UMEÅ UNIVERSITY

REHABILITATION NEEDS AFTER TRANSIENT ISCHEMIC ATTACK

A Perspective of Patient-Reported Outcome Measures

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Dedication / Quote

To my parents

Contents

Abstract

Background: Transient ischemic attack (TIA) has drawn increased interest in the last 20 years concerning sequalae. However, the long-term consequences and rehabilitation needs of TIA remain largely unknown. The overall aims of this thesis were to evaluate long-term disabilities after TIA and their effects on patients' daily activities, social participation, and health-related quality of life (HRQoL).

Methods: This thesis involved two cohorts from two different observational studies. The first cohort included 47 community-dwelling individuals in the sub-acute phase (4 months) after TIA who were included in a prospective cohort study (Study I). The second cohort was from a retrospective cohort study (Studies II–IV) assessing 431 community-dwelling adults' rehabilitation needs, mainly in the chronic phase (1–13 years) after TIA onset.

Patient comorbidities, such as hypertension and atrial fibrillation, were collected from the Riksstroke Registry in Study I and patients' medical records in Studies II–IV. The multidimensional consequences of TIA and rehabilitation needs after TIA were assessed by five well-validated patient-reported outcome measures (PROMS), including the Fatigue Assessment Scale with added sleep-related questions, Hospital Anxiety Depression scale, simplified Modified Rankin Scale, Stroke Impact Scale 3.0 (SIS), and the EQ-5D three-level version (EQ-5D-3L). Statistical analyses were performed using SPSS v.27 and GraphPad Prism 10.

Results: Assessments with PROMS were feasible among community-dwelling persons after a first-ever TIA in an outpatient setting (Study I). At the sub-acute stage, the most common parameter affected was mood (reported by 89% of participants), followed by bladder function (70%), sexual life (52%), strength (51%), and fatigue (26%). Symptoms of depression and anxiety were reported by 6% and 17% of participants, respectively.

In Study II, long-term patient-reported fatigue was evident among 37.8% of the community-dwelling adults from 6 months up to 13 years following a TIA. Among first-ever TIA patients, 35% were fatigued, with higher mean scores than the general age-matched population. Additionally, depression, anxiety, heart disease, and atrial fibrillation were independently associated with increased perceived fatigue in the

same group. This elevated perceived fatigue was significantly associated with fewer activities in everyday life.

In Study III, the most reported perceived disabilities assessed by the SIS belonged to the emotions (80.6 SD 15.5), strength (84.2 SD 24.0), and participation (89.1 SD 18.5) domains up to the 10-year follow-up. No significant differences in SIS domains were observed over time when comparing data between the three groups (i.e. < 1 year post-TIA; 1 - 5 years post-TIA; and 5 – 10 years post-TIA). Perceived disabilities and their correlations with Activities of Daily Living / instrumental Activities of Daily Living ADL/IADL and participation were demonstrated consistently up to 10 years after TIA.

In Study IV, we demonstrated that most first-ever TIA patients were not affected regarding HRQoL (mean 0.88 SD 0.2) as measured by index scores of the EQ-5D-3L. However, the index scores were significantly lower in the TIA with stroke group (0.77 (0.3); $p < 0.001$) compared to the first-ever TIA group. A preserved HRQoL was observed at a similar level from 1 to more than 10 years after the first-ever TIA ($p = 0.643$). The most reported sub-domain problem was pain, followed by depression/anxiety and mobility. Factors associated significantly with poorer HRQoL in this cohort ($p < 0.001$) were persons with recurrent TIA and stroke (odds ratio (95% CI) 0.67 (0.53–0.83)), more depression (0.59 (0.53–0.66)), anxiety (0.73 (0.68–0.79)), and perceived fatigue (0.81 (0.77-0.85)).

Conclusion: Our findings support the screening of long-term consequences of TIA among community-dwelling individuals. Besides secondary prevention measures after TIA, tailored rehabilitation interventions could improve the everyday lives of TIA patients.

Keywords: transient ischemic attack, fatigue, activities of daily living, participation, health-related quality of life, long-term consequence

Sammanfattning på svenska

Övergående ischemisk attack (TIA) är ett tillfälligt stopp av blodflöde till ett kärl i centrala nervsystemet. Neurologiska symtom som då uppstår, till exempel övergående blindhet (Amaurosis Fugax) eller sensomotoriska symtom såsom pares i en arm eller ett ben går enligt definitionen av TIA över inom 24 timmar. Om symtomen kvarstår är det en stroke. Dock kan mindre uppenbara funktionsnedsättningar såsom trötthet (fatigue) eller emotionell påverkan kvarstå.

Intresset för TIA har de senaste 20 åren ökat. Dock är konsekvenserna över tid och rehabiliteringsbehoven efter en TIA fortfarande till stor del okända. De övergripande målen med denna avhandling var att utvärdera funktionsnedsättningar över längre tid efter en TIA, deras effekter på aktiviteter i dagliga livet, vid social medverkan och hälsorelaterad livskvalitet (HRQoL).

Denna avhandling består av två kohorter som har undersökts i fyra studier (Studie I – IV). Den första kohorten var del i en prospektiv (framåtblickande) kohortstudie (Studie I), där 47 personer med eget boende som upplevt en TIA cirka 4 månader tidigare, deltog. Den andra kohorten var del i en retrospektiv (backåtblickande) kohortstudie (Studie II – IV) där 431 vuxna (med eget boende) individers rehabiliteringsbehov utvärderats, framför allt ur ett långvarigt perspektiv (1 – 13 år post-TIA).

Samsjuklighet samlades in från Riksstroke registret i studie I och från patientjournaler i studie II – IV. De multi-dimensionella konsekvenserna och rehabiliteringsbehoven efter en TIA bedömdes genom 5 väl validerade enkäter. Fatigue Assessment Scale med extra frågor för sömn, Hospital Anxiety and Depression scale, simplified Modified Rankin Scale, Stroke Impact Scale 3.0 och EQ-5D-3L. Statistik utfördes med hjälp av SPSS ver. 27 och Graphpad Prism 10.

Resultaten visade att utvärdering med enkäter var genomförbart 4 månader efter en (förstagångs) TIA i Studie I. I det sub-akuta skedet var den vanligaste funktionsnedsättningen negativt påverkat känsloliv (89%), följt av urinblåse-funktion (70%), sexuallivet (52%), styrka (51%) och trötthet (26%). Symtom av depression och ångest rapporterades av 6% respektive 17% av medverkande.

För studie II skattade 37.8% av deltagare med subjektivt rapporterad trötthet, från 6 månader till 13 år efter en TIA. Hos de med förstagångs TIA sågs 35% med trötthet, med ett högre medelvärde i gruppen än i den generella åldersmatchade populationen. Och depression, ångest, hjärtsjukdom och förmaksflimmer var oberoende associerade med ökad trötthet i denna grupp. Denna förhöjt upplevda trötthet var signifikant associerad med mindre aktiviteter i det dagliga livet.

I studie III var de till största delen påverkade domänerna känsloliv (80.6 SD 15.5), styrka (84.2 SD 24.0), och medverkan (89.1 SD 18.5), vid upp till 10 års uppföljning. Inga signifikanta skillnader bland SIS domäner sågs över tid när data jämfördes mellan tre tidsfaser. Subjektivt uppfattade funktionsnedsättningar och deras korrelationer med ADL / iADL och medverkan sågs konsistent upp till 10 år efter en TIA.

I studie IV kunde observeras att de flesta med en förstagångs-TIA inte påverkades vad det gällde HRQoL (medelvärde 0.88 (SD 0.2), mätt via EQ-5D-3L index. Dock var index-poängen signifikant lägre i TIA med stroke subgruppen (0.77 (SD 0.3) $p<0.001$) jämfört med förstagångs-TIA subgruppen. Det gick att se liknande nivåer av HRQoL över 10 års tid efter en förstagångs-TIA ($p = 0.64$. Den vanligaste påverkade sub-domänen var smärta, följt av depression/ångest och rörlighet. Faktorer som var signifikant associerade med sämre HRQoL i denna kohort ($p<0.001$) var personer med återkommande TIA och stroke (odds ratio (95% CI) 0,67 (0.53-0.83), mer depression (0.59 (0.53-0.66), ångest (0.73 (0.68-0.79) och upplevd trötthet (0.81 (0.77-0.85).

Följande slutsatser dras: TIA patienter föreslås genomgå screening för dolda symtom såsom till exempel trötthet och emotionella besvär. Utöver sekundärprevention efter TIA så skulle patient-anpassad rehabilitering kunna förbättra det dagliga livet för denna patient-grupp.

Nyckelord: TIA, fatigue, dagliga aktiviteter, delaktighet, hälsorelaterad livskvalitet, kroniska konsekvenser

Abbreviations

ADL / iADL	Activities of Daily Living / instrumental Activities of Daily Living
BMI	Body Mass Index
CHF	Chronic heart failure
CI	Confidence Interval
CNS	Central nervous system
ECG	Electrocardiogram (i.e. EKG in Swedish)
EQ-5D-3L	European Quality of Life 5 Dimensions 3 Level Version
FAS	Fatigue Assessment Scale
GAD-7	Generalized Anxiety Disorder 7-item scale
HADS	Hospital Anxiety and Depression Scale
HRQoL	Health-related quality of life
ICD	International Classification of Diseases, by the World Health Organization
ICF	International Classification of Functioning, Disability and Health, by the World Health Organization
IQR	Interquartile range
LUTS	Lower urinary tract symptoms
MRI DWI	Diffusion-weighted magnetic resonance imaging
mRSq	simple modified Rankin Scale questionnaire
OR	Odds-ratio
PSF	Post-stroke fatigue

PROMs	Patient-reported outcome measures
SD	Standard deviation
SIS	Stroke Impact Scale version 3.0
TIA	Transient ischemic attack
WHO	World Health Organization

Original studies

I. **Gustaf Magaard**, Britt-Marie Stålnacke, Ann Sörlin, Fredrik Öhberg, Stina Berggren, Emma Grollmuss & Xiaolei Hu*. Identifying Rehabilitation Needs Among Individuals after Transient Ischemic Attack with a Rehab-Compass as a Simple Screening Tool in the Outpatient Clinic, **Journal of Rehabilitation Medicine - Clinical Communications**, 2019 Oct 14;2:1000018. doi: 10.2340/20030711-1000018

II. **Gustaf Magaard**, Fredrik Öhberg, Britt-Marie Stålnacke, Ann Sörlin, Per Liv & Xiaolei Hu. Long-term perceived fatigue after transient ischaemic attack. Manuscript re-submitted to **Frontiers of Neurology** after revision.

III. Jenni Andersson, Britt-Marie Stålnacke, Ann Sörlin, **Gustaf Magaard** & Xiaolei Hu. Long-Term Perceived Disabilities up to 10 Years after Transient Ischaemic Attack, **Journal of Rehabilitation Medicine**, 2021 53(3):jrm00167. Epub 20210322. doi: 10.2340/16501977-2808.

IV. **Gustaf Magaard**, Fredrik Öhberg, Ann Sörlin, Britt-Marie Stålnacke, Fredrik Norström & Xiaolei Hu. Lack of observed effect on health-related quality of life after transient ischemic attack. Manuscript under preparation.

My contributions

Study I: Gustaf Magaard (GM) was actively involved in several steps, including participant recruitment. GM was responsible for collecting data, all statistical analysis under supervision, and manuscript writing and was involved in revisions. GM is the first author.

Study II: GM was actively involved in all study stages, including design, planning, participant recruitment, data collection, analysis, manuscript preparation and submission, and correspondence with the journal. GM is the first author.

Study III: GM was actively involved in several stages, including design, planning, participant recruitment, and data collection. He also participated in analysis and manuscript preparation and revision. GM is a co-author.

Study IV: GM was actively involved in all stages, including design, planning, participant recruitment, data collection, analysis, manuscript preparation and submission, and correspondence with the journal. GM is the first author.

Introduction

Author's Preface

As a child, asking "why" rather than only trying to memorize information came naturally to me. Early on during my studies to become a physician, I tried to get involved in research and finally achieved this goal. I applied to conduct my research project in Term 10 of the medical program without high hopes that I would get my first choice, but I did. I wanted to learn more about neurological diseases and their consequences, and not only was my work that term published but I was also accepted for a PhD project in this research area. My aim in life was always to help people, and I could see the highest potential to do so in the field of rehabilitation. I put my love into my work, as it matters to me only if it is also meaningful to others. Hopefully, this is reflected in the present thesis, and the reader can gain from it.

Transient Ischemic Attack (TIA)

Definition

TIA was defined by the World Health Organization (WHO) (1) as "a sudden, focal neurological deficit of presumed vascular origin that resolves within 24 hours." A blood vessel supplying blood to the central nervous system (CNS; the brain or spinal cord) would be temporarily blocked or have impaired blood flow. Neurological symptoms would then follow, such as blindness in an eye (i.e., amaurosis fugax), paresis of a limb, sensory changes or speech impairments (i.e., aphasia), and other focal neurological symptoms, all depending on the location of the affected tissue in the brain. According to the definition of TIA, all symptoms resolve within 24 hours. As radiology advanced, a tissue-based definition of TIA was developed (i.e., a lesion on diffusion-weighted magnetic resonance imaging [MRI DWI] indicates stroke) (2). In Sweden, the time-based definition is still used since MRI DWI is not commonly applied in the acute phase, even though up to 50% of TIA patients have lesions on MRI DWI in the acute phase (3). A limitation of using the time-based definition and not the tissue-based one is that minor strokes could still occur in the TIA population. There are currently no routinely used blood biomarkers for TIA (4).

Relation to stroke

Stroke is a potentially deadly illness, with 14% of stroke patients dying within 28 days after a first-time stroke in Sweden in 2022 (5). The event involves hemorrhage or infarct in the CNS, with sequelae lasting more than 24 hours. The International Classification of Diseases version 11 (ICD-11) definition includes patients with symptoms for less than 24 hours and evidence of stroke on neuroimaging (6). Of stroke patients, 7 – 40 % experienced a TIA before their stroke (7). Differing from a TIA defined as a National Institute of Health Stroke Scale (NIHSS) score of 0, a minor stroke is generally considered for an NIHSS score of three or less (8).

The risk of stroke increases five-fold after a TIA (9), with the highest risk in the first 48 hours (half of incident strokes), declining with time. Every year, 20% of stroke patients re-experience a stroke. Since TIA and stroke share the same risk factors, screening for risk factors after TIA has been widely implemented as a clinical routine, including ECG findings (telemetry), hypertension control, and blood sugar and lipid control. Secondary stroke prevention strategies, such as platelet inhibitor use and interventions to minimize the mentioned risk factors are then applied, which can lower the risk of stroke by up to 80% (10). Moreover, evidence of a reduction in stroke risk following TIA is emerging.

Epidemiology

The worldwide incidence of TIA is 1.19/1000 person-years (11). In Sweden, the incidence is 1/1000 person-years (5), although that number could be higher, as it is estimated that only about 50% of people who experience a TIA search medical attention within 24 hours (12). For stroke, the numbers are about twice as high in Sweden as official TIA numbers, that is, 21,000 patients per year (5).

Consequences

In the acute phase after TIA, patients often subjectively experience deep-seated anxiety about future uncertainties/disruption to normality, loss of confidence, frustration, TIA as a wake-up call, a sense of loss and sadness, and embarrassment (13).

Since symptoms seemed to completely resolve within 24 hours, no further rehabilitation was considered necessary. However, as clinicians met TIA patients, they noticed that this was not always the case. Growing evidence has shown that sequelae could occur post-TIA. Stroke-like

symptoms could be found but were much attenuated and “hidden.” Such “hidden” symptoms were usually emotional or cognitive or involved unexplained fatigue (14 - 17). However, long-term impairment is seldom studied, and no rehabilitation is commonly initiated after TIA.

Fatigue

Fatigue comes from the Latin word “fatigare,” meaning “to tire out” (18) and is commonly used in many different areas. In this thesis, the medical definition of fatigue is used, that is, a “…lack of energy, and increased need to rest…affecting everyday life…” (19), as measured subjectively by the Fatigue Assessment Scale (FAS). Fatigue occurs in the normal population with a rough prevalence of 15–22% (20). The FAS was chosen since it is quick and easy to finish and is recommended for patients with stroke (21) (among many other illnesses). Other Patient Reported Outcome Measures (PROMs) explore more dimensions of fatigue, taking into consideration situational or environmental factors, and are therefore more extensive and harder to finish. They are usually not assigned the highest recommendation for stroke patients.

Fatigue after a stroke (post-stroke fatigue [PSF]) is extensively studied. The cause of this sequala is not known, but the etiology is thought to be multi-factorial (22). In stroke patients, the prevalence of fatigue could be as high as 92% (23), but 50 % is commonly estimated (24). Among TIA patients, the risk to consult for fatigue was estimated to 43% compared with controls (25) and the prevalence ranges between 20 and 40 % depending on measurement and cohort (26). However, most studies have only evaluated acute or sub-acute phases. The long-term consequences of post-TIA-fatigue remain largely unknown, along with the prevalence of fatigue over time.

Rehabilitation Medicine

Rehabilitation medicine has been a medical specialty since 1969, focused on patients with conditions that are chronic and complex. Rehabilitation was defined as “a set of interventions designed to optimize functioning and reduce disability in individuals with health conditions in interaction with their environment” by the WHO (27). The International

Classification of Functioning, Disability and Health (ICF) is the common framework used in this field, and multidisciplinary teamwork with goal-oriented interventions is standard.

The activity-driven neuro-remodeling process (neuroplasticity) (28) is one of the most important theoretical bases for rehabilitation medicine. It involves the ability of the CNS to re-organize and change its structures and functions after disease or injury. For example, the most intense neuroplastic activity occurs within 3–4 months post-stroke. During this time, evidence-based interventions are commonly used to help the patient make the most of this temporary advantage. Nevertheless, the rehabilitation therapeutic window never closes since neuroplasticity remains even among older individuals. A chronic phase of activity carries on, although at a slower rate.

International Classification of Functioning, Disability and Health

The ICF classification was created by the WHO as a theoretical foundation in rehabilitation. It aimed to provide an objective, holistic view of a patient's health without considering etiologies. This made it possible to share a patient's health status more easily between different health events. Moreover, there is no judgment of the reason for the patient's disease. The ICF consists of different inter-related domains (Figure 1). ICF is much like a spider web since if one domain is affected, the effects are noticed in the other domains. It can also be used with ICD to include etiologies.

We have applied the ICF framework in this thesis. In Study I (29), all the major ICF domains were covered by PROMs. An illness like TIA that impairs body structure or function could limit activity or participation and affect the patient's Health-Related Quality of Life (HRQoL). As shown in Figure 2, we studied fatigue in Study II (30) , which is one of many impairments of bodily function and structure. In Study III (31), my co-workers and I studied activities and participation among TIA patients. In Study IV (32), HRQoL was evaluated among participants after TIA.

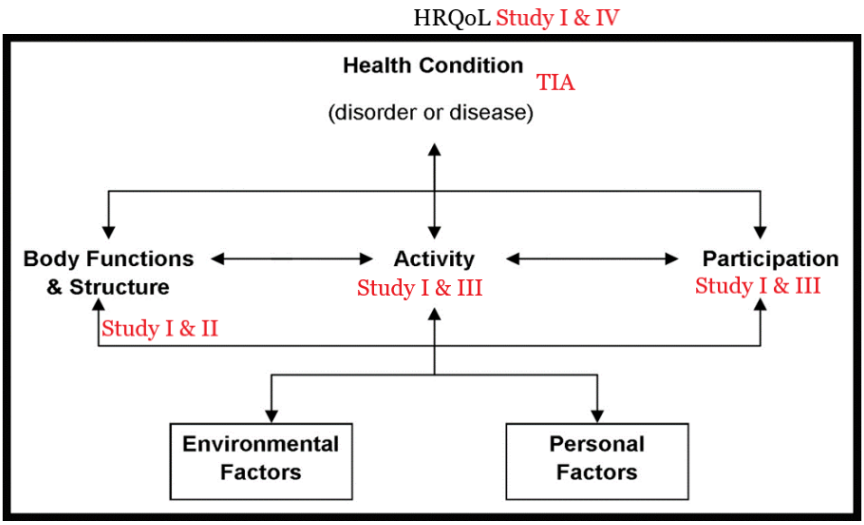

Figure 1. ICF model with associated studies

Patient-Reported Outcome Measures

PROMs collect health information from patients directly and are thus patient-centered. They are usually quick to fill out and can supply important information from the patient. This could enhance the communication between the patient and caretaker. PROMs could also facilitate understanding and improve healthcare. The subjective nature of these tools could be considered both a strength and a weakness. Since they can provide a lot of information directly from the patient, they are well-suited for research. On the other hand, variables could be under- or overestimated by non-professionals more easily. In this thesis, several well-validated PROMs were used to cover the different domains of the ICF (Table 1).

Table 1. PROMs covering different domains of the ICF within the studies.

ICF	PROMs	Studies
Body function/structure	FAS/HADS/SIS/sleep disturbance	I & II

ICF	PROMs	Studies
Activities	SIS 1–7/mRSq	I & III
Participation	SIS domain 8	I & III
Quality of life	EQ-5D-3L	I & IV

SIS – Stroke Impace Scale; FAS – Fatigue Assessment Scale; HADS – Hospital Anxiety and Depression scale; EQ-5D-3L – European Quality of Life 5 Dimensions 3 Level Version; mRSq – simple modified Rankin Scale questionnaire

Rehab-Compass

This measure with a group of PROMs questionnaires with graphic illustrations has also been called "Rehab-Compass" (33). The PROMs used can differ depending on the patient group studied. In this thesis, we used a group of the same PROMs that were applied among stroke patients, such as the FAS, Hospital Anxiety and Depression Scale (HADS), Generalized Anxiety Disorder 7-item scale (GAD-7), simple modified Rankin Scale questionnaire (mRSq), Stroke impact scale 3.0 (SIS) and European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3L). Instead of utilizing the Rehabkompassen graphic illustrations, we focused on various impairments, daily activity, participation, and HRQoL in this thesis.

Gaps/Problems to Solve

The rationale for this thesis builds on the need for a deeper understanding of the long-term consequences of TIA and their effects on activities of daily living (ADL), participation, and HRQoL. While numerous studies have mapped disabilities in TIA patients, a significant knowledge gap persists in long-term consequences and their effects on daily activities and HRQoL.

In this context, individuals with TIA comprise a forgotten group concerning rehabilitation needs. For example, secondary stroke prevention for TIA patients is mentioned in the guidelines of the Swedish National Board of Health and Welfare (from 2020) (34), but no rehabilitation guidelines exist. Globally, the European Stroke Organisation (35) did not mention rehabilitation for TIA patients in 2021. The American Stroke Association (ASA), using the tissue-based definition where DWI MRI is mandatory (around 40% of TIA patients have a lesion seen on this modality), did not recommend rehabilitation in 2024 for TIA patients either. Large journals (e.g., Lancet or Stroke) published few or no rehabilitation strategies for TIA patients, although "hidden symptoms," such as cognitive impairment, depression, fatigue, and sleep problems, were recognized in some studies (36 - 40).

Furthermore, little is known about which factors influence long-term impairments after TIA. Such factors would be of interest for targeted interventions to improve outcomes among persons after TIA.

Aims

The overall aim of the thesis was to identify multidimensional rehabilitation needs, including impairments, limitations in daily activities, restrictions in social participation, and the quality of life after TIA, and to facilitate the rehabilitation of TIA patients.

Study I: To evaluate whether PROMs could identify comprehensive rehabilitation needs among individuals in the sub-acute stage after the onset of first-ever TIA.

Study II: To investigate the extent of perceived fatigue among patients after a TIA and evaluate the potential risk factors and consequences of such an impairment.

Study III: to assess the long-term perceived impact of a first-ever TIA and explore the influence of sex and age on these perceptions, as well as to evaluate the relationships of ADL, participation, and overall recovery with the other domains of the Stroke Impact Scale 3.0 (SIS).

Study IV: To investigate HRQoL using the EQ-5D-3L in TIA patients, as well as factors that could influence it.

Materials and Methods

Study Design and Data Collection

This thesis builds on two different cohorts. The first cohort was from an observational prospective cohort study in an outpatient clinic setting at the University Hospital of Umeå (Study I). In Study I, participants were followed at the sub-acute phase (approximately 4 months) after TIA onset during 1 July 2016–1 July 2017 (29). This study indicated that persons after TIA had several impairments in functioning, which led to the assessment of our second cohort.

The second cohort was assessed in a retrospective cohort study (Studies II–IV). The participants were community-dwelling adults admitted to the Stroke Center at the University Hospital of Umeå (31) with a TIA diagnosis between January 2005 and June 2018. Physicians determined TIA diagnoses according to the time-based definition of TIA. Data were collected during the autumn of 2018, which means participants were mainly in the chronic phase (1 to 13 years) after TIA onset.

Study Population

In Study I, 210 first-ever TIA patients, in the sub-acute phase (~4 months after the TIA event) were assessed for inclusion. Of these, 33% returned the questionnaires (69 patients), and 47 patients (22%) met the inclusion and exclusion criteria (29).

In Studies II–IV, a total of 431 persons (23%), mainly in the long-term phase after TIA (i.e., more than 1 year post the event) were included in the cohort after 1894 patients with TIA were assessed, with a response rate of 25%. The cohort was then divided into three subgroups: individuals with a first-ever TIA (n = 299, Studies II–IV), individuals with recurrent TIA (n = 54, Studies II and IV), and individuals with a TIA and stroke (n = 78, Studies II and IV). Since four values were missing on the EQ-5D, a total of 427 participants were included in Study IV (Figure 2).

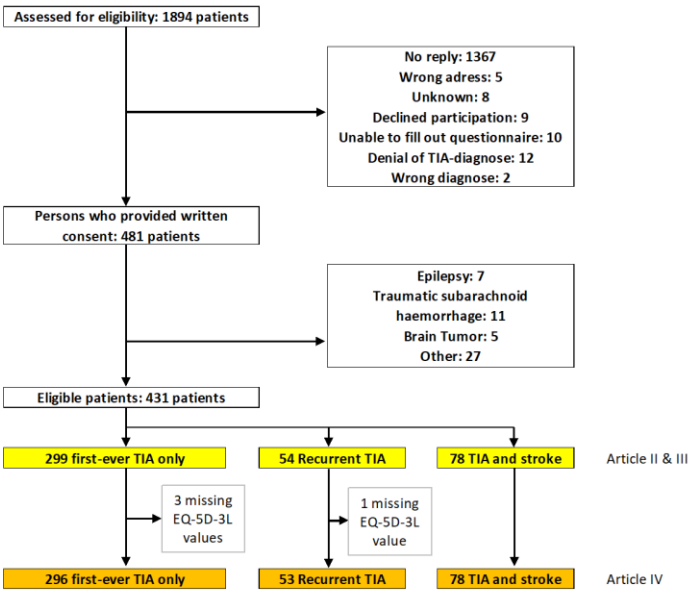

Figure 2. Flowchart of the inclusion/exclusion process for Studies II– IV

Variables

Clinical characteristics

Demographic data, such as age and sex, were assessed by patient personal number. Years after TIA were determined by journal entry. Comorbidities, such as atrial fibrillation, hypertension, hyperlipidemia, heart disease, diabetes, and smoking, were recorded from the Riksstroke registry in Study I. For Studies II–IV, comorbidities were screened in journals as well, since hyperlipidemia and heart disease were missing in Riksstroke and smoking was missing in the journals (Table 3).

Outcomes

To comprehensively evaluate unmet rehabilitation needs after TIA, a group of well-validated PROM questionnaires was used, with graphic illustrations, namely Rehab-Compass, as a novel follow-up instrument for persons with stroke (33). To cover diverse deficits in functioning, daily activity, participation, and quality of life according to the concept of ICF, five validated and reliable PROMS were included: the Hospital Anxiety and Depression Scale (HADS); the Fatigue Assessment Scale (FAS); the modified Rankin Scale questionnaire (mRSq); the SIS with

additional questions related to sensory disturbances, sleep disturbances, and natural topics; and the EQ-5D. The questionnaires used to cover various ICF domains in this thesis are described previously in Table 1.

Symptoms of **depression and anxiety** (Studies I and II) were assessed with the HADS (41, 42). The HADS is a 14-item questionnaire, taking 2–5 minutes to complete and recording depression and anxiety during "the past week." A four-point Likert scale (0–3) is utilized for answers. Scores range from 0–21 for depression and 0–21 for anxiety. It seems to perform well for both women and men across ages (43 - 45), as well as in non-psychiatric hospital clinic settings. It demonstrates a robust internal consistency (41). Scores of 8–10 suggest the presence of the state investigated (i.e., the presence of symptoms of depression or anxiety) and higher values indicate the probable presence thereof.

Fatigue (Studies I and II) was assessed by the FAS (46), recommended recently for use in stroke cohorts by the National Institute for Health and Care Excellence (NICE) (47). It has been widely used in interventional post-stroke fatigue research studies (48) and is available in at least 15 different languages. The FAS is a 10-item questionnaire with five questions on physical fatigue and five on mental fatigue that are answered using a five-item Likert scale (49) ranging from "Never" to "Always." The developers mixed the physical and mental fatigue questions, and two questions were reverse-scored to maintain their validity. The total FAS score ranges from 10 to 50. It has been used and validated for many diseases, including stroke and TIA, and is considered unidimensional. The Swedish version of the FAS demonstrated high and good internal consistency and convergent validity with a limited number of questions, thus minimizing its completion time (50). Floor or ceiling effects or sex bias were not apparent. Two FAS score cutoffs have previously been reported (22 and 24 points) to define fatigue; a cutoff of 24 points was chosen for this study (51).

Disability (Studies I and III, Figure 1) was evaluated with the mRSq, a standardized, pragmatic, validated and reliable tool (52). Five questions are answered with "Yes" or "No" by the individual. A scale ranging from 0 (no symptoms) to 5 (total physical dependence) is rated using the mRSq flowchart; mRSq scores ≤ 2 are considered to represent total independence (53).

Various activity-related limitations (Studies I and III) in stroke survivors were assessed by the SIS. The SIS consists of eight domains with 59 questions (54, 55). The domains include strength, memory and thinking, emotions, communication, mobility, hand function, ADL/instrumental ADL (IADL), and social participation. Four additional domains were added, dealing with sensory, sleep disturbance, bladder/bowel, and sexual function items (utilized only in Study I). Each question is answered using a Likert scale ranging from 1 to 5. The ratings range from "No strength at all" to "A lot of strength" for the strength domain; "None of the time" to "All of the time;" for emotions and participation; and "Extremely difficult/cannot do at all" to "Not difficult at all" for the remaining domains. The initial score is summed up for each domain and linearly converted to a 0–100 scale. A visual analog scale (VAS) is included as well, where 100 represents full recovery. Scores < 100 were defined as not fully recovered and 0 as no perceived recovery.

HRQoL (Studies I and IV) was assessed using the EQ-5D-3L (56), a two-page questionnaire. Page 1 is named "descriptive" and Page 2 consists of instructions and a VAS. The descriptive page consists of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension contains three statements, indicating no problems, some problems, and extreme problems. The answers can be converted to an index value, which is country-specific (57). Index score 1 indicates full health. It is possible to obtain numbers lower than 0, which indicates death (i.e., HRQoL estimated to be worse than death). It is also possible to keep the original data, displaying them and drawing inferences therefrom. Different states of health can still be estimated: for example, "11111" translates to index score 1 or full health. On Page 2, a VAS score of 100 represents "best imaginable health state" and 0 represents "worst imaginable health state."

Data Presentation

Binary outcomes (comorbidities) were presented as frequency (%) for a quick overview. Sex was presented as whole numbers (men/women) and/or frequency (%). Continuous variables, such as age, Body Mass Index (BMI), and SIS score, were presented as mean with standard deviation (SD) in tables and as median (inter-quartile range [IQR]) in figures. This gave a detailed picture of the data, including consideration

of outliers. Ordinal regression results were presented as odds ratios (ORs) with 95% confidence intervals (CIs).

Statistics

The statistical methods used in this thesis are described in Table 2. When comparing mean scores, the t-test for independent samples was used for two groups when a normal data distribution was assumed. The Mann–Whitney U test was used otherwise.

Three groups were compared using a one-way analysis of variance (ANOVA) for continuous variables in Studies II and III. The Krukal–Wallis H test was used instead in Study IV as EQ-5D-3L data were non-normally distributed. The chi-square test was used for categorical variables, except in Study I, which had small population numbers, where Fisher's exact test was used instead. For ANOVA, Levene's test was utilized for testing homogeneity of variance and Welch's test was initiated if Levene's test was significant. The Bonferroni post hoc test was utilized after chi-square tests and ANOVA to identify differing groups if the tests were significant.

Spearman's correlation coefficients examined relationships in non-normally distributed data for correlation analysis in Study IV. Pearson's correlation coefficients were used in Study III (< 0.5 = low correlation, 0.5–0.7 = moderate correlation, and > 0.7 = high correlation) (58).

Univariate ordinal regression was used for assessing associations between dependent outcomes and independent variables (59). Adjustment for age was done in multivariate ordinal regression tests.

Alpha was set to 0.05.

Table 2. Statistical methods used in Studies I–IV.

	Study I	Study II	Study III	Study IV
T-test	X		X	
Fisher's exact test	X			
Chi-square test		X	X	X
ANOVA		X	X	X
Ordinal regression		X		X
Pearson's correlation coefficient			X	
Spearman's correlation coefficient				X

Ethics

The studies included in this thesis were approved by the Regional Ethical Review Board in Umea, Sweden (Dnr 2016-355-80 32M). Written informed consent was obtained from all participants. This study conformed to the principles of the Declaration of Helsinki.

To respect the patient's autonomy and right to informed choice, the patients were provided general information on why and how the study was to be carried out. Data regulations were covered, as well as the possibility of opting out for any reason, at any time. This helped protect both participants and researchers, build trust, exhibit transparency, and follow the regulatory rules. Written consent was mandatory for participation.

Results

Participant Characteristics

The participant demographic characteristics and clinical data in this thesis are summarized in Table 3. The participants in Study I were in the sub-acute stage after TIA (4 months after the TIA event). Participants in Studies II–IV were mostly in the chronic phase (92.3%; ≥ 1 year after the TIA event). Certain variables were available for all cohorts; however, some variables, such as BMI, hyperlipidemia, and heart disease, were not collected in Study I as they were in Studies II–IV.

Table 3. Demographics and clinical data from Study I – IV. Study I was not included in total scores (only collected from Studies II – IV).

	Study I	Study II - IV	Subgroups			
Patient characteristics	First-ever TIA	Total	First-ever TIA	Recurrent TIA	TIA and stroke	*p*-value
Participants, *n*	47	431	299	54	78	
Year after transient ischaemic attack, mean (SD)	4 months	4,8 (3,6)	4,8 (3,7)	4,7 (3,3)	5,0 (3,4)	0,851
Age, years, mean (SD)	71 (12)	73 (11)	72 (11)	73 (9)	76 (9) #	**0,009**
Sex, male/female, *n*	27 / 20	266 / 165	168 / 131	40 / 14 *	58 / 20 #	**0,002**
BMI, mean (SD)		25,6 (7,4)	26,3 (7,0)	26,3 (3,8)	22,8 (10,0) # +	**0,001**
Comorbidities, cases, *n* (%)						
Hypertension		248 (58)	164 (55)	34 (63)	50 (64)	0,223
Diabetes	5 (11)	56 (13)	36 (12)	7 (13)	13 (17)	0,557
Atrial fibrillation	4 (9)	52 (12)	34 (11)	4 (7)	14 (18)	0,151
Hyperlipidaemia		124 (29)	75 (25)	14 (26)	35 (45) #	**0,002**
Heart diseases		71 (17)	42 (14)	11 (20)	18 (23)	0,114
Modified Rankin Scale questionnaire, mean (SD)		0,5 (1,0)	0,4 (0,9)	0,4 (0,7)	1,1 (1,4) #+	**< 0,001**
HADS depression, mean (SD)		2,5 (2,8)	2,1 (2,3)	3,5 (4,0) *	3,3 (3,4) #	**< 0,001**
HADS anxiety, mean (SD)		2,9 (3,0)	2,8 (2,9)	3,6 (3,1)	3,0 (3,5)	0,204
Sleep problems, mean (SD)		61 (18)	62 (18)	59 (15)	61 (22)	0,501

In Study I, the mean age of 71 (SD 12) years was close to that in the large studies' (Studies II–IV) mean age of 73 (SD 11) years. Men were more frequent (57%). The participants were sent the survey by mail 3 months

post-TIA, and data were collected thereafter. Unfortunately, not all information was available from Study I at the time for this thesis. All available data are listed in Table 3.

In Studies II–IV, the mean number of participants per year was 21 (SD 12). To increase the statistical power for comparing various outcomes over time, participants were divided into three groups: < 1 year post-TIA, 1–5 years post-TIA, and > 5 years post-TIA. The mean age in the entire study population was 73 (SD 11) years, with mostly male participants (62%). In the TIA with stroke group, participants were slightly older (4 years) than in the first-ever TIA group. Female participation was significantly higher among first-ever TIA patients (44%) than among recurrent TIA patients (26%) or TIA with stroke patients (26%).

Hypertension was the most common comorbidity (58%). Hyperlipidemia was seen in 29% of patients, with a 20% higher prevalence in TIA with stroke patients than in first-ever TIA patients. Heart disease was observed in 17% of patients. Diabetes was observed in 13% of participants. Atrial fibrillation was seen only in 12% of patients. The TIA with stroke participants had significantly less independence (with higher variability) than the participants in the recurrent TIA and first-ever TIA groups.

Multidimensional Consequences in the Sub-Acute Phase

In Study I, 47 persons at 4 months after TIA reported that the most affected domain was mood (reported by 89% of participants). However, symptoms of depression and anxiety were less frequent and only reported by 6% and 17% of participants, respectively. The sexual life domain was affected to a higher degree, but its prevalence (52%) was lower than that of some other domains. Other domains with a high prevalence of disability were bladder function (70%), strength (51%), and fatigue (26%). We found that most participants (90%) were independent in their daily lives (mRSq 0–1) but with restrictions in participation (57%; Figure 3) in their daily lives despite a good quality of life, with a median EQ-5D-3L index score of 0.85.

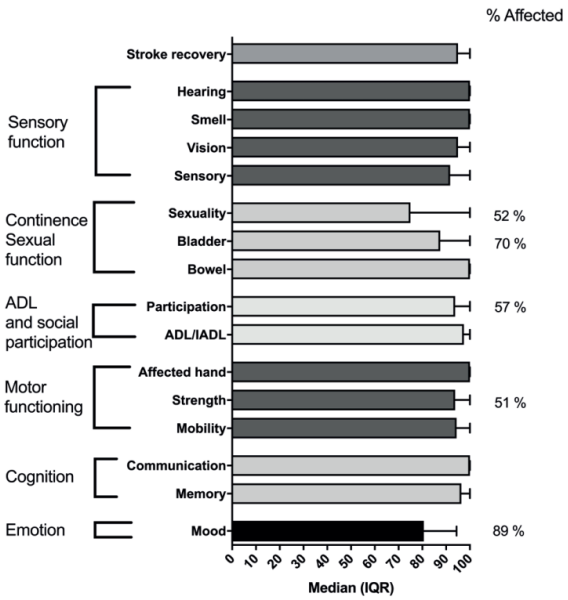

Figure 3 (with permission from the Journal of Rehabilitation Medicine – Clinical Communications). Extents and frequencies of unmet rehabilitation needs identified by the Rehab-Compass questionnaires 4 months after first-ever transient ischemic attack (TIA). The bar graph represents the extent (median +interquartile range [IQR]) of unmet rehabilitation needs, ranging from 0 (worst outcome/unmet need) to 100 (best outcome/no need). The numbers on the right side of the graph represent some of the frequencies of various conditions. ADL: activities of daily living.

Effects on Fatigue

In Study II, 431 community-dwelling participants after TIA reported certain fatigue, with a group mean score (21.8 SD 5.2) below the cutoff for fatigue assessed by the FAS. However, 35% of the first-ever TIA group experienced perceived fatigue (cutoff ≥ 24 points). Fatigue was reported at similar levels from several months up to 13 years after TIA onset. The mean score of perceived fatigue for the first-ever TIA group was significantly lower than that for the recurrent TIA group (23.9 SD 5.7; $p < 0.05$) and the TIA with stroke group (23.8 SD 6.5; $p < 0.05$; Figure 4A).

Similar levels across different time phases (< 1 year: 22.1 SD 5.2; 1 to 5 years: 22.0 SD 5.3; and > 5 years: 21.4 SD 5.0) were observed after a first-ever TIA (Figure 4B).

Perceived fatigue was associated with higher scores of anxiety (OR 1.3, 95% CI 1.2–1.4; p < 0.001; measured by the HADS), greater scores of depression (OR 1.6, 95% CI 1.5–1.8; p < 0.001; measured by HADS), heart disease (OR 2.0, 95% CI 1.3–3.3; p < 0.001), and atrial fibrillation (OR 2.5, 95% CI 1.3–5.0; p < 0.001).

Notably, higher patient-reported fatigue was significantly associated with lower daily activities (OR 0.85, 95% CI 0.82–0.88; p < 0.001) and SIS social participation (OR 0.84, 95% CI 0.81–0.97; p < 0.001) scores after adjustments for age.

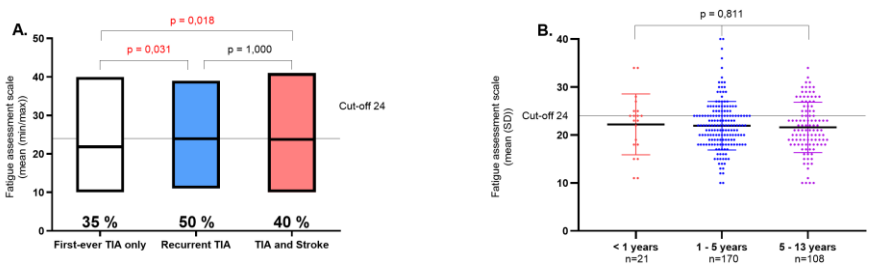

Figure 4. (A) The bar graph presents the perceived fatigue mean score assessed by the FAS for the three subgroups with the minimum/maximum in each subgroup. (B) The plot shows perceived fatigue as mean scores (lines) and individual scores (dots) for the first-ever TIA group stratified over 13 years after TIA. FAS: Fatigue Assessment Scale; TIA: transient ischemic attack.

Negative Effect on Participation

In Study III, we examined daily activity and participation among 299 community-dwelling individuals with first-ever TIA. Of the eight SIS domains, three mean scores were between 80 and 90. Most participants (83%) had problems with emotion, followed by problems with strength (43%) and restrictions of participation (37%). Subtle perceived difficulties were found in memory/thinking, mobility, hand function, and communication (see Table 4). Stable mean scores were seen after

dividing the first-ever TIA participants into smaller groups (i.e., < 1 year, 1–5 years, and > 5 years after TIA), and no significant results were observed upon comparison (see Table 4). Women reported significantly more disabilities for emotion (p = 0.03) and hand function (p = 0.03), while older subjects (age > 65 years) reported more disabilities for strength (p = 0.04), mobility (p = 0.001), hand function (p = 0.02), ADL/IADL (p = 0.002), and participation (p = 0.01). The ADL, participation, and overall recovery in this cohort demonstrated significant, low-to-moderate associations with other SIS domains.

Table 4 (With permission of Journal of Rehabilitation Medicine) SIS data from first-ever TIA patients.

Table III. Degree of disability presented by Stroke Impact Scale (SIS) scores (Mean (standard deviation; SD)). *p*-value tested by analysis of variance (ANOVA) test between 3 groups

SIS domains	Total Mean (SD)	N of non-limitation, (%)	< 1 year post-TIA Mean (SD)	1–5 years post-TIA Mean (SD)	> 5 years post-TIA Mean (SD)	*p*-value
Participants, *n*	299		21	170	108	
Strength	84.2 (24.0)	169 (57)	83.3 (28.0)	84.3 (24.9)	84.3 (21.8)	0.98
Memory and thinking	92.0 (11.7)	168 (56)	92.2 (10.6)	92.8 (10.0)	90.7 (14.1)	0.36
Emotion	80.6 (15.5)	52 (17)	82.3 (14.4)	80.5 (15.5)	80.4 (16.0)	0.87
Communication	94.2 (9.3)	201 (67)	93.4 (7.4)	94.4 (9.0)	94.0 (10.3)	0.86
ADL/IADL	94.9 (10.4)	232 (78)	96.1 (8.0)	94.7 (11.0)	94.9 (9.8)	0.85
Mobility	92.0 (14.9)	188 (63)	91.0 (21.1)	91.3 (15.5)	93.4 (12.3)	0.47
Hand function	95.4 (12.7)	252 (84)	94.8 (12.8)	95.2 (14.2)	95.9 (10.0)	0.87
Participation	89.1 (18.5)	187 (63)	89.4 (17.5)	89.0 (19.3)	89.1 (17.5)	1.00
Recovery	91.6 (15.0)	198 (66)	88.6 (21.9)	92.1 (14.4)	91.4 (14)	0.60

ADL/IADL: activities of daily living/instrumental activities of daily living.

Lack of Observed Effect on Quality of Life

In Study IV, most first-ever TIA patients were not affected regarding the HRQoL (mean 0.88 SD 0.2) index score (EQ-5D-3L). In the TIA with stroke group (0.77 (0.3); p < 0.001), the score was significantly lower than in the first-ever TIA group. After division into three time groups from 1 to more than 10 years after the first-ever TIA (p = 0.643; Figure 4), no significant differences were observed between mean scores. Pain, followed by depression/anxiety and mobility, was the most reported problem. The factors associated significantly with poorer HRQoL in this cohort (p < 0.001) included patients with recurrent TIA and stroke (OR (95% CI) 0.67 (0.53–0.83)), worse symptoms of depression as measured by the HADS (0.59 (0.53–0.66)), worse symptoms of anxiety as measured by the HADS (0.73 (0.68–0.79)), and higher levels of fatigue as measured by the FAS (0.81 (0.77–0.85)).

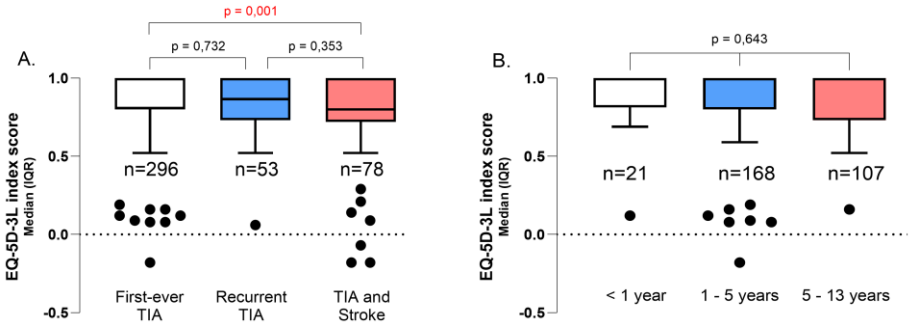

Figure 5. (A) Three subgroups of TIA patients compared based on median EQ-5D-3L scores (IQR). (B) Time-group comparison of first-ever TIA patients over 0–13 years.

Discussion

Key Findings

This thesis evaluated the long-term consequences of TIA with comorbidities, as well as their effects on patients' daily activities, participation, and HRQoL among community-dwelling individuals from the sub-acute phase to more than 10 years after a TIA event.

The key findings indicated that assessment of rehabilitation needs with PROMS was feasible in the outpatient clinic. In the sub-acute stage, we observed multidimensional patient-reported consequences, including bladder function, sexual life, strength, and fatigue. However, symptoms of depression and anxiety were less reported in the sub-acute stage.

In the chronic phase, long-term perceived fatigue was evident after 1 year up to 13 years after a TIA. This increased perceived fatigue after TIA was independently associated with depression, anxiety, heart disease, and atrial fibrillation. Elevated perceived fatigue was significantly associated with lower activity levels in everyday life.

Besides fatigue, the most perceived disabilities were reported in the emotion's domain, strength domain, and participation domain. No significant differences in all SIS domains were observed over time between the three time groups. The remaining perceived disabilities and their associations with ADL/IADL and participation were noted consistently up to 10 years after TIA. However, these perceived impairments and limitations in daily activity and participation did not make a statistically significant difference to the EQ-5D-3L index score.

These findings highlight that the timely screening of long-term consequences is needed among community-dwelling individuals after TIA. Besides secondary prevention after TIA, patient-tailored rehabilitation interventions could improve their everyday life and HRQoL.

Impairments of body function and structure after TIA

In the sub-acute stage (Study I), we observed patient-reported multidimensional consequences, including those related to bladder function (70%), sexual life (52%), strength (51%), and fatigue, with fewer symptoms of depression and anxiety. Lower urinary tract symptoms were common in older patients (60), and their age could explain these symptoms. However, since it is a common sequela in stroke (61), a TIA could also hypothetically contribute. Sexual life issues are poorly studied in TIA patients but are known to be common in stroke survivors (62). Perhaps cardiovascular pathology could explain some of the perceived disability in this area. Affected strength, also seen in Study I, is known to be common in stroke survivors (63) but is not commonly known to affect TIA patients. Fatigue was also common (26%) and was researched further in Study II, as were participation and ADL, which were also negatively affected, especially participation (57%). A known risk factor for fatigue is cardiovascular disease, which is also common in TIA and stroke patients (64). To a certain degree, old age and comorbidity could explain some of these symptoms.

In the chronic stage (Study II), long-term perceived fatigue was evident after 1 year up to 13 years after a TIA. Higher FAS scores among patients who experienced a stroke in the acute to sub-acute stages (65) are known to exist. Therefore, the severity of vascular events could explain recurrent TIA patients' higher levels of fatigue compared to first-ever TIA patients since multiple TIA events may cause more damage than one (66).

Unexpectedly, perceived fatigue levels were similar in the three time-phase groups up to 13 years post-TIA. Taking neuroplasticity into account, fatigue would be expected to be alleviated in the sub-acute and chronic phases after TIA (67). One reason could be that neuroplasticity is less efficient in old age. Another reason could be known comorbidities that induce fatigue, such as hypertension, diabetes, and heart disease, which were common in the cohort (see Table 3) (68, 69). However, minor stroke cases were likely to be present in Study II's cohort, since a time-based rather than a tissue-based TIA diagnosis method was used. The inference was that long-term post-TIA fatigue may share some common mechanisms with post-stroke fatigue.

This increased perceived fatigue after TIA was independently associated with depression, anxiety, heart disease, and atrial fibrillation. Post-stroke fatigue is considered multidimensional, which also seems to be the case for post-TIA fatigue. Depression and anxiety were independently associated with higher perceived fatigue scores, and a connection is known to exist in post-stroke fatigue as well (70). Heart disease and atrial fibrillation had an increased OR for fatigue, which can be seen for heart disease alone in other studies (69, 71). Our data suggested these treatable factors, such as depression, anxiety, and heart disease, may provide new treatment avenues for persons with fatigue after TIA.

Elevated perceived fatigue had a significant adverse association with the SIS, ADL, and social participation (as seen in the ICF, Figure 1) in first-ever TIA patients in Study II. Patients with fatigue were more likely to experience ADL limitations, such as decreased mobility and reduced independence. This resonates with another study (72). Additionally, in Study III, emotions and strength, among others, had low to moderate associations with ADL and social participation.

Even though sleep problems were often reported among TIA and stroke patients in a systematic review and meta-analysis (73), they were not associated with fatigue levels in first-ever TIA patients in Study II.

Limitations of daily activities and participation restrictions

Besides fatigue, the most perceived disabilities were reported in the emotions, muscular strength, and participation domains. Emotional problems, as measured by the SIS, were most common, and these results were confirmed by other studies, in which TIA increased psychological impairments 6–48 months after TIA onset (17, 25, 26). However, the impairments seemed less prominent after looking at mean HADS scores. Therefore, most participants seemed not to be psychologically clinically ill post-TIA, as would be indicated by higher HADS scores. Instead, the affected SIS domain hints at subtler impairments, which could be explained by temporary situations in life or mood swings.

However, problems were present across all 10 years, indicating that they could be sequelae of TIA. Female participants reported significantly

more emotional difficulties, also seen in another stroke study (74). This could mean that women express their emotional issues better than men. Screening for emotional issues among TIA survivors could assist in recovery.

Surprisingly, reduced strength was the second most perceived impairment among more than 40% of participants up to 10 years post-TIA. This is consistent with another cohort study that reported reduced strength 12 months after TIA (75) and is common in stroke survivors. Therefore, minor strokes and reduced physical activity may partly contribute to mobility limitations, mostly among older participants. Rehabilitation focusing on physical activity could improve motor impairment and mitigate long-term negative impacts on daily life among individuals after a TIA, especially among older subjects.

Independent living (mRSq values 0–2), which was most common, was not surprising since other studies confirm it (25, 39, 72, 76). Despite independence, close to one-third of participants reported participation restrictions, especially older patients (age > 65 years). This could mean that these individuals may struggle with more complex activities, including various family, social, and work situations, while living an independent life. More association with the perception of incomplete recovery was seen than with other SIS domains. This was consistent with stroke survivors, among whom social participation was considered a major aspect of recovery in another study (77). These findings indicate a need for rehabilitation interventions focusing on participation issues among TIA patients.

Older subjects (age > 65 years), no matter their sex, reported more disabilities in muscular strength, mobility, hand function, ADL/IADL, and social participation. Higher age could be a potential risk factor for the deterioration of outcomes after a TIA. Limitations in mobility and hand function were moderately related to limitations in ADL/IADL, re-emphasizing the need for physical activity for a person after a TIA. Moreover, many weak and significant associations were observed between ADL and participation (such as the impairment of muscular strength and limitations in memory and thinking, emotions, and communication), indicating that subtle disabilities after TIA may play a significant meaningful role in everyday life and recovery in the chronic phase of TIA. Similar to the approach in stroke research, a multiprofessional follow-up with holistic rehabilitation may be required to reduce these negative effects on ADL/IADL and participation and improve overall recovery (78).

Lack of observed effect on Health-Related Quality of Life

HRQoL was not statistically significantly affected by a first-ever TIA in this cohort, despite participation limitations, as previously demonstrated. Our results are consistent with another study (79). It was suggested that TIA may be a diagnosis where change is not detected by the EQ-5D-3L. Compared to age-matched Swedish population norms, first-ever TIA patients had higher levels of HRQoL. The reason for this is unknown. It could reflect the presence of more comorbidities in the general population than in the present TIA cohort. Meanwhile, we demonstrated an unfavorable HRQoL in the TIA and stroke groups. Our findings were in line with a trial (CHANCE trial) wherein recurrent stroke was associated with a poor quality of life in patients after TIA or minor stroke (80).

The HRQoL data were collected more than 6 months and up to 13 years after TIA, providing long-term results on HRQoL preservation after TIA, in contrast to most other studies reporting on the acute and sub-acute phases after TIA (80) (79). No significant differences were observed between different time periods after TIA in the present study.

The most reported sub-domain problem in the present study was pain/discomfort, followed by depression/anxiety and mobility. We speculate that this may not be related to the TIA diagnosis directly, and a possible reason could be that pain/discomfort is a common issue among older individuals (81). These sub-domains' results were somewhat consistent with our previous studies wherein participants reported limitations of participation in daily life, with various hidden symptoms, such as those related to fatigue, sexual life, bladder function, strength, and anxiety in Studies II and III (29 - 31).

Besides the severity of vascular events, we found that more depression, anxiety, and perceived fatigue played a significant role in poor HRQoL in this unique cohort. Even though the TIA did not significantly worsen HRQoL, our results still indicated that active treatment and rehabilitation for depression, anxiety, and fatigue may further improve HRQoL.

Discussion of Methodology

This thesis is based on observational studies with two different study designs. Study I was a prospective cohort study that provided relatively strong evidence, while Studies II–IV were retrospective cohort studies that were more time-efficient and less costly. In Studies II–IV, we collected data from all persons who fulfilled the selection criteria between 6 months and 10 years after TIA onset in a single period. Since the participants were recruited at different time points after TIA onset, the study was not designed to evaluate changes in consequences over time. Still, mapping TIA patients' rehabilitation needs over a very long period was considered a strength of this thesis since 78 participants suffered a TIA at least 5 years ago.

The main strength of this thesis is its relatively large cohort size in Studies II–IV, with demographic and medical comorbidity information with wide time phases after TIA onset. Our cohorts provided valuable opportunities to understand the multidimensional consequences from the sub-acute to the late chronic phases after TIA events. Even though we intended to study persons with TIA, we cannot rule out persons with minor stroke since the TIA diagnosis was mainly based on clinical symptoms without MRI examination per the clinical routine in Sweden.

Another methodological constraint arises from using only PROMs as assessment tools to evaluate the consequences of TIA. For example, since studies on biomarkers are advancing, an objective way to measure fatigue could lead to new conclusions and therapies. Even then, it seems that no completely objective measurement of "hidden" symptoms will be available soon, if ever. PROMs can help the patient to achieve greater self-awareness, create better patient involvement, facilitate goal setting, help the clinician to understand the patient's situation better, and permit the discussion of sensitive topics. They can be helpful as a screening tool, cover patients' needs, are time-efficient, can assist in diagnosis, are beneficial for a holistic understanding of the patient's life, can follow up treatment, can assist in monitoring changes and tracking progress, and reassure the patient that they are cared for, among other advantages. Until new objective measurements arise, PROMs are of great assistance and together with qualitative research help scientists understand the world better. Some downsides of PROMs are the risks of misunderstanding or inability to answer the question. Not telling the truth is also a risk. PROMs only provide one piece of the picture and can over- and underestimate patients' problems. Certain questions can seem unclear or irrelevant to the patient. Additionally, they are not suitable for

all patients, especially very sick individuals who cannot concentrate enough and older, cognitively impaired, or low-literacy patients, due to their complexity (82).

Generalizability/clinical implications

Furthermore, we are aware of the relatively low response rate in this thesis of only 30% (Study I) and 25% (Studies II–IV) in the catchment area represented in the thesis. This might increase the risk of bias since we were unable to perform missing data comparisons due to a lack of consent from those who did not participate in the studies. One way of investigating whether the sample population was representative of the total population could be to look at demographic data and other comparable variables (such as comorbidities) from the national registry Riksstroke (5). When comparing mean age in TIA patients, our cohort matched that of another large study (11), further validating the studies conducted.

As illustrated in Table 5, it could be suggested that patients with fewer comorbidities chose to participate. However, not all data were available in Riksstroke, such as data on hyperlipidemia and heart disease, which were both highly prevalent in the Study II–IV cohort. Moreover, Riksstroke could obtain data from multiple sources, adding to the saturation of their variables, which was not the case with Studies II–IV, where medical records were screened by medical students. The hypertension data in Table 5 were on treated patients in the Framingham Heart Study, perhaps resonating more with the method of collecting data for Studies II–IV. Reasons for not participating were the number of questions to answer in the Rehabkompassen©, layout of the survey, and participant age.

Table 5. Comparison of Riksstroke data with Study I–IV cohort data. NA - not available

	Age (mean)	Men (%)	Hypertension (%)	Atrial fibrillation (%)	Diabetes (%)	Heart disease (%)
Studie I	71	51	NA	9	11	NA
Study II - IV	73 (11)	62	58	12	13	17
First-ever TIA patients subgroup	72	56	55	11	12	14
General TIA Sweden (Riksstroke)	74	52	62	22	20	NA
General Stroke Sweden (Riksstroke)	75	54	64	28	23	NA
Framingham Heart Study	72 (12)	48	47	10	16	24

Clinical Implications and Future Perspectives

In this thesis, broadly perceived disabilities were demonstrated consistently and played a significant, meaningful role in the everyday lives and recovery of community-dwelling individuals from 6 months up to 13 years after TIA. The results presented in this thesis show the importance of screening for various consequences/rehabilitation needs after TIA onset. In the current clinical route in Sweden, screening of stroke risk factors and initiating secondary preventions to minimize the risk of subsequent stroke are considered important. However, much less attention has been paid to various consequences since TIA is commonly considered with only temporal symptoms. The results presented in this thesis indicate a need to establish structured follow-up for the screening of various consequences/rehabilitation needs among persons after TIA onset. The results in this thesis also support PROMs as feasible outcome measures in the outpatient clinic setting to identify the multidimensional rehabilitation needs of individuals after TIA.

Furthermore, multiple dimensional impairments, including long-term patient-reported fatigue, were evident for community-dwelling adults after TIA. No clinical rehabilitation interventions are routinely provided to TIA survivors in Sweden, which may need to be reconsidered, especially regarding fatigue management. Depression, anxiety, heart disease, and atrial fibrillation were independently associated with increased perceived fatigue. Reduced ADL were also significantly associated with perceived fatigue. These findings indicate a need for long-term, multiprofessional follow-up with holistic rehabilitation interventions, including information on handling fatigue, actively treating mood disorders, and training on daily activity and social participation, to improve overall recovery among survivors of TIA.

A large prospective longitudinal study with persons after TIA should be carried out in the near future to identify the longitudinal alterations in rehabilitation needs among large numbers of patients with TIA. MRI imaging data imaging from TIA patients could also rule out persons with potential stroke.

Conclusions

This thesis revealed that PROMs are feasible outcome measures in the outpatient clinic setting to identify the multidimensional rehabilitation needs of individuals after TIA.

Broadly perceived disabilities, including impairments such as fatigue, were consistently demonstrated to be associated with ADL and participation and play a significant meaningful role in everyday life among community-dwelling individuals up to 13 years after TIA.

Certain comorbidities were associated with increased perceived fatigue, and mean FAS scores were higher in patients than in the age-matched healthy population. Women and older individuals were more prone to reporting difficulties in muscular strength, ADL/iADL, mobility, hand function, and participation. However, TIA did not statistically significantly affect HRQoL.

These findings indicate the need for long-term multiprofessional follow-up with holistic rehabilitation and comorbidity treatment to improve daily activities among TIA patients.

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References

1. Coupland AP, Thapar A, Qureshi MI, Jenkins H, Davies AH. The definition of stroke. J R Soc Med. 2017;110(1):9-12.
2. Albers GW, Caplan LR, Easton JD, Fayad PB, Mohr JP, Saver JL, et al. Transient ischemic attack--proposal for a new definition. The New England journal of medicine. 2002;347(21):1713-6.
3. Clissold B, Phan TG, Ly J, Singhal S, Srikanth V, Ma H. Current aspects of TIA management. J Clin Neurosci. 2020;72:20-5.
4. Foschi M, Padroni M, Abu-Rumeileh S, Abdelhak A, Russo M, D'Anna L, et al. Diagnostic and Prognostic Blood Biomarkers in Transient Ischemic Attack and Minor Ischemic Stroke: An Up-To-Date Narrative Review. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2022;31(3):106292.
5. The Swedish Stroke Register (Riksstroke) - Statistics [Internet]. 2024. Available from: https://statistik.incanet.se/riksstroke/.
6. Groff H, Yousfani S, Pantoja-Ruiz C, Douiri A, Bhalla A, Wolfe C, et al. A systematic review of the incidence and outcomes of ICD-11 defined stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2024;33(8):107784.
7. Easton JD, et al. Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/Ame... - PubMed - NCBI. 2018.
8. Fischer U, Baumgartner A, Arnold M, Nedeltchev K, Gralla J, De Marchis GM, et al. What is a minor stroke? Stroke. 2010;41(4):661-6.
9. Vinding NE, Butt JH, Lauridsen MD, Kristensen SL, Johnsen SP, Kroll J, et al. Long-Term Incidence of Ischemic Stroke After Transient Ischemic Attack: A Nationwide Study From 2014 to 2020. Circulation. 2023;148(13):1000-10.
10. Shahjouei S, Li J, Koza E, Abedi V, Sadr AV, Chen Q, et al. Risk of Subsequent Stroke Among Patients Receiving Outpatient vs Inpatient Care for Transient Ischemic Attack: A Systematic Review and Meta-analysis. JAMA Netw Open. 2022;5(1):e2136644.
11. Lioutas VA, Ivan CS, Himali JJ, Aparicio HJ, Leveille T, Romero JR, et al. Incidence of Transient Ischemic Attack and Association With Long-term Risk of Stroke. JAMA. 2021;325(4):373-81.
12. Giles MF, Flossman E, Rothwell PM. Patient behavior immediately after transient ischemic attack according to clinical characteristics, perception of the event, and predicted risk of stroke. Stroke. 2006;37(5):1254-60.
13. Spurgeon L, James G, Sackley C. Subjective experiences of transient ischaemic attack: a repertory grid approach. Disability and rehabilitation. 2013;35(26):2205-12.

14. Broomfield NM, Quinn TJ, Abdul-Rahim AH, Walters MR, Evans JJ. Depression and anxiety symptoms post-stroke/TIA: prevalence and associations in cross-sectional data from a regional stroke registry. BMC neurology. 2014;14:198.
15. Turner GM, et al. Establishing research priorities relating to the long-term impact of TIA and minor stroke through stakeholder-centred consensus. - PubMed - NCBI. 2018.
16. Spurgeon L, Humphreys G, James G, Sackley C. A Q-Methodology Study of Patients' Subjective Experiences of TIA. Stroke research and treatment. 2012;2012:486261.
17. van Rooij FG, Plaizier NO, Vermeer SE, Goraj BM, Koudstaal PJ, Richard E, et al. Subjective Cognitive Impairment, Depressive Symptoms, and Fatigue after a TIA or Transient Neurological Attack: A Prospective Study. Behav Neurol. 2017;2017:5181024.
18. Merriam-Webster: America's Most Trusted Dictionary. 2025.
19. Lynch J, Mead G, Greig C, Young A, Lewis S, Sharpe M. Fatigue after stroke: the development and evaluation of a case definition. Journal of psychosomatic research. 2007;63(5):539-44.
20. De Vries J, Michielsen HJ, Van Heck GL. Assessment of fatigue among working people: a comparison of six questionnaires. Occup Environ Med. 2003;60 Suppl 1(Suppl 1):i10-5.
21. Brandal A, Eriksson M, Wester P, Lundin-Olsson L. Reliability and validity of the Swedish Fatigue Assessment Scale when self-administrered by persons with mild to moderate stroke. Top Stroke Rehabil. 2016;23(2):90-7.
22. Kuppuswamy A, Billinger S, Coupland KG, English C, Kutlubaev MA, Moseley L, et al. Mechanisms of Post-Stroke Fatigue: A Follow-Up From the Third Stroke Recovery and Rehabilitation Roundtable. Neurorehabil Neural Repair. 2024;38(1):52-61.
23. Duncan F, Wu S, Mead GE. Frequency and natural history of fatigue after stroke: a systematic review of longitudinal studies. Journal of psychosomatic research. 2012;73(1):18-27.
24. Cumming TB, Packer M, Kramer SF, English C. The prevalence of fatigue after stroke: A systematic review and meta-analysis. International journal of stroke : official journal of the International Stroke Society. 2016;11(9):968-77.
25. Turner GM, Calvert M, Feltham MG, Ryan R, Marshall T. Ongoing impairments following transient ischaemic attack: retrospective cohort study. European journal of neurology. 2016;23(11):1642-50.
26. Moran GM, Fletcher B, Feltham MG, Calvert M, Sackley C, Marshall T. Fatigue, psychological and cognitive impairment following transient ischaemic attack and minor stroke: a systematic review. European journal of neurology. 2014;21(10):1258-67.

27. Who. World Health Organization - International Classification of Functioning, Disability and Health (ICF) © 2001 - 2024 https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health2024 [
28. Dabrowski J, Czajka A, Zielinska-Turek J, Jaroszynski J, Furtak-Niczyporuk M, Mela A, et al. Brain Functional Reserve in the Context of Neuroplasticity after Stroke. Neural Plast. 2019;2019:9708905.
29. Magaard G, Stålnacke BM, Sörlin A, Öhberg F, Berggren S, Grollmuss E, et al. Identifying Sub-Acute Rehabilitation Needs Among Individuals After Transient Ischaemic Attack Using Rehab-Compass as a Simple Screening Tool in the Outpatient Clinic. Journal of rehabilitation medicine Clinical communications. 2019;2.
30. Magaard G, Öhberg F, Sörlin A, Stalnacke BM, Liv P, Hu X. Long-term perceived fatigue after transient ischaemic attack. In: Rehabilitation DoCMa, editor. 2024. p. 22.
31. Andersson J, Stålnacke BM, Sörlin A, Magaard G, Hu X. Long-term perceived disabilities up to 10 years after transient ischaemic attack. Journal of rehabilitation medicine. 2021;53(3).
32. Magaard G, Öhberg F, Sörlin A, Stalnacke BM, Norstrom F, Hu X. Lack of observed effect on health-related quality of life after transient ischemic attack. In: Rehabilitation DoCMa, editor. 2025.
33. Magaard G, Wester P, Levi R, Lindvall P, Gustafsson E, Nazemroaya Sedeh A, et al. Identifying Unmet Rehabilitation Needs in Patients After Stroke With a Graphic Rehab-Compass(TM). Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2018;27(11):3224-35.
34. Socialstyrelsen. Nationella riktlinjer stroke och TIA - [Internet] 2020 [Available from: https://www.socialstyrelsen.se/kunskapsstod-och-regler/regler-och-riktlinjer/nationella-riktlinjer/riktlinjer-och-utvarderingar/stroke/.
35. Fonseca AC, Merwick A, Dennis M, Ferrari J, Ferro JM, Kelly P, et al. European Stroke Organisation (ESO) guidelines on management of transient ischaemic attack. Eur Stroke J. 2021;6(2):CLXIII-CLXXXVI.
36. Luijendijk HJ, Stricker BH, Wieberdink RG, Koudstaal PJ, Hofman A, Breteler MM, et al. Transient ischemic attack and incident depression. Stroke. 2011;42(7):1857-61.
37. Olive-Gadea M, Cano D, Rodrigo-Gisbert M, Muchada M, Montiel E, Baladas M, et al. Redefining Disability: Patient-Reported Outcome Measures After Minor Stroke and Transient Ischemic Attack. Stroke. 2023;54(1):144-50.
38. Winward C, Sackley C, Metha Z, Rothwell PM. A population-based study of the prevalence of fatigue after transient ischemic attack and minor stroke. Stroke. 2009;40(3):757-61.

39. van Rooij FG, Schaapsmeerders P, Maaijwee NA, van Duijnhoven DA, de Leeuw FE, Kessels RP, et al. Persistent cognitive impairment after transient ischemic attack. Stroke. 2014;45(8):2270-4.
40. El Husseini N, Goldstein LB, Peterson ED, Zhao X, Pan W, Olson DM, et al. Depression and antidepressant use after stroke and transient ischemic attack. Stroke. 2012;43(6):1609-16.
41. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. Journal of psychosomatic research. 2002;52(2):69-77.
42. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 1983;67(6):361-70.
43. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. Psychol Med. 1997;27(2):363-70.
44. Lisspers J, Nygren A, Soderman E. Hospital Anxiety and Depression Scale (HAD): some psychometric data for a Swedish sample. Acta psychiatrica Scandinavica. 1997;96(4):281-6.
45. Djukanovic I, Carlsson J, Arestedt K. Is the Hospital Anxiety and Depression Scale (HADS) a valid measure in a general population 65-80 years old? A psychometric evaluation study. Health Qual Life Outcomes. 2017;15(1):193.
46. De Vries J, Michielsen H, Van Heck GL, Drent M. Measuring fatigue in sarcoidosis: the Fatigue Assessment Scale (FAS). Br J Health Psychol. 2004;9(Pt 3):279-91.
47. Evidence reviews for the optimal tool for the assessment of fatigue: Stroke rehabilitation in adults (update). 2023.
48. Aali G, Drummond A, das Nair R, Shokraneh F. Post-stroke fatigue: a scoping review. F1000Res. 2020;9:242.
49. Clark LA, Watson D. Constructing validity: New developments in creating objective measuring instruments. Psychol Assess. 2019;31(12):1412-27.
50. Brändal A, Eriksson M, Wester P, Lundin-Olsson L. Reliability and validity of the Swedish Fatigue Assessment Scale when self-administrered by persons with mild to moderate stroke. Topics in stroke rehabilitation. 2016;23(2):90-7.
51. Cumming TB, Mead G. Classifying post-stroke fatigue: Optimal cut-off on the Fatigue Assessment Scale. Journal of psychosomatic research. 2017;103:147-9.
52. Bruno A, Shah N, Lin C, Close B, Hess DC, Davis K, et al. Improving modified Rankin Scale assessment with a simplified questionnaire. Stroke. 2010;41(5):1048-50.
53. Modified Rankin Scale (MRS) [Internet] 2024 [Available from: https://strokengine.ca/en/assessments/modified-rankin-scale-mrs/.

54. Duncan PW, Wallace D, Lai SM, Johnson D, Embretson S, Laster LJ. The stroke impact scale version 2.0. Evaluation of reliability, validity, and sensitivity to change. Stroke. 1999;30(10):2131-40.
55. Duncan PW, Bode RK, Min Lai S, Perera S, Glycine Antagonist in Neuroprotection Americans I. Rasch analysis of a new stroke-specific outcome scale: the Stroke Impact Scale. Archives of physical medicine and rehabilitation. 2003;84(7):950-63.
56. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-43.
57. Burström K, Sun S, Gerdtham U-G, Henriksson M, Johannesson M, Levin L-Å, et al. Swedish experience-based value sets for EQ-5D health states. Quality of Life Research. 2014;23(2):431-42.
58. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in medical research. Malawi medical journal : the journal of Medical Association of Malawi. 2012;24(3).
59. Westreich D, Greenland S. The table 2 fallacy: presenting and interpreting confounder and modifier coefficients. Am J Epidemiol. 2013;177(4):292-8.
60. Gibson W, Wagg A. New horizons: urinary incontinence in older people. Age Ageing. 2014;43(2):157-63.
61. Zhang X, Mai Y, Hu X. Effect of pelvic floor muscle training on pelvic floor muscle function and lower urinary tract symptoms in stroke patients: a systematic review. Physiother Theory Pract. 2023;39(7):1342-54.
62. Grenier-Genest A, Gerard M, Courtois F. Stroke and sexual functioning: A literature review. NeuroRehabilitation. 2017;41(2):293-315.
63. E. LK, Choi M, Jeoung. Effectiveness of Rehabilitation Exercise in Improving Physical Function of Stroke Patients: A Systematic Review. International journal of environmental research and public health. 2022;19(19).
64. Hankey GJ. Secondary stroke prevention. The Lancet Neurology. 2014;13(2):178-94.
65. Ramirez-Moreno JM, Munoz-Vega P, Alberca SB, Peral-Pacheco D. Health-Related Quality of Life and Fatigue After Transient Ischemic Attack and Minor Stroke. Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association. 2019;28(2):276-84.
66. Wang L, Chaudhari K, Winters A, Sun Y, Berry R, Tang C, et al. Recurrent Transient Ischemic Attack Induces Neural Cytoskeleton Modification and Gliosis in an Experimental Model. Transl Stroke Res. 2023;14(5):740-51.
67. Bernhardt J, Hayward KS, Kwakkel G, Ward NS, Wolf SL, Borschmann K, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and

Rehabilitation Roundtable taskforce. International journal of stroke : official journal of the International Stroke Society. 2017;12(5):444-50.
68. Fritschi C, Quinn L, Hacker ED, Penckofer SM, Wang E, Foreman M, et al. Fatigue in women with type 2 diabetes. Diabetes Educ. 2012;38(5):662-72.
69. Smith OR, Michielsen HJ, Pelle AJ, Schiffer AA, Winter JB, Denollet J. Symptoms of fatigue in chronic heart failure patients: clinical and psychological predictors. Eur J Heart Fail. 2007;9(9):922-7.
70. Duncan F, Lewis SJ, Greig CA, Dennis MS, Sharpe M, MacLullich AM, et al. Exploratory longitudinal cohort study of associations of fatigue after stroke. Stroke. 2015;46(4):1052-8.
71. Smith OR, van den Broek KC, Renkens M, Denollet J. Comparison of fatigue levels in patients with stroke and patients with end-stage heart failure: application of the fatigue assessment scale. J Am Geriatr Soc. 2008;56(10):1915-9.
72. Kjork E, Blomstrand C, Carlsson G, Lundgren-Nilsson A, Gustafsson C. Daily life consequences, cognitive impairment, and fatigue after transient ischemic attack. Acta neurologica Scandinavica. 2016;133(2):103-10.
73. Ho LYW, Lai CKY, Ng SSM. Contribution of sleep quality to fatigue following a stroke: a cross-sectional study. BMC neurology. 2021;21(1):151.
74. Volz M, Ladwig S, Werheid K. Gender differences in post-stroke depression: A longitudinal analysis of prevalence, persistence and predictive value of known risk factors. Neuropsychol Rehabil. 2021;31(1):1-17.
75. Croot EJ, Ryan TW, Read J, Campbell F, O'Cathain A, Venables G. Transient ischaemic attack: a qualitative study of the long term consequences for patients. BMC Fam Pract. 2014;15:174.
76. Guyomard V, Metcalf AK, Naguib MF, Fulcher RA, Potter JF, Myint PK. Transient ischaemic attack, vascular risk factors and cognitive impairment: a case-controlled study. Age Ageing. 2011;40(5):641-4.
77. Woodman P, Riazi A, Pereira C, Jones F. Social participation post stroke: a meta-ethnographic review of the experiences and views of community-dwelling stroke survivors. Disability and rehabilitation. 2014;36(24):2031-43.
78. Quinn TJ, Paolucci S, Sunnerhagen KS, Sivenius J, Walker MF, Toni D, et al. Evidence-based stroke r-ehabilitation: an expanded guidance document from the european stroke organisation (ESO) guidelines for management of ischaemic stroke and transient ischaemic attack 2008. J Rehabil Med. 2009;41(2):99-111.
79. Labberton AS, Augestad LA, Thommessen B, Barra M. The association of stroke severity with health-related quality of life in survivors of acute cerebrovascular disease and their informal caregivers

during the first year post stroke: a survey study. Qual Life Res. 2020;29(10):2679-93.
80. Wang YL, Pan YS, Zhao XQ, Wang D, Johnston SC, Liu LP, et al. Recurrent stroke was associated with poor quality of life in patients with transient ischemic attack or minor stroke: finding from the CHANCE trial. CNS Neurosci Ther. 2014;20(12):1029-35.
81. Leung DKY, Fong APC, Wong FHC, Liu T, Wong GHY, Lum TYS. Nonpharmacological Interventions for Chronic Pain in Older Adults: A Systematic Review and Meta-Analysis. Gerontologist. 2024;64(6).
82. Campbell R, Ju A, King MT, Rutherford C. Perceived benefits and limitations of using patient-reported outcome measures in clinical practice with individual patients: a systematic review of qualitative studies. Qual Life Res. 2022;31(6):1597-620.