifically refugees from Eritrea, Ethiopia, Somalia and former Yugoslavian countries. Any comparable finding was lacking in the literature when study I was conducted. A recent study generated some evidence in this regard, and showed a lower risk of hospitalisation for suicide attempt among refugees than among the Swedish-born individuals, even after stratifying by groups with or without specific mental disorders (267).

Interestingly, the multivariate-adjusted risk (aHR) of suicide attempt was higher among refugees from Iran in study I. This result was somewhat comparable with higher HRs (adjusted for age, sex, income and marital status) of hospitalisation for suicide attempt for Iranian migrants to Sweden reported by Westman et al. (2003) (165). Refugees who resettled in Sweden from Iran were found to be more educated and have more secularised views than their origin population in Iran (268). A further investigation into the educational level of different refugee groups in study I also revealed similar findings; 36% of refugees from Iran had high educational level vs 11% of refugees from Somalia (data not shown). Reasons behind this apparent surplus risk of hospitalisation for suicide attempt among refugees from Iran require further investigation.

5.2.1.2 Risk of suicide

In both study I and IV, almost all refugee groups by their region/country of birth had lower risk estimates for death by suicide compared with their respective host country peers. Although the associations were measured differently, according to the study design of the respective study, the aHRs and aORs for death by suicide in refugee groups were quite similar in both studies. However, for some country of birth groups, inadequate statistical power limited the possibility of making valid comparisons. Up until study I, no previous study examined suicide risk among refugees resettled in HIC by their country of birth. However, the finding of lower risk of suicide for all refugees, irrespective of country of birth, partially agreed with the results from Norredam et al. (2013). In their study, only male refugees had a lower risk of suicide than Danish-born individuals; the risk for female refugees was not statistically significant (180). Suicide rates were lower among refugees than among the host population in Ontario, Canada (125). Recently, after study I was conducted, the findings from this thesis were replicated by Hollander et al. (2020), Björkenstam et al. (2019) and Geirsdottir et al. (2021), showing a lower risk of suicide, both among all refugees (255), and when stratified by specific mental disorders (267) or educational level (269).

5.2.1.3 Influence of covariates

In both study I and IV, adjusting for the different factors related to socio-demographics, LMM and morbidity did not explain any major part of the risk of suicidal behaviour among refugees. Even after considering potential residual confounding in some of the covariates, these results are still surprising because the baseline differences between refugees and the host population regarding these factors were significant. It is, therefore, likely that the lower risk among refugees is driven by other unmeasured factors such as resiliency or attitude towards suicidal behaviour.

Further investigation of any modifying role of age or sex in study IV did not show any significant results for sex. However, stratification by age groups revealed that the risk of suicide for individuals aged 18-24 years was similar for refugees and their respective host population peers in Sweden and Norway; contrary to the findings of lower risk among refugees who belonged to the other age groups. Additional analyses into the role of age and sex in study I disclosed somewhat similar results, i.e. female refugees aged 16-24 years had the same risk of suicide as their Swedish-born counterparts. This might suggest that the apparent suicide mortality advantage among refugees than the host population is not equally favourable for younger refugees as it is for older refugees. These results are partially supported by what Guillot and colleagues found in their study of all-cause mortality among immigrants (270). Their results have shown that the cultural and health selection effects on migrant mortality advantage are more prominent among older than younger individuals (270). Religious beliefs could be weaker in younger birth cohorts than in older cohorts (271). Moreover, acceptability of suicidal behaviour may vary by age, and cultural taboo can be more prevalent among older individuals than among the youth (272). As neither resilience factors nor culture/religion-bound attitudes were measured in our study, these notions are

rather speculative. Therefore, future studies should investigate which factors influence suicidal behaviour among refugee youth.

Convergence theory states that the longer migrants reside in the host country, the more acculturation occurs, and that they embrace more and more the lifestyle and health behaviours of the host population. Therefore, the health disparities and mortality differences between recent migrants and the host population converge after a certain period (70). An inquiry into any modifying role of duration of residence on the risk of suicidal behaviour was beyond the scope of study I because the refugees in all three cohorts were relatively homogenous regarding this variable (approximately 85% refugees were residents for >5 years in Sweden). However, in study IV this hypothesis was tested, and no evidence of a modifying role of duration of residence was found for refugees regarding suicide mortality. In studies not distinguishing between refugees and non-refugee migrants, suicide rates among migrants were found to be converging with that among long-term residents (163, 255). The results in study IV contradicted these findings and highlighted the importance of considering the heterogeneous nature of immigrant populations when testing certain hypotheses. Interestingly, a somewhat constant suicide risk for refugees with recent as well as long-term resident status in Sweden and Norway reinforces another hypothesis: intrinsic factors such as resiliency and culture- and religion-bound attitude toward suicidal behaviour has probably more influence on the suicide risk among refugees than extrinsic factors such as adverse life experiences in the post-resettlement period.

5.2.1.4   Temporal effects on the risk of suicidal behaviour

A chronological decrease of the risk of hospitalisation for suicide attempt among refugees was observed across three cohorts (1999, 2004 and 2009 cohort) in study I showing minor time period effects. On the other hand, the risk of suicide among refugees did not vary across these cohorts. It is, therefore, unlikely that changes in national policies concerning psychiatric healthcare and social insurance regulations that occurred in Sweden during the studied years had any major influence on the risk of suicidal behaviour among refugees.

5.2.1.5   Host country of resettlement and suicide risk

In study IV, the aOR of suicide among refugees in Sweden vs Swedish-born was slightly higher than that for refugees in Norway vs the Norwegian-born. Compared to refugees in Sweden, refugees in Norway were reported to experience comparatively better situations in the post-resettlement period regarding integration in the labour market (189) and access to psychiatric healthcare (69, 194). Therefore, it was hypothesised that refugees in Norway might have more favourable outcome regarding suicide mortality than refugees in Sweden. However, the results did not support this hypothesis from several perspectives. First, adjusting for LMM factors in the regression models revealed only minor contributions from these factors on the suicide risk estimates, and such findings were similar for both host-country specific analyses. Despite the analytical models lacking statistical power for some country of birth groups and the fact that suicide risk for refugees from Eritrea varied by host country of resettlement, the analyses by specific region/country of birth did not show major differences in the risk estimates for most refugee groups in Norway and their counterparts in

Sweden. Additionally, person-time could only be calculated in a 25% representative sample in Norway, instead of the entire population. For this limitation, we could not estimate and compare absolute differences regarding the risk of suicide among refugees residing in Sweden and Norway. Therefore, any definitive conclusions regarding the differences in aORs for suicide mortality between refugees resettled in these host countries could not be drawn. Thus, the findings from study IV suggest a somewhat similar suicide risk for resettled refugees in Sweden and Norway. These results hint at a more protective effect of inherent resiliency and negative attitudes towards suicidal behaviour than external factors such as structural factors in the host country.

5.2.2 Healthcare use among refugees

Specialised healthcare use during three years before and after a suicide attempt was generally lower among refugees than among the Swedish-born despite the patterns being fairly similar in both groups, i.e. healthcare use increased until the first year following index attempt and then decreased for the rest of the follow-up years. Similar patterns of increase and decrease were observed one year before and after a suicide attempt among individuals (irrespective of migrant status) treated in hospital emergency departments from 1997-1998 in Helsinki, Finland (206). The results from study II showed that these patterns of healthcare use are also similar for refugees who attempted suicide.

5.2.2.1 *Specialised psychiatric and somatic healthcare use before and after a suicide attempt*

The finding of lower crude and adjusted prevalence rates of specialised psychiatric healthcare use among refugees than among the Swedish-born in study II was not directly comparable due to the lack of previous similar studies. Nonetheless, some relatable findings from studies on migrant populations showed that in seven European nations, immigrants from non-European countries received less referral to specialised healthcare following a suicide attempt than the host populations (211). Additionally, specialised psychiatric healthcare was less often offered to migrants from south Asia following self-harm than the majority host population in the UK (212). Contrary to the findings for crude and adjusted prevalence estimates, there was little difference between refugees and the Swedish-born regarding the mean number of visits to inpatient and specialised outpatient healthcare and the mean duration of hospitalisations for psychiatric diagnoses. Among the individuals who used specialised healthcare during the different observation years in study II, it appears as if the differences in psychiatric healthcare use between refugees and the Swedish-born are less prominent than the findings from the whole cohort. Access to healthcare is universal through Sweden's national health insurance system, and resettled refugees have the same rights as the Swedish-born. In general, lower healthcare use among refugees could be perceived due to several deterrents. Inadequate language skills and lack of knowledge to navigate the social and healthcare systems in Sweden may deter refugees from seeking help. Moreover, the stigma associated with mental disorders and perceived negative encounters with healthcare personnel (273) may discourage refugees from continuing adequate care after a suicide attempt.

Deterrents to access healthcare may also exist on the side of the service providers. Differences in language skills and cultural expressions may lead to misinterpretation of the information provided by refugees to the healthcare personnel during a consultation (273). Moreover, clinicians may generalise a suicide attempt among refugees as a 'natural' process following their traumatic past and, therefore, may miss the opportunity to identify other precipitating factors behind their suicidal behaviour. Such preconceptions may hinder adequate referral to specialised healthcare and, consequently, lower healthcare use among refugees. Such barriers to healthcare access can be overcome by increasing cultural competency among service providers. Additionally, promoting health literacy among refugees, especially regarding mental health, may reduce the disparity observed between the Swedish-born and the refugees who attempted suicide. Although costs for healthcare are capped with a ceiling for high costs in Sweden, low income and job insecurity among refugees may still negatively affect their willingness to seek help (274). The welfare and social support system may, therefore, play an important role in this regard.

Some variations in specialised somatic healthcare use were observed in study II for refugees who attempted suicide. While inpatient somatic healthcare was lower among refugees than among the Swedish-born individuals across all six follow-up years, both the adjusted prevalence and mean number of visits to specialised outpatient somatic healthcare were rather similar between refugees and the Swedish-born during the years before a suicide attempt. Moreover, the results showed that adjusted prevalence of specialised outpatient somatic healthcare use was slightly higher among refugees after the index attempt. Several factors may have influenced such over or underrepresentation of healthcare use among refugees. Idioms of distress were found to be expressed as somatic symptoms in refugee populations (275, 276). Additionally, cultural views regarding mental ill-health may vary among refugees (274), and there could be a lack of confidence in how mental disorders are managed in the western healthcare system. Such factors may lead refugees to express somatic instead of psychiatric symptoms. Due to the lack of equivalent studies in refugees with a suicide attempt, these results were not directly comparable with any previous findings on somatic healthcare use among refugees who attempted suicide.

5.2.2.2 Determinants of healthcare use among refugees who attempted suicide

Among refugees with a suicide attempt, specialised healthcare use was higher among DP recipients at baseline than among the non-recipients. Individuals are granted DP in Sweden when a disease or injury has led to reduced work capacity (227). Such underlying disease or injury among refugees who attempted suicide could be the primary reason for their healthcare needs. Therefore, slight variations were observed in the pattern of healthcare use in this group of refugees.

5.2.2.3 Trajectories of antidepressant use

In study III, antidepressant use was constantly low among most refugees (64.9%) and the Swedish-born (59.7%) who attempted suicide. However, this 'low use' was slightly more

prevalent among refugees than among the Swedish-born. Similar marginal differences in the prevalence of other psychotropic drug use were observed between refugees and the Swedish-born during the year before suicide attempt. Trajectory groups of antidepressants use among refugees with a suicide attempt has never been investigated before this study, which limited comparability of the results from study III with previous findings. In 2009, the prevalence of antidepressant use in a national cohort of immigrants from major refugee-generating countries to Sweden was significantly lower than among the Swedish-born (3.8% vs 7.3%, respectively) (194). Among youth aged 16-25 years with common mental disorders, significant differences between refugees and their Swedish-born peers were identified regarding initiation (277) and persistence (278) of antidepressant medications. Results concerning the strength of the association between antidepressant medication among refugees could be partly due to the differences in the populations under study, i.e. differences between the general population and specific diagnostic groups. Moreover, other explanatory factors could be the differences in the baseline factors related to socio-demographics and morbidity in the study populations.

A somewhat lower proportion of refugees (5.9%) belonged to the 'Low increasing' trajectory group than their Swedish-born peers (10.8%). Moreover, antidepressants use in this group following the index attempt rose more sharply among refugees than among the Swedish-born. A potential explanation for this sharper increase in antidepressant use among refugees compared to the Swedish-born could be differences in the severity of the method of suicide attempt, i.e. use of more severe methods among refugees leading to comparatively higher need of treatment following the index attempt. Differences in reattempts between the groups during the follow-up could also be a potential reason. However, some findings from study II and III contradict such explanations. Refugees more frequently used self-poisoning than the Swedish-born in both studies. An additional investigation in study II revealed that the mean number of hospitalisations for reattempts during the follow-up after the index attempt was nearly half among refugees than among their Swedish-born counterparts (data not shown). This result was comparable with findings reported by Niederkrotenthaler and colleagues (2020), who showed that the risk of reattempt among refugees with a suicide attempt was lower (HR: 0.74, 95% CIs: 0.67-0.81) than that among the Swedish-born who attempted suicide (279). A more likely explanation could be that some refugees may have lacked adequate treatment before the index attempt. This discrepancy was probably compensated with appropriate dosage with antidepressants following the index attempt.

In terms of proportions, refugees were slightly underrepresented than the Swedish-born in the 'Low constant' and 'Low increasing' trajectory groups. These results from study III correspond to findings from study II regarding somewhat lower specialised psychiatric healthcare use among refugees. Moreover, other studies also found such disparity between refugees and the host population concerning psychiatric healthcare use (208) and medication use (277, 278). Apart from the barriers to access healthcare discussed in section 5.2.2.1, several other factors related to medication use may have contributed to these disparities among refugees. Socio-cultural preferences may lead to refugees discontinuing medications

more than the Swedish-born due to adverse effects. Moreover, refugees might wish to have alternative therapies such as herbal remedies etc. instead of pharmacotherapy (280).

Even after considering so many deterrents for refugees to access healthcare, the differences in antidepressant use among the trajectory groups in refugees vs the Swedish-born were minimal. The healthcare system in Sweden may probably have succeeded, to some extent, in reducing the disparities in treatment for refugees, especially among those who attempted suicide. However, it can also be that only those refugees with higher medical severity sought help for a suicide attempt due to the barriers to access healthcare. As data on the severity of the mental disorder or the index attempt was not available, this assumption could not be tested. In future studies, data on these clinical factors are required to test such associations. Finally, duration of residence may underlie another potential explanation for these findings of apparent comparability than a discrepancy in the patterns and compositions of the trajectory groups among refugees and their Swedish-born peers. In study III, the majority of the refugees with a suicide attempt were long-term residents in Sweden (>5 years). The longer refugees live in the host country, the easier it may get for them to overcome some of the barriers to access healthcare. Brendler-Lindqvist et al. reported a positive association between longer duration of residence and healthcare use in terms of dispensed psychotropic drug use among refugees (194).

Among the clinical factors, any use of psychotropic drugs at the baseline year, particularly anxiolytic or sedative/hypnotic drugs had the most influence in explaining the variability among the trajectory groups in both refugees and their Swedish-born counterparts. This may suggest higher severity of any underlying mental disorder. The Nagelkerke pseudo R^2 value for the use of sedatives/hypnotics was also higher for refugees compared with the Swedish-born. Regarding this covariate, the identified trajectory groups among refugees were somewhat more skewed than those among the Swedish-born, primarily concerning the differences between the 'Low increasing' trajectory group in refugees vs the Swedish-born. The 'Low increasing' trajectory group also had the largest differences in the changes in DDD levels across time during the follow-up period, suggesting discrepancies regarding the medical severity of the underlying disorder between refugees and the Swedish-born.

5.3 METHODOLOGICAL CONSIDERATIONS

In all four studies of this thesis, data was obtained from high-quality registers (227, 246, 248, 250, 281, 282) with nationwide coverage in Sweden and Norway. Moreover, population-based studies in this thesis allowed the investigation of associations between relatively rare outcome measures (suicidal behaviour) in a minority group like refugees. Furthermore, we could test several hypotheses that required multiple stratified analyses; without nationwide coverage and long follow-up periods, it would have been impossible to make such inquiries. An additional strength of the studies was the availability of data on a broad range of covariates regarding socio-demographics, LMM and morbidity/healthcare use. Apart from these strengths, the results should be interpreted considering some limitations. In the following sections, key sources of error in epidemiological studies and how they may have affected the validity of the findings of this thesis are discussed.

Random error refers to inconsistent variations in the data that may have happened out of chance (283). Such error usually occurs when conclusions drawn from a sample do not reflect the actual scenario of the population from which the sample was drawn. Because all four studies of this thesis were population-based, random errors could be reduced in the best possible way.

Contrary to random error, systematic bias does not depend on sampling errors but results from incorrect estimation of the association between the exposure and the outcome variables (284). Such bias may be introduced when identifying and selecting subjects in the study, collecting and analysing data, or classifying the exposure or outcome variables. There are two major forms of systematic bias: selection bias and information bias (284).

Selection bias may occur when the probability of selection and/or being in the study following selection (subject-selection and loss to follow-up, respectively) leads to a biased result due to error (284). Inclusion of the entire study population from administrative registers minimised such bias in the studies of this thesis. Even then, some selection bias is likely in study II and III as the study population of individuals with a suicide attempt were selected from specialised healthcare. In Sweden, hospitalisations seem to cover only about half of the suicide attempts (285). Also, refugees are likely to be underrepresented compared with Swedish-born when suicide attempt is measured from specialised healthcare because of higher levels of stigma towards suicidal behaviour (126). Thus, the exposed group and the comparison group may have been selected differentially in these studies. Therefore, individuals with events of undetermined intent (ICD-10 codes: Y10-Y34) were included to minimise bias from this source.

Information bias results from errors in exposure or outcome measurement leading to exposure or outcome misclassification (284). If exposure misclassification differs between those who had the outcome versus those who did not, it is called differential misclassification and otherwise, non-differential (284). Similarly, outcome misclassification can be differential or non-differential based on its relationship with the exposure status. As register data was used

in this thesis, it is unlikely to have recall bias or interviewer/recorder bias leading to misclassification of the exposure or the outcome. The exposed group in this thesis comprised not only convention refugees but also individuals who were granted residence due to 'in need of protection' or on 'humanitarian grounds'. Refugees in the 'humanitarian grounds' category were reported to have higher psychiatric morbidity (218) and may, therefore, have a differential risk of the outcome measures in this thesis. To check if any bias was introduced from this source, several sensitivity analyses were conducted. These analyses did not show any reason for concern regarding exposure misclassification.

Some differential misclassification of the outcome leading to overestimation of the risk estimates may have occurred in study I. In that study, hospitalisation for suicide attempt was the outcome of interest, and due to higher levels of stigma associated with suicidal behaviour (126), refugees were more likely to underreport than the Swedish-born. Including events of undetermined intent may have reduced such information bias to some extent. In study III, some underestimation of the outcome, prescribed antidepressant use, was likely because the registered data cannot consider secondary non-adherence. Moreover, the prescribed drug register does not contain information on antidepressant use during an episode of hospitalisation or unregistered purchases, e.g., from the internet. Additionally, the indications for antidepressant use can be different than affective and anxiety disorders, e.g. chronic pain. In study IV, outcome misclassification could have occurred because ascertaining suicide cases may have significant temporal and spatial variations. Nonetheless, in both host countries (Sweden and Norway), somewhat similar measures are taken following a suspected death by suicide (92, 248, 250). According to the findings from Tøllefsen et al. (2015), the use of 'undetermined intent' as a cause of death varies considerably between the Swedish and the Norwegian cause of death registers (92). Therefore, to reduce the extent of misclassification bias, deaths with undetermined intent were not included in this study.

Moreover, the lower suicide mortality among refugees in study I and IV could be biased if the risk of death by non-suicidal causes is higher among refugees than in the host population. However, such bias can be deemed unlikely for two reasons. First, an investigation into the risk of all-cause and cause-specific mortality due to somatic and psychiatric disorders among refugees in Sweden revealed that refugees had a consistent mortality advantage over the Swedish-born population for all investigated categories (78). Second, Hollander et al. (2020) tested and rejected this competing risk theory regarding suicide mortality among refugees in Sweden (255). In their study, the risk estimates (aHR) for death by suicide among refugees compared with the Swedish-born were similar to what was found in study I of this thesis.

Confounding distorts the association between two factors (exposure and outcome) when the study groups are imbalanced regarding other factors (confounders) which are associated with the outcome and do not fall in the causal pathway from the exposure to the outcome (284). Contrary to selection or information bias, confounding can be controlled for in the analysis phase if the information on the potential confounding factors is available. On the other hand, residual confounding may arise if potential confounders are not adjusted for in the analysis or

are adjusted for but not measured correctly. In this regard, residual confounding may have affected the results in study I. In that study, morbidity factors were measured from specialised healthcare, and refugees are likely to be underrepresented there compared with the Swedish-born. Sundvall et al. (2015) reported lower access to specialised healthcare for refugees (210). Later, in study II of this thesis, similar findings were observed. However, the difference in healthcare use between refugees and the Swedish-born was not extreme. To account for missingness regarding educational level, a separate category for individuals with missing data was introduced in all adjusted analyses. Another source of residual confounding could be unmeasured confounders in study I, e.g., alcohol consumption. Because data was lacking for this variable, it was not adjusted for in the analysis. Nevertheless, the magnitude of bias from this source was investigated using a quantitative bias analysis method proposed by Lash and colleagues (2009) (286). Using secondary data regarding the prevalence of alcohol use disorder among refugees and Swedish-born (287) and the strength of the association between alcohol use disorder and suicidal behaviour (288), the bias analysis showed similar results to the main analysis in study I. In the comparative study between Sweden and Norway (study IV), differences in measurement practices in the host countries may have introduced residual confounding for the measured covariates. For example, social insurance regulations are not the same in Sweden and Norway (192, 193) and, therefore, the LMM factors in the registers could have been differentially measured. Still, any substantial bias from this source is not expected because, in both host countries, these factors only influenced the ORs to a minor extent.

One may determine good internal validity if the findings of a study were not or minimally affected by any of three main sources of error, i.e. random error, systematic bias, and confounding. In this regard, all four studies in this thesis can be considered to have good internal validity. However, internal validity does not confirm generalisability (external validity), which denotes whether the study results can be generalised to other circumstances. The findings of this thesis are only generalisable to refugees who have resettled in a host country with a similar immigration policy, healthcare, and welfare system as that in Sweden or Norway. Moreover, the results are not generalisable to refugees who have not resettled yet, e.g., asylum-seekers, refugees staying in camps or even refugees resettled in LMIC. In these settings, the risk of suicidal behaviour and healthcare use for refugees could be significantly different than the resettled refugees in Sweden or Norway. In study II, data on healthcare use was not available from primary healthcare, limiting the results' generalisability to only severe forms of morbidity.

6 CONCLUSIONS

- This thesis revealed that the risk of hospitalisation for suicide attempt and death by suicide was lower among resettled refugees in Sweden than their Swedish-born peers, even though previous studies found a higher burden of mental ill-health among refugee populations. These associations were similarly lower among refugee groups from specific country of birth except for refugees from Iran who had higher risk for suicide attempt than the Swedish-born, and for refugees from Eritrea with similar risk for death by suicide as that among the Swedish-born.

- Across three time period cohorts in study I, the lower suicide mortality among refugees did not vary much. On the other hand, a minor change across time period regarding the risk of hospitalisation for suicide attempt was observed.

- Resettled refugees in Sweden and Norway had comparative advantage regarding suicide mortality with regard to the respective host populations. These findings were relatively consistent when the analyses were stratified by refugees' region/country of birth, i.e. refugees from the same country of birth migrating to different host countries had an almost similar risk of suicide.

- Duration of residence and sex did not modify the risk of suicide among refugees in study IV. Some modifying role of age was observed: refugee youth aged 18-24 years had a similar relative risk for suicide mortality than their same-aged Swedish-born or Norwegian-born peers.

- In both study I and IV, several socio-demographic, LMM and morbidity factors did not explain a major part of the lower suicide mortality among refugees in Sweden and Norway; nor did these covariates have any major influence on the risk of hospitalisation for suicide attempt among refugees in Sweden in study I.

- Regarding specialised healthcare use for psychiatric diagnoses three years before and after a suicide attempt, this thesis revealed a slight disparity between refugees and the host population in Sweden. While prevalence rates for such healthcare use were somewhat lower among refugees who attempted suicide, the mean number of visits to specialised healthcare settings and mean duration of hospitalisations for psychiatric disorders did not show major differences between refugees and the Swedish-born.

- Differences between refugees and the Swedish-born concerning specialised healthcare use for somatic diagnoses three years before and after a suicide attempt showed mixed findings. While prevalence rates, mean numbers and durations of hospitalisations for somatic diagnoses were generally slightly lower among refugees than among the Swedish-born, specialised outpatient healthcare following a suicide attempt was rather similar between these groups.

- Among refugees who attempted suicide in study II, specialised healthcare use did not differ according to their age, sex or educational level but differed by receipt of disability pension (DP) at baseline, i.e. DP recipients had higher specialised healthcare use than non-recipients.

- In study III, differences in antidepressant use three years before and after a suicide attempt were marginal between refugees and the Swedish-born: the patterns and compositions of the identified trajectory groups of antidepressant use were comparable between these groups.

7 FUTURE RESEARCH

The findings generated by the studies in this thesis regarding suicidal behaviour and healthcare use among refugees can be considered the forerunners in this research field. There were very few comparable studies, and for some of the results, there were none for direct comparison. Therefore, it is essential to test the replicability of these findings. When designing such studies, several factors are important to consider:

Even after including the entire population in Sweden and Norway as the study population and with observation periods of nine and 21 years in study I and IV, respectively, some stratified analyses lacked statistical power in this thesis due to the comparative rarity of suicidal behaviour as an outcome and refugees being a minority population. Therefore, conclusive remarks could not be made regarding some variations in the results, i.e. a higher risk of suicide attempt and suicide among refugees from Iran and Eritrea, respectively. Longer follow-up periods in a specific host country or aggregated data from several host countries may help overcome such issues.

The rates of suicidal behaviour among refugees in Sweden found in study I could vary considerably in comparison with the rates in the refugees' country of birth. However, the lack of quality studies in refugees' origin countries limits the possibility to make valid comparisons. One key obstacle is that accurate registration systems for fatal and non-fatal suicidal behaviour are almost non-existent in many countries from which refugees migrate. Countries with adequate resources and experience of functioning registration systems should, therefore, help develop such effective systems in countries where they are lacking. This will allow the possibility to conduct comparative studies in the future, and the results can contribute to devising targeted suicide prevention strategies in those countries.

The generalisability of the results of this thesis is limited to mainly resettled refugees in countries with a similar economy, migration policy and welfare systems as in Sweden and Norway. Therefore, future studies should also cover the periods before resettlement, i.e. during the stay in refugee camps and the asylum-seeking period. Moreover, a vast majority of refugees migrate to neighbouring LMIC. It is paramount to have more evidence regarding the suicidal behaviour among refugees living in different conditions than the study population in this thesis.

Although register data in this thesis enabled us to account for several socio-demographic, LMM and morbidity factors, some important information was missing in the administrative registers. Future research should combine other data sources on measurements of resilience and attitudes towards suicidal behaviour, religiousness, social connectedness, and alcohol consumption to better understand the suicidal process among refugees.

In study II, data was collected from inpatient and specialised outpatient healthcare, which restricts the generalisability to healthcare use due to comparatively more severe psychiatric or somatic morbidities. In future studies, it will be interesting to compare the primary healthcare use between refugees and the host population. It is also vital to identify which specific factors hinder access to healthcare for refugees who attempted suicide and how preventable measures may improve their healthcare use.

In study III, around 40% of the variance across the identified trajectory groups among refugees and Swedish-born was explained by the factors related to socio-demographics, LMM and clinical characteristics. These results may hint towards other unmeasured factors such as the severity of the underlying mental disorder etc., that are probable determinants of the trajectory groups of antidepressant use for refugees and the Swedish-born. Information on the severity of the mental disorder or suicide attempt will also help to elucidate if refugees seeking specialised healthcare are a selected group because the known barriers to healthcare access may have differentially affected healthcare-seeking according to the severity of illness. Future studies should include data on such factors.

For international comparison of suicide mortality among refugee groups, further investigations should adopt study designs that allow calculating person-time to estimate absolute rates. This way, more robust conclusions regarding the differences in suicide mortality among refugees can be drawn through such cross-national comparisons.

In response to the unusually high number of asylum applications during 2014-2015, Sweden has adopted highly restrictive policies regarding asylum and family reunification in 2016, which was a rather dramatic shift from its historically generous asylum regulations. In future research, it will be imperative to analyse how such drastic policy changes may affect mental health and suicidal behaviour among refugees and asylum-seeking populations.

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