

Annual Report 2023

Stress in Action is a multidisciplinary 10-year research project funded by the Dutch Research Council (NWO) Gravitation Programme.

Seven institutes collaborate in the Science of Stress in Daily life.















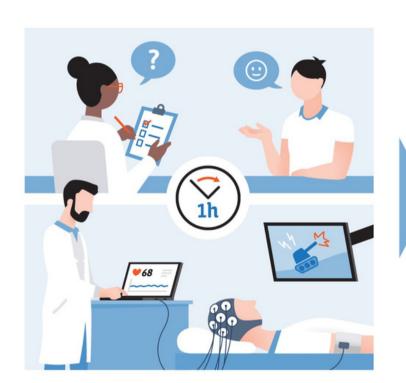




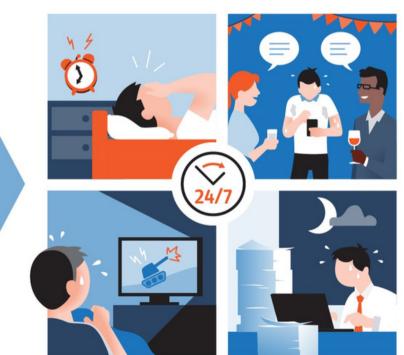
CONTENTS

Mission	02
• Executive Summary	03
 Over-arching goal 	06
 Organisation 	07
• Governance	14
• Finance	19
 Dissemination 	20
• SWOT	23
• Appendix	24

From Lab...



...to Daily Life





MISSION

The Stress in Action (SiA) consortium aims to undertake ground-breaking research to better measure, understand, and intervene on the detrimental effects of daily life stress on health. Our consortium is comprised of a multidisciplinary group of researchers from seven academic institutes: Amsterdam UMC, VU Amsterdam, UMC Groningen, University of Groningen, Utrecht University, University of Twente and Erasmus MC.

We develop and evaluate innovative ambulatory methods to measure affective, cognitive, biological, and behavioural responses to daily life stress. By conducting studies within large-scale cohorts, we aim to identify the contextual and personal factors that influence these stress responses and understand how daily life stress contributes to the development and course of mental and cardiometabolic diseases. SiA's research will pave the way for the development of novel monitoring techniques and personalized intervention strategies to

Stress in Action is funded by a 10-year Gravitation grant from the Dutch Research Council and the Dutch Ministry of Education, Culture and Science.

track and alleviate daily life stress, ultimately improving overall health

Coordinating Researcher/PI

Prof. dr. Brenda Penninx

and well-being.

EXECUTIVE SUMMARY

Team

In our first SiA year, we extended the consortium to 81 researchers and staff members. The Stress in Action consortium was initially formed as a team of 25 senior researchers who encompass a diverse range of expertise in the fields of genetics, psychiatry, internal medicine, psychology, sociology, longitudinal data analytics, machine learning, engineering, and interaction design. In 2023, 14 mid-career researchers joined the consortium, all experts in the aforementioned fields.

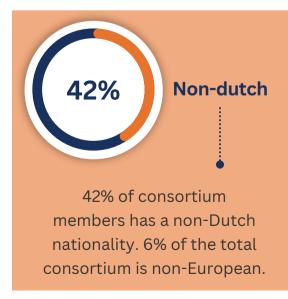
We hired 16 PhD students and five postdoctoral researchers through the SiA grant and an additional seven PhD students and two postdoctoral researchers were added through in-kind arrangements. Also, two data managers, five research assistants and two local project secretaries have been hired to ensure the efficient organization and analysis of our research data. Finally, our project office comprising of a project manager, a communications officer and a project assistant, was established.

We are excited to have created a balanced and diverse consortium within our first year (63% female, 42% non-Dutch, members with 19 nationalities). The hired junior researchers have all started their research projects as can be seen in the Appendix where their first study activities are described.

Consortium members



Nationalities



PhD students



Consortium meetings

In 2023 we hosted two full consortium meetings which provided a great opportunity for all consortium members to share their progress and learn from each other's projects.

The first meeting in June with over 60 researchers saw lots of interactions in different group compositions that helped us get to know each other and exchange ideas about first research ideas and collaborations. At this meeting we had the privilege of hosting our Scientific Advisory Board (SAB) who provided feedback and direction on our first phase of the research.

The second meeting in December concentrated on addressing the feedback we had received from our SAB members. This meeting aimed to foster integration by discussing our common terminology, hosting in-depth discussions around how each researcher will contribute to the central research aim and discussing the differences in between- and within-subject variability.

Monthly online lab meetings

Stimulating collaboration and integration between all consortium members is one of the main goals of SiA in this starting phase. Therefore, we started organising monthly online SiA lab meetings, which provide a platform that will encourage more integration and exchange between the researchers from the different research teams and institutes. The online SiA lab meetings consist of sharing general SiA news and updates, a senior expert lecture and two junior lectures with recent SiA research findings. In view of the SAB suggestion that we form a tight community, we strongly encourage all consortium members to join the monthly lab meetings.

In November 2023, we hosted our first lab meeting and have planned eight meetings to be held in 2024.



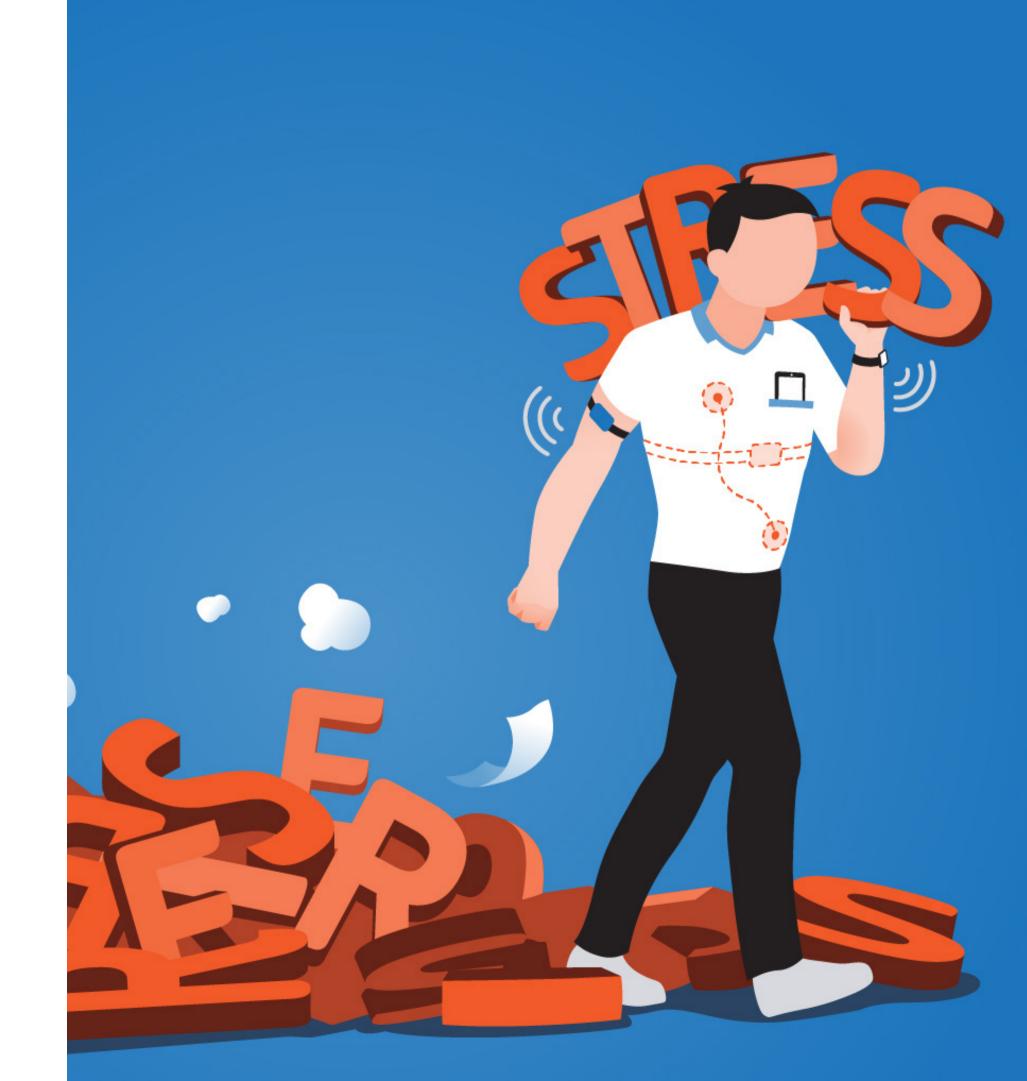


OVER-ARCHING GOAL

Stress in Action capitalizes on the fast advances in technology and big data analytics to move stress research from the lab to daily life. A theoretical framework of daily life stress will be developed using the novel insights from ambulatory assessments in large, long-running Dutch cohorts and from experimental validation studies.

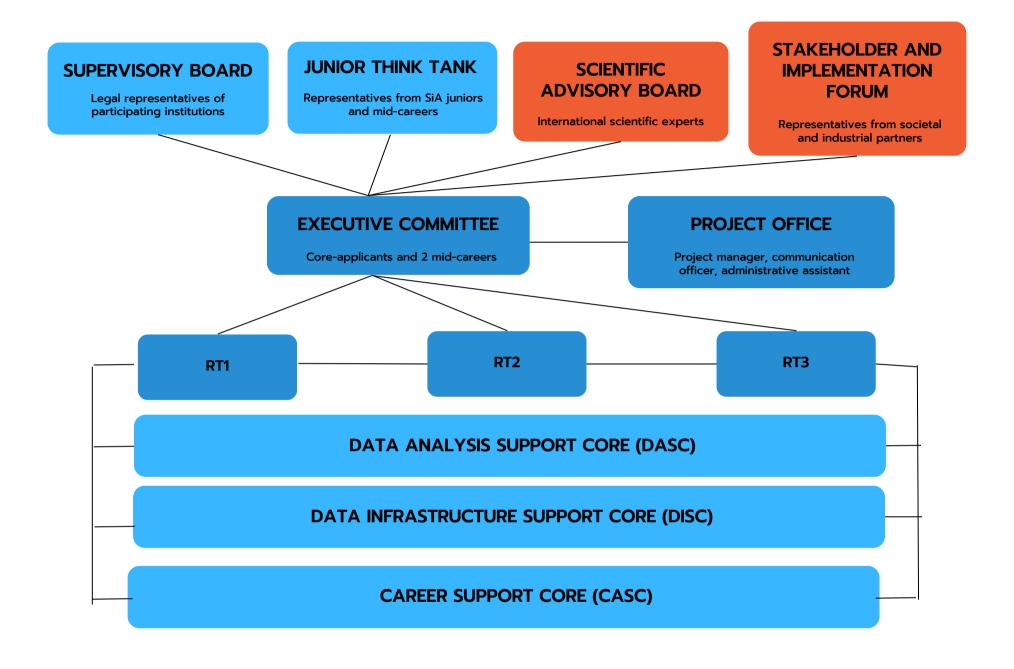
This generates novel, mechanistic understanding of:

- 1. How responses to daily life stress arise from the temporal, dynamic interplay between context and person-specific factors.
- 2. How daily life stress can be reliably measured in a specific individual in real-time.
- 3. How and when potential beneficial stress-response mechanisms turn into detrimental effects on mental and cardio metabolic health. This will enable the development of novel monitoring and intervention strategies to track and reduce daily life stress and its health impact.



ORGANISATION

Our first SiA year served to establish a clear organisational structure within our consortium. All research theme and support core groups started their activities, as can be read in this annual report. In addition, the Executive Committee, the Scientific Advisory Board and the Junior Think Tank were established and had their first meetings (see next pages). In 2024, we will have our first Supervisory Board meeting and work on setting up a stakeholder implementation forum.



















RESEARCH THEME 1: STRESS IN CONTEXT

The primary objectives of Research Theme 1 (RT1) are to 1) develop a comprehensive evidence-based theory of daily life stress, 2) determine the key contextual factors in the aetiology of daily life stress, and 3) test how these stress responses are moderated by evoking/buffering environmental factors and person-specific vulnerability and resilience characteristics.

In 2023, we appointed two PhD students and one postdoctoral researcher. We worked on the development of an (online) Stress wiki, in which we collect summaries of important concepts and theories from stress research. We envision that the Stress wiki will grow from a platform for wider collaboration and knowledge sharing within SiA to a publicly shared, and authoritative source on stress theory.





Interactive presentation of RT1 during the consortium day in December 2023

A key milestone was the successful provision of the interactive session 'Concept mapping and discussion of core concepts and definitions within the SiA project' at the consortium meeting in December. This session was organized to tackle the challenge of defining a common 'stress' nomenclature. We are currently synthesizing the input and reflections from all consortium members in a 'SiA Manifesto', to be used as a guideline by the consortium members, and will prepare a publication on this manifest for an international audience.



Interactive presentation of RT1 during the consortium day in December 2023

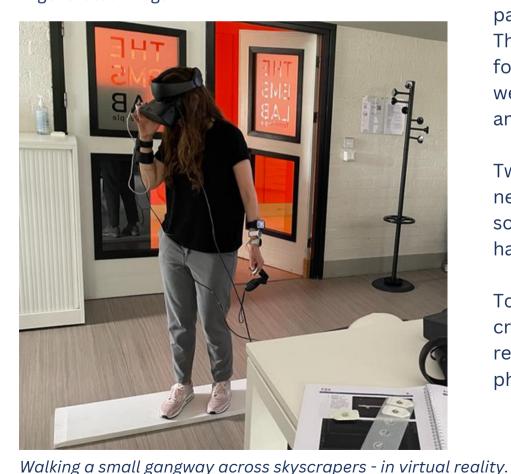
Moreover, we collectively started with three reviews:

- 1. An umbrella review on theories, hypotheses, and models describing the relationship between stress exposures, stress responses and mental health.
- 2. A systematic review of original longitudinal studies on stress and mental health.
- 3. A systematic review of the conceptualization, classification and contextualization of daily life stressors as a first step towards the development of a taxonomy of stress exposures in modern life. Next to these Stress wiki and review activities, we started with an empirical article to test the stress generation hypothesis in relation to mental health.

Next year

In 2024, we will mainly focus on the wiki, the reviews and the initiated empirical research activities. Two new PhD students will start: one to address the topic of stress responses and cardiometabolic health (in collaboration with RT3) and another one to address the measurement of daily life stressors and contextual factors (in collaboration with RT2).

Measuring the 'fight-flight' response with wearables. Al generated image



UTwente BMS lab.

RESEARCH THEME 2: STRESS ASSESSMENT AND INTERVENTION

The aim of Research Theme 2 (RT2) is to develop increasingly sophisticated versions of a cutting-edge, low-burden, ecologically valid ambulatory assessment toolkit to quantify stress in daily life. In 2023, RT2 appointed six PhD students and two postdoctoral researchers to design an ambulatory assessment toolkit to quantify stress in daily life. We have been working on various tasks aiming to develop an ambulatory assessment toolkit.

We created the Stress in Action wearables database (SiA-WD) of wearable ambulatory monitoring devices, which are both consumer and research-oriented, with a comprehensive overview of 30 aspects relevant for research purposes (e.g., signals/variables assessed, participant burden, cost, practical use issues and scientific validity). The SiA-WD will facilitate the selection of the most suitable devices for the upcoming cohort studies that measure stress in daily life, as well as provide the best candidate devices for subsequent in-lab and ambulatory validation.

Two lab-based validation pipelines for wearable stress sensors have nearly been completed (local lab design, protocol, hardware, software, instructions), and umbrella ethical permission requests have been submitted.

To correct the physiological stress effects for confounders, we created new algorithms to compute adjusted physiological stress reactivity scores that account for the many changes in posture and physical activity occurring in daily life.

Responsible design of wearables: The inclusion and initial analysis is finished for a narrative review on current insights into how people wear, use and experience wearables that offer some form of stress feedback and management.

Next year

In 2024, we aim to continue developing the toolkit by expanding our team and focussing on our ambitions and deliverables. Our plans are as follows:

- 1. In January 2024 a new PhD student will start on the cognitive stress response.
- 2. Create an online forum study which investigates current users' attitudes towards stress management technology.
- 3. Launch the SiA wearables database (version 1.0 beta) as part of the publication on the database.
- 4. Use our validation pipeline to examine the most promising low-burden wearables for inclusion in the large cohort studies in phase II of Stress in Action.
- 5. Provide proof of concept for new ambulatory monitoring technology.
- 6. Recruit a PhD student to work on the validation of contextual assessments relevant for the stress response in daily life.
- 7. Publish the seven papers currently in preparation.





RESEARCH THEME 3: STRESS IMPACT ON HEALTH

Research Theme 3 (RT3) investigates the impact of daily life stress responses on mental and cardiometabolic health. The focus is on both positive (wellbeing, normotension) and negative (depression, anxiety, cardiometabolic disease, obesity) health outcomes. We will can collaborate across databases and synchronize their stress examine potential moderation by personal factors like early-life stressors, sex and genetics and mediation through multi-omics analyses. Finally, we seek proof-of-concept evidence on how interventions targeting daily stress can positively influence health outcomes.

In 2023, we appointed ten junior researchers (nine PhD students, one postdoctoral researcher), and an additional seven junior researchers (five PhD students, two postdoctoral researchers) were embedded with in-kind resources. Researchers have started to analyse existing data from our cohort and intervention studies to gain a deeper understanding of 1) how daily life affect and behavioural responses (VU Amsterdam and Erasmus MC) and 2) physiological stress measures and genetics (Amsterdam UMC, UMC Groningen and Erasmus MC) are linked to mental and cardiometabolic health.

Most junior researchers have progressed to data analysis or even writing stages. A first SiA article, reviewing and meta-analysing hair cortisol and cortisone levels with cardiometabolic health outcomes. has recently been published in a high-ranked peer-reviewed journal (PMID: 37926862, Ref. 1).

In 2023 there were two physical RT3 meetings, attended by over 20 persons, in which we specifically addressed how individual projects contribute to the overall RT3 aims and how individual researchers assessments.

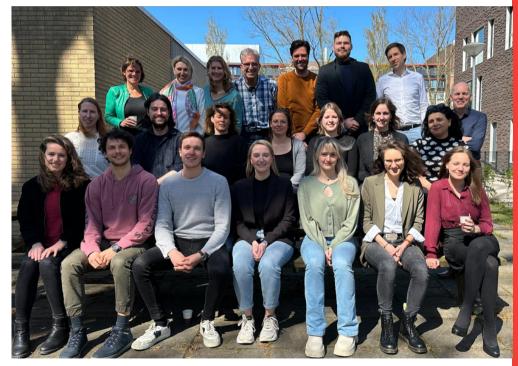
In addition to within-RT3 collaborations, first collaborations with other SiA research groups have also started. For instance, Robin Lengton (Erasmus MC, RT3) and Myrte Schoenmakers (VU Amsterdam, RT2) are currently writing a review regarding the stress-obesity connection and relevant opportunities offered by novel stress measures in this context. In addition, there is a collaborative effort of various SiA members across RT2 and RT3 to examine the cross-talk between autonomic nerve activity and the HPA-axis output using dense sampling of both systems in daily life using new ambulatory monitoring solutions (low burden impedance cardiography paired to a portable micro dialysis system) in a diverse population.

Next year

For 2024, we expect that RT3 will deliver more individual project results and papers that will point towards the most important daily life stress response measurements that determine mental and cardiometabolic health outcomes. Results will contribute to improve decision making regarding data enrichment in a later stage of the SiA project.



Measurements of glucocorticoid sensitivity in blood samples



Group picture of all RT3 members in Amsterdam in April 2023

Ref. 1: Long-term glucocorticoids in relation to the metabolic syndrome and cardiovascular disease: A systematic review and meta-analysis. Kuckuck S, Lengton R, Boon MR, Boersma E, Penninx BWJH, Kavousi M, van Rossum EFC. J Intern Med. 2024 Jan;295(1):2-19. doi: 10.1111/joim.13739. Epub 2023 Nov 5. PMID: 37926862.



DATA ANALYSIS SUPPORT CORE

The Data Analysis Support Core (DASC) aims to help SiA researchers make use of optimal analytic strategies in their research. This requires an alignment between one's research question, data, and analytical technique. Hence, the DASC is concerned with:

- 1. Raising awareness about how to best align these components of empirical research and how to make methodological decisions.
- 2. Identifying data analytical challenges and developing new techniques to tackle these, by innovating the individual techniques and by combining dynamic modelling and machine learning techniques.

Thus far, the DASC has been meeting once every month (online) to discuss ideas, progress, and challenges. Specifically, we:

- Start the meeting with one of the DASC researchers presenting their work (e.g., about survival analysis) to allow DASC researchers to learn from/about each other's expertise.
- Allow the PhD students and postdoctoral researchers to discuss their activities.
- Discuss questions that have arisen in the RTs that DASC members are part of or that have been posed directly to the DASC via email or Slack (e.g., questions about nested cross-validation and the random intercept cross-lagged panel model).

In 2023, four PhD students and one postdoctoral researcher started within the DASC. They currently work on:

- Jointly modelling longitudinal and survival outcomes through the Super Learner paradigm to optimize predictions.
- Techniques that can detect overfitting in dynamic modelling.
- A combination of vector autoregressive modelling and joint modelling for better predictions.
- Ability to explain deep learning models, especially in the context of time series data.
- Using machine learning to aid causal inference from both longitudinal panel data and intensive longitudinal data.

Because each senior DASC member is also part of one of the three RTs, short lines of communication to other teams are guaranteed. The DASC members have also been sharing insights regarding important methodological issues at the SiA consortium meetings. For instance, we have had group discussions about the kind of questions SiA researchers try to answer (e.g., description, prediction, explanation) and the crucial role of timescales in gathering and analysing data. Furthermore, a presentation was given about the importance of separating within-person processes from betweenperson differences.

Next year

In 2024, we aim to develop our connections within the consortium and foster exchanges between the DASC and the RTs (e.g., through courses and workshops, but also consultation). Furthermore, we want to explore how the DASC and the DISC can cooperate in the future.

DATA INFRASTRUCTURE **SUPPORT CORE**

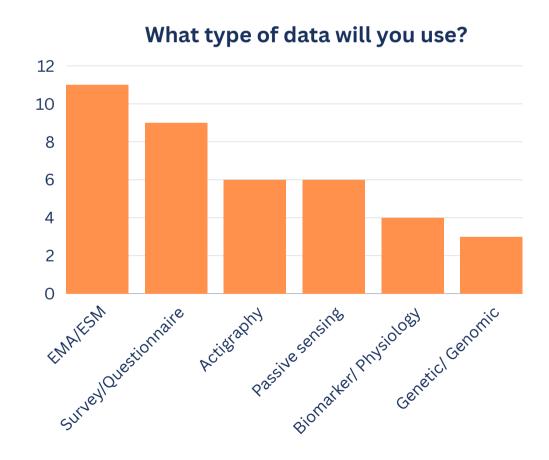
The overall goal of the Data Infrastructure Support Core (DISC) is to provide a central coordinating hub for data collection, data management, and data delivery processes within Stress in Action. In phase I, the DISC catalogues the existing datasets and provides meta-data annotation. In phase II, we will create the Data Governance Framework and the Standard Operational Procedures for the new data collection.

Members of the DISC are also part of RT2 and RT3, and as such we are well connected with other groups allowing for good alignment of DISC products and RT members' needs.

studies 703 **EMA items** 5593 subjects

EMA data inventory

DISC has done an inventory on EMA studies. Currently, we have 8 studies catalogued. They have collected 703 EMA items in 5593 subjects.



Progress year 1

- We have used a survey amongst consortium members to see what data sources are needed in phase 1 (see figure 1).
- We have released a first version of the inventory of existing Ecological Momentary Assessment (EMA) items and provided a harmonization scheme.
- We have started the inventory of existing Actigraphy datasets and providing a harmonization scheme.
- We have updated the Data management plan (DMP) and resubmitted to NWO.



Next year

In 2024, a new postdoctoral researcher will be hired to expand the cataloguing of existing survey/questionnaire data (in particular exposure and health outcomes) and the conceptual harmonization process following the SiA manifesto on a joint terminology of concepts. We will create a list of cohort contact details and a collection of guidelines for cohort-specific data access procedures. The latter collection is a starting point for the phase II SiA Data Governance Framework and the Standard Operational Procedures.

The eight studies catalogued are NESDA, MARIO, REAL-HEARING, three EMA Well-being studies of NTR, RADAR (v3) and the Grow it! covid studies.

Figure 1. DISC survey results revealed that in phase I most people will work with EMA data and actigraphy, starting to harmonize these data should have priority

CAREER SUPPORT CORE

In 2023, the Stress in Action consortium was extended with 16 new PhD students and five new postdoctoral researchers. The Career Support Score (CASC) aims to stimulate the careers of these early-career scientists in order to let them excel and grow into well-trained stress scientists. So far, the CASC has provided the following activities:

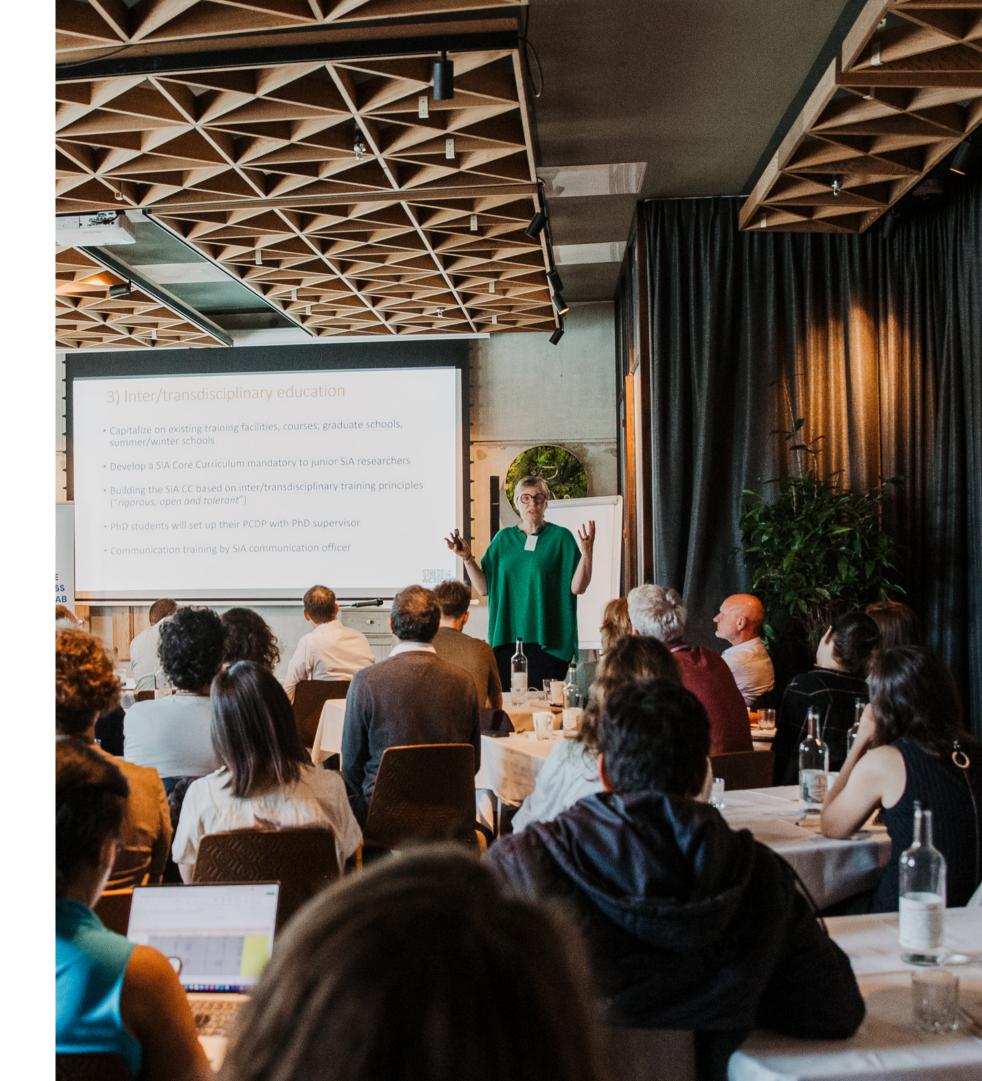
All early-career scientists received a personal onboarding by the project manager in order to teach them about the project's structure, management and (internal) communication.

An inventory of the standard support and mentoring activities provided by the academic institutes has been created. This shows what the universities and UMCs already offer to early-career scientist. Based on this, the CASC will discuss what additional needs the early-career scientists have in terms of support and mentoring from within the consortium.

A living document with relevant (postdoctoral) courses has been set-up and shared with all consortium members. This is constantly updated with new information.

CASC is working on setting up a postdoctoral course for stress research to be held in 2024. In interaction with the Junior Think Tank, the course programme is currently being developed.

CASC stimulates and oversees the SiA exchange programme. Early-career scientists will be stimulated to spend time abroad at another academic institute during their career. There is a bit of financial support for this, when needed.



GOVERNANCE







EXECUTIVE COMMITTEE

The Executive Committee (EC) is made up of the senior researchers, who were the core applicants and are now the principal investigators on behalf of their institutes, and two mid-career researchers. The Executive Committee played a pivotal role in the first SiA year in; overseeing consortium composition and organization of consortium meetings, discussing adequate interaction between institutes, the progress within RTs/SCs, and all matters regarding communication.

In 2023, we had ten EC meetings, with two meetings on locations in Groningen (UMC Groningen and University of Groningen) and Enschede (University of Twente) where facility tours and interactions with deans and other researchers of participating departments were organized.



BRENDA PENNINX

Professor of Psychiatry and Epidemiology

Amsterdam UMC



ECO DE GEUS

Professor of Biological Psychology

VU Amsterdam



PETER DE JONGE

Professor of Developmental Psychology University of

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UTE BÜLTMANN

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LIESBETH VAN ROSSUM

Professor of Medicine

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MANON **HILLEGERS**

Professor of Child and Adolescent Psychiatry

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MATTHIJS NOORDZIJ

Professor of Health Psychology & Technology

University of Twente



FEMKE LAMERS

Associate Professor

Amsterdam UMC



LAURA **BRINGMANN**

Associate Professor

University of Groningen

SCIENTIFIC ADVISORY BOARD

Stress in Action has invited a team of experts within our fields of research from across the world, to take part in our Scientific Advisory Board (SAB). During the consortium meeting in June 2023 the SAB joined us in Amsterdam. On the first day the Scientific Advisory Board was introduced to the project and presented their backgrounds and expertise. Over the following two days the SAB members joined presentations from the RTs and SCs and provided feedback to the challenges each group had encountered. On the last day, the SAB members held a closed session where they discussed their feedback and advice, which were then shared with the whole consortium.

The SAB was impressed with the ambitions of SiA. They offered guidance and advice to ensure that our project is well-integrated and remains at the forefront of scientific innovation. The feedback and guidance provided by the Scientific Advisory Board will play a crucial role in ensuring that SiA continues to progress in the right direction.



PROF. JOSHUA SMYTH

Ohio State University,
USA; Psychology, and
president of the
Society for Ambulatory
Assessment



PROF. VIOLA VACCARINO

Director at Rollins
School of Public
Health, Atlanta, USA;
Behavioural medicine
in cardiology

PROF. PETER KUPPENS

University of Leuven,
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statistical methodology
for ambulatory
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PROF. MARCELLA RIETSCHEL

Central Institute of
Mental Health,
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Genetics



PROF. MATTHIAS MEHL

University of Arizona, USA; Ambulatory research methods



University of
Düsseldorf, Germany;
Sociology, Work stress
models



SUPERVISORY BOARD

In our first year we invited seven deans from each institute to join our Supervisory Board. The Supervisory Board (SB) will meet once a year, starting in 2024, and will play a crucial role in guiding and supporting the Executive Committee (EC) as they integrate Stress in Action within participating institutions and faculties.

At the yearly meeting, the SB will monitor the quality and scientific progress of SiA, assessing the need for adjustments in structure, scientific direction, and consortium composition. The SB will evaluate and approve changes to the consortium's composition and the new annual budget proposed by the EC. In case of unresolved conflicts, the SB will make final decisions through majority voting. Additionally, the SB will be committed to systematically embedding SiA programme activities within participating institutions.



PROJECT OFFICE

GOVERNANCE

To support Stress in Action, we have hired dedicated project staff, including a project manager, communications officer, and project assistant. These individuals play a crucial role in coordinating our activities, managing communications channels, and providing administrative support.

They organise and manage the weekly meetings with the management team where all operational SiA tasks are discussed. These range from organising all consortium and executive committee meetings to onboarding our newest researchers to creating and managing all the communications channels such as the website.



Anna Silvestrin, Project manager Anouk Weverling, Communications officer Marianne Knudsen, Project assistant

JUNIOR THINK TANK

The Junior Think Tank (JTT) was established in June 2023 to represent and support the PhD candidates and postdoctoral researchers (postdocs) of SiA. It provides both solicited and unsolicited advice to the Executive Committee (EC) and the Career Support Core (CASC) on matters that impact the work, and wellbeing of junior researchers. Currently, the JTT consists of seven members, representing all universities and research teams (including the DASC) involved in SiA: Merel van den Berg (PhD, RT2, UT), Lino von Klipstein (postdoc, RT1, RUG), Robin Lengton (PhD, RT3, Erasmus MC), Jeroen Mulder (postdoc, DASC, UU), Felix Reichelt (PhD, RT3, UMCG), Marcos Ross (PhD, RT2 and RT3, Amsterdam UMC), and Melisa Saygin (PhD, RT2, VU).

The JTT holds monthly meetings in which developments and plans for PhDs and postdocs within SiA are discussed. In 2023, important topics included (a) the creation of a SiA expertise page, which contains an overview of the each SiA-member's main area of expertise, and can serve as a basis for collaborations; (b) issuing a survey amongst junior researchers to get an overview of workshop topics that are of interest; and (c) providing feedback on suggested CASC activities for junior researchers, which included the setup of an exchange programme, and a SiA summer school.

Within the CASC and the EC, many of the plans for supporting junior researchers are still in development. For the year 2024, JTT will continue providing feedback on these plans, and help with implementing them in a manner that is supportive for PhDs and postdocs. To this end, we will hold a meeting with the EC in 2024. The JTT will also suggest plans on its own discretion when it has ideas how to improve the working environment of juniors. Particular focus areas include fostering collaborations among junior researchers, and creating plans for disseminating work by PhD's and postdocs.

Members of the Junior Think Tank 2023

Jeroen Mulder, Robin Lengton, Felix Reichelt, Marcos Ross, Lino von Klipstein, Merel van den Berg and Melisa Saygin.



FINANCE

In the first year of the project, Stress in Action budgeted a total of € 2.949.973. Of this total, € 2.727.338 was designated for Personnel Costs and € 222.635 for Material Costs.

The first year is characterized by underspending, which was expected by projecting the experience of longerrunning Gravitation grant programmes on SiA. The main reason for underspending was that personnel were hired during the course of the year and were not employed from the beginning of 2023.

While overall spending was lower than planned, the pattern of spending closely followed the predicted pattern in the 10year budget scheme. This means that in the budget plan for 2024, no repairs or transfers between cost categories are required.

Percent of the budget used in 2023

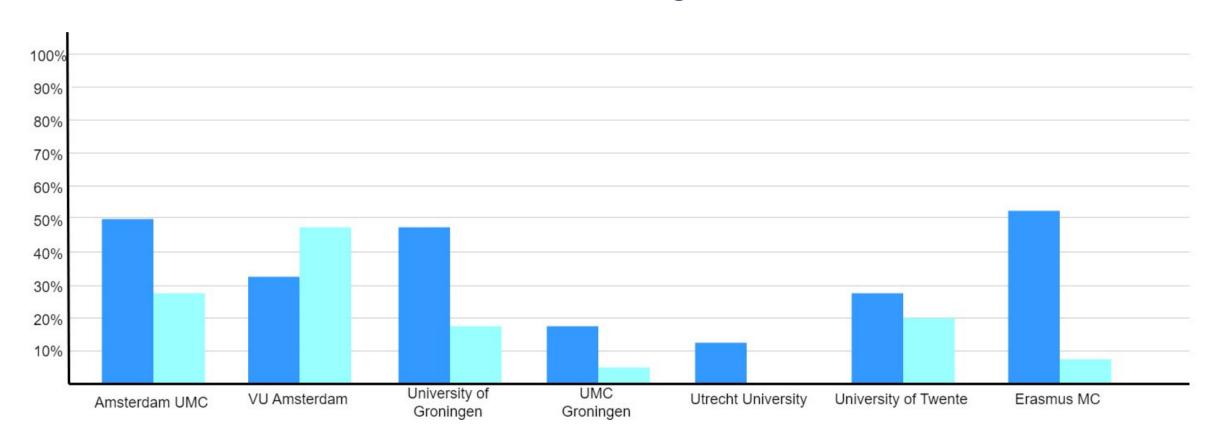


Figure 2. The graph depicts the percentage of the budget allocated for the year 2023, that has been utilized by each institute.



COMMUNICATION & DISSEMINATION

In 2023, our main objective was to lay a solid base of internal communication, community and knowledge transfer in order to be successful in external dissemination. Therefore, in 2023 our focus was on internal dissemination. We have done this in various ways, some of which will also serve external goals. The Stress in Action website and social media platforms (X, LinkedIn) are serving either the internal and external audience, whereas the newsletter, lab meetings and consortium meetings serve an internal audience.

In internal meetings we aim to share updates on projects, progress, results, events, new colleagues and encourage community building. The lab meetings are hosted monthly in an online setting. However, the physical consortium meetings, are hosted on location twice a year (two days in June and one day in December) to foster and encourage connection within the consortium, improve collaboration and allow the opportunity for socialisation.. Apart from the meetings we share the latest news and updates in a monthly newsletter.

Stress in Action aims for all consortium members to become engaged in (inter)national dissemination of research results.

On the website and social media, we aim to actively spread information about the objectives, approach, and results of our research to the broader scientific community and to the general public thereby raising interest in, understanding of, and support for our science goals and results in general. Apart from a complete listing of our open access scientific publications, in 2024 we will see the start of dissemination of SiA products like a searchable database of stress wearables, the Stress wiki, and a number of data analytic scripts.

HIGHLIGHTS

In 2023 we have celebrated some great highlights of scientific and societal activities, of which we are very proud to share with you.

The Stress in Action consortium was initially formed as a team of 25 senior researchers. In our first year, we extended the consortium to 81 researchers and staff members.

The annual meeting of the international Society of Ambulatory Assessment (SAA) took place in Amsterdam, organized by prof. dr. Eco de Geus. Its central theme was Stress in Action, and many SiA consortium members presented during this meeting.

The first SiA paper was published. Long-term glucocorticoids in relation to the metabolic syndrome and cardiovascular disease: A systematic review and meta-analysis. Kuckuck S., Lengton R., Boon M.R., Boersma E., Penninx B.W.J.H., Kavousi M., van Rossum E.F.C. J Intern Med. 2024 Jan;295(1):2-19.

We held two well-attended consortium meetings. At the first meeting in June we were happy to have great discussions and feedback from the members of our international Scientific Advisory Board.



Award ceremony of the Gravitation projects by dr. Robbert Dijkgraaf, minister of Education, Culture and Science, in 2022

MEDIA

In 2023, many consortium members featured in newspapers, radio, websites and other media, indicating the relevance and impact of our research into stress.

Manon Hillegers - 'Generatie Z(en) Stress en Gezondheid', Podcast Stadswandelingen, 14 June 2023

In an episode of <u>Stadswandelingen</u> titled 'Generation Z(en) Stress and Health' Prof. Dr. Manon Hillegers (Erasmus MC) talks about her research on stress. Core questions are discussed like what is stress? What are the causes of stress? Is stress positive or negative? Hillegers talks about Stress in Action and how the city of Rotterdam (and other cities) will serve as a lab for our study where stress in daily life will be measured and studied.



Brenda Penninx – 'Miljoenen voor wetenschappelijk onderzoek naar stress', NPO Radio 1, 3 May 2022

In May 2022 the Dutch Research Council (NWO) has announced the awarded projects of the Gravitation Grant. One of the Gravitation projects is Stress in Action. Stress in Action will receive 19,6 million euros for the next 10 years. Live at NPO Radio 1, PI of the project prof. dr. Brenda Penninx explains that Stress in Action aims to measure stress in daily life and to learn more about stress on a personal level, looking at various factors like emotional, cognitive, physiological and behavioural stress responses.

Bertus Jeronimus - 'De Stressgeneratie', OOG Groningen, 21 September 2023

During a lecture 'The stress generation' the main question addressed was 'How to grow up stressfree?' This question was discussed by a Dutch author of young adult books, Francine Oomen, and SiA researcher Bertus Jeronimus. The lecture was held at Forum Groningen and covered by the regional news OOG Groningen.



Christiaan Vinkers - 'What is burn out?'

There is a lot of media coverage on the topic of stress, it is a buzzword in modern life. SiA researcher Christiaan Vinkers, professor of stress and resilience, is a popular guest in various media coverages on this theme. This year, Vinkers recorded an explainer video on stress with the Brain Foundation (Hersenstichting) and another one on burn out with Amsterdam UMC. He has also appeared in other TV programmes, such as an episode about burn out by Kassa (BNNVARA).

AWARDS, GRANTS & PROMOTIONS

Prof. dr. Matthijs Noordzij was appointed professor in Health Psychology and Technology at University of Twente after successfully completing his inaugural lecture on the 12th of October 2023.

Prof. dr. Meike Bartels (Professor of Genetics and Well-being, VU Amsterdam) received a VICI-grant from the Dutch Research Council (NWO). Bartels will use this grant to research a better understanding of the causes of differences in happiness and well-being.

Prof. dr. Geke Ludden was appointed Professor in Interaction Design (University of Twente). Her inaugural lecture will take place in 2024.

Prof. dr. Liesbeth van Rossum (Professor of Medicine, Erasmus MC) received the 'Christina Fleetwood Award' of the European Coalition for people living with obesity (ECPO) for communication and research concerning the obesity stigma at the European Congress of Obesity. This widespread societal stigma is one of the major stressors many patients with obesity suffer from.

Two SiA colleagues were promoted to assistant professor: dr. Iris Arends and dr. Mariëtte Boon. Prof. dr. Liesbeth van Rossum (Professor of Medicine, Erasmus MC) is part of the OBCT project which received an EU Horizon Grant. This project aims to support sustainable prevention of obesity. A substantial part of this project is stress measurements.

Dr. Femke Lamers (Amsterdam UMC) was promoted to Associate Professor.

> Yong Zhang (PhD student, University of Groningen) has won the Jan Brouwer thesis prize for the category behavioural science.

Prof. dr. Susanne Scheibe (Professor in Organisational Psychology, University of Groningen) received a COST Action grant for her project 'LeverAge': A European Network to Leverage the Multi-Age Workforce.

Dr. Maryam Kavousi (Associate Professor, Erasmus MC) received a 'Heart 4 Women Award' for her research on women's health. Kavousi will work on innovative research into the influence of stress and psychosocial factors on cardiovascular disease in women.



Prof. dr. Monique Tabak was appointed Professor in Personalised eHealth Technology (University of Twente). Her inaugural lecture will take place in 2024.

Dr. Mariëtte Boon (Assistant Professor, Erasmus MC) was awarded a Senior Fellowship from the Dutch Diabetes Foundation. This grant enables important diabetes research in the Netherlands. Boon's research focuses on the role of stress hormones in type 2 diabetes.

SWOT ANALYSIS

Strengths

- Funding for long-term research without distraction,
- Top tier researchers who are strongly committed,
- Rapid growth of a diverse consortium in first year with strong governance structure,
- Many new cross-institute connections due to (1) mixed PhD supervisory teams,(2) exchange of datasets, (3) shared terminology and (4) harmonization of cross-lab experimental approaches to stress measurement.

Weaknesses

- Risk of disconnect between individual projects and overall project aims,
- Geographic & organizational distribution of the team,
- Stakeholder interactions not yet developed.

Opportunities

- Importance of theme of stress further increased with societal insecurity about the maintenance of standards of living due to geopolitical developments, climate change, and reduced social cohesion and challenges related to migration,
- Increased interest of the public in self-monitoring,
- Much common ground with relevant other gravitation programmes, NWA (Dutch Science Agenda), programmes and international stress networks
- Advances in applications of 'AI for health' in academia and beyond.

Threats

- Local rules and research climate sometimes oppose crossinstitute collaboration,
- Financial risks as salary raises and overheads are higher than expected,
- Medical-ethical and privacy regulations make ambulatory monitoring for research more complicated,
- Talented junior staff moving away due to limited tenured positions in academia,
- Governmental pressure to reduce international students and staff.







APPENDIX PHD/PD PROJECTS

George Aalbers Postdoctoral researcher, Amsterdam UMC



"To what extent can we predict the presence of depression and/or anxiety disorders from smartphone- and wearable-based data, and what are the most important features for doing so?"

In three studies I will apply an explainable machine learning approach to multi-modal Dutch and international cohort data, quantifying the link from smartphone- (location, phone use, in-app surveys) and wearable-based (sleep, physical activity) data to gold-standard measures of depression and anxiety disorders. By combining feature selection with cross-validation and explanation of machine learning models, I aim to identify behavioural predictors of psychiatric status that might be useful for monitoring daily life stress.

Merel van den Berg, PhD student, University of Twente



"How can we establish standards for responsible design of technology for stress monitoring and interventions?"

I am working on a narrative review that captures users' needs and concerns, ways to consider these in the design process, and corresponding design recommendations. To better understand the lived experiences of end users, I conduct an explorative study on user attitudes towards (wearable) stress management technology. An example of a relevant information source is a forum thread where users exchange their experiences with the stress tracking feature of the Garmin smartwatch. Results of these two activities will contribute to developing user-centered technology for stress monitoring and interventions, and establishing guidelines for responsible design.

Caroline Broeder, PhD student, Amsterdam UMC



"Does 1-week add-on treatment with the GR-antagonist mifepristone improve stress system dynamics in adults with depression following childhood trauma?"

Childhood trauma significantly impacts the risk and course of stress-related disorders, including depression. With this randomized clinical trial I investigate the effects of 1-week addon treatment with the GR-antagonist mifepristone on stress system dynamics in adults with depression following childhood trauma. Stress system dynamics will be assessed using resting-state and task-based functional magnetic resonance imaging (fMRI), salivary cortisol and alphaamylase, subjective stress and mood during the acute (0-40 minutes) and recovery phase (60-100 minutes) of psychosocial stress before and 6 weeks after treatment. If effective, this would be the first hypothesis-driven drug treatment for depression following childhood trauma.

Shannon Dickson, PhD student, Erasmus MC



"Can we identify risk for emotional problems at a much earlier stage using experience sampling and daily diary methods?"

The advent of mobile technologies has facilitated real-time studies of individuals' emotions, behaviours, and interactions in their daily lives, such as through experience sampling methods. Risk factors can be classified as static or dynamic. Static risk factors are fixed and unchanging, measured at a single time-point, while dynamic risk factors fluctuate over seconds to hours and are best measured at multiple time-points throughout the day. Using cutting-edge technology to monitor real-time emotions, behaviours, and interactions of adolescents and emerging adults (aged 12-25), I will develop a theoretical framework of static and dynamic risk factors for emotional problems that is empirically verified using real-life data. My longer-term goal is to develop a new toolbox with to monitor real-time functioning of adolescents with smartphone apps and create a centre of methodological and clinical expertise around experience sampling methods. This allows us to identify whether a given individual is at risk in real-time, in real settings, leading to earlier diagnostics.

Nina van Gerwen, PhD student, Erasmus MC

"Does ensemble learning lead to an improvement of prediction accuracy in settings with both longitudinal and time-to-event outcomes?"



In biomedical statistics, it often occurs that data consists of both time-to-event outcomes (e.g., time to death) and longitudinal outcomes (e.g., biomarker values measured annually), and then the interest lies in estimating a patient's survival probability. There are currently diverse methods available to analyse this type of data. In this study I explore whether combining these different techniques through stacking, an ensemble learning technique from machine learning literature, can lead to an improvement in the prediction of survival probability.

Lino von Klipstein, Postdoctoral researcher, University of Groningen

"How is stress conceptualized in the existing theoretical literature?"

RT1 is tasked with developing a new extendible framework that conceptualizes stress as resulting from continuous interactions between key environmental exposures and four subsystems: emotions, cognitive appraisal and regulation strategies, physiological responses, and behavioural reactions. To start this process, I am performing a scoping review of existing stress theories in the literature. An important goal of this review is to distinguish between theories that describe differences between people versus processes within people and (where possible) to identify the timescale within-person processes are thought to take place on.

Susanne Kuckuck, PhD student, Erasmus MC

"How do potential vulnerability and resilience factors influence the relationship between stress and cardiometabolic health?"



My project focuses on the relation of biological stress measures with cardiometabolic health, and potential determinants of this association. Recently, we published a systematic review and meta-analysis investigating the association of long-term glucocorticoid levels in scalp hair with the metabolic syndrome and cardiovascular disease. We saw that hair glucocorticoids were closely linked to cardiovascular disease and age might be a potential moderator of this relationship, as the association was strongest among younger individuals. Currently, I am investigating the association of other long-term measures of the daily life stress response in relation to hormonal and behavioural correlates of appetite and eating behaviour, as well as metabolic deterioration. In these associations, I will determine the extent of moderation by sex and age, along with other factors (e.g., socioeconomic position).

Robin Lengton, PhD student, Erasmus MC

"How do novel biological stress measures correlate with daily life stress responses? and what is the relationship between (novel) biological stress indicators and cardiometabolic health status in diverse populations?"



This project focuses on the validation of novel biological stress measures in different populations. Furthermore, daily life stress responses in relation to cardiometabolic health status will be assessed in existing large cohort studies. By assessing the relationship between these measures and cardiometabolic health status, my research aims to contribute valuable insights into the intricate connections between biological stress indicators and cardiometabolic health. My study seeks to enhance our understanding of how these (novel) stress measures can serve as reliable markers for assessing and managing cardiometabolic health, providing a foundation for more targeted interventions and improved health outcomes.

Julius März, PhD student, Erasmus MC

"What are predictors for compliance with the Experience Sampling Method in children and adolescents and how does this compliance affect mental health outcomes?"



Many mobile mental Health (mHealth) interventions use the Experience Sampling Method (ESM), in which participants respond to multiple surveys per day to self-monitor their mental state. It is important to ensure participants compliance with this procedure to ensure mHealth interventions efficacy. My study examines various factors that can impact ESM compliance in children and adolescents and explores how it relates to the development of well-being and positive and negative affect. Hereby, I not only examine compliance as the average number of completed surveys, but also explore different temporal patterns of compliance, and its relation to momentary emotional states.

Malin Meyer, PhD student, UMC Groningen

"What are key daily life stressors and contextual factors in the aetiology of daily life stress responses?"



The main goal of my project is to develop an interdisciplinary taxonomy that conceptualizes, identifies, and contextualizes daily life stressors across multiple life domains (e.g., work, family). Further, my project will identify new daily life stressors that arise from contemporary societal changes (e.g., digitalization of work). The first step towards this taxonomy is an interdisciplinary literature review on the existing conceptualizations, classifications, and contextualization of daily life stressors. With this review I aim to provide an interdisciplinary overview, identify gaps, and integrate knowledge whenever possible.

Jeroen Mulder, Postdoctoral researcher, Utrecht University

"How can we improve causal inference from (intensive) longitudinal data in stress research?"



The website of Stress in Action states that "(...) we aim to gain insight into the causes and consequences of daily life stress, and to provide a path towards more stress-resilient citizens." The investigation of causes, and the development of effect treatments for stress requires robust causal inference methodology. In my postdoctoral project I investigate how machine learning techniques can best be used to aid causal inference from longitudinal, nonexperimental data (both panel data, and intensive longitudinal data). A specific focus is on the estimation of propensity scores for time-varying exposures, which can be used to adjust for time-varying confounding.

Solomiia Myroniuk, PhD Student, University of Groningen

"How is everyday stress (i.e., stressors and stress responses) conceptualized and measured, and what is the pattern of the dynamic associations between daily stress and depression and anxiety disorders?"



To address these questions, I am conducting a series of systematic reviews to map all ambulatory studies on the topic of stress and mental health into a database. My first aim is to provide a general overview of these studies with a special emphasis on the conceptualization and operationalization of stress, the measurement timescale, and the measured stress response components. The second goal is to zoom into the studies that assess depression or anxiety diagnoses, and daily stress. Based on the outcomes of this first overview, future in-depth studies will follow.

Noluthando Ntlapo, PhD student, Erasmus MC

"Is there a bidirectional relationship between depression, anxiety with Atrial Fibrillation?"



My study investigates a bidirectional association between depression and anxiety with newonset atrial fibrillation (AF). Firstly, I analyse the associations of depression symptoms and anxiety with AF using a cox regression model, with depression symptoms and anxiety taken as the independent variables. Then, I analyse AF with depression and anxiety, with AF as the independent variables. Finally, drawing from this, I evaluate causal relationships using a twosample Mendelian Randomisation (MR) method. This will provide a comprehensive understanding of these relationships which currently remains unclear.

Jasmin Pasteuning, PhD student, Amsterdam UMC

"How do daily-life ambulatory assessments of stress response correlate to neuroimaging patterns and lab-induced (acute) stress responses, and are these differential in persons with and without early life trauma?"



In this study I explore the mechanism behind stress dynamics on multiple levels in people with depression and childhood trauma, people without depression and childhood trauma, and healthy controls. We collect imaging (fMRI) and biological data (cortisol, alpha-amylase), as well as ecological momentary assessment and wearables. This way, we are able to study stress dynamics both in a lab-setting after induction of social stress and in everyday life.

Fridtjof Petersen PhD student, University of Groningen

"Can we improve the prediction of health outcomes by taking into account the arising temporal dynamics?"



Joint models allow for dynamic prediction of time-to-event outcomes (such as disease onset or relapse), while taking into account time-varying covariates. As classical joint models are designed for only few longitudinal measurement occasions, we aim to model the covariates via vector autoregressive models. This extension can account for the temporal dependency arising in the intensive longitudinal data from the SiA project (e.g., ESM measure of affect/stress response). Additionally, the derived temporal dynamics can potentially improve the accuracy of time-to-event predictions.

Emma Pruin, PhD student, Amsterdam UMC

"Which continuous indicator of family history has the strongest predictive power of disorder risk?"



Family history is an important factor of individual vulnerability for psychiatric disorders, but how to summarise information about relatives most accurately is unclear. The aim of my current project is to establish the best way of quantifying family history for prediction of mental health outcomes. Through systematic comparison of various indicators and using databases such as Lifelines and NESDA, the best predictor of developing anxiety or depression will be identified. Results can support recommendations of indicators to use for existing data, as well as which family-related data to collect in the future.

Felix Reichelt, PhD Student, UMC Groningen

"How does heritability impact stress exposure, and what insights do gene X stress exposure interactions offer regarding their link to cardiometabolic health?"



In the multigenerational large-scale (N>~160,000) LifeLines cohort, we examined with genetic heritability analysis the extent to which our stress exposures (i.e., long-term difficulties, stressful life events, childhood trauma, loneliness, and lack of social support) can be attributed to our genetic makeup, shared environment and unique environment. Future analysis will focus on the influence of gene X stress interaction analysis on cardiometabolic health.

Marcos Ross, PhD student, Amsterdam UMC

"What is the relationship between ambulatory assessments of cognitive performance and mental health?"



The study explores the association between depression severity and cognitive performance in the context of remote ambulatory assessment. During a follow-up period between one and two years, participants from the RADAR-MDD project provided data every couple of weeks with their smartphone. They answered the PHQ-8 to assess depression severity and played a mobile game called THINC-it to assess cognitive performance, both subjectively and objectively. By using the Random Intercept Cross-Lagged Panel Model, my research will investigate the relationships between these variables at the between-person and within-person levels. Ultimately, it will provide insights for remote assessment of cognitive performance and whether it can be used as a marker for changes in mental health status.

Melisa Saygin, PhD student, VU Amsterdam

"How can we accurately measure physiological stress responses, and furthermore obtain a more precise index of cardiac vagal activity, in daily life using wearable monitors?"



My project involves validation of wearables in daily and laboratory settings to see if autonomic nervous system responses in the face of differing psychosocial stressors, including those personally significant, can be captured. Among the autonomic parameters repeatedly linked with stress, mental and organic diseases comes heart rate variability (HRV). It is delved deeper into controlling for HRV, measured as peak-valley respiratory sinus arrhythmia (RSA), so that phenomena (e.g., speaking, respiratory rate) known to mask the measurement of true vagal tone during stress periods are minimized. Multilevel modelling and machine learning are utilized to test whether stress period identification reliability may be enhanced.

Myrte Schoenmakers, PhD student, VU Amsterdam

"How accurately can the blood pressure (BP) be determined using a continuous, non-invasive monitoring system via the pulse transit time?"



Instead of the ambulatory BP monitoring cuff system, I aim to determine blood pressure values using impedance cardiography, bio-impedance and photoplethysmography techniques that can potentially be used more non-invasively in daily life. In addition, I will also contribute to developing a wearables-database, which is a dynamic, regularly updated overview of available wearable devices which perform continuous measurement of physiological signals. This database provides a method for well-informed selection of a wearable for (stress) research used for the SiA-toolkit that will be implemented in cohorts in a later phase of the Stress in Action project.

Milou Sep, Postdoctoral researcher, Amsterdam UMC

"Is early-life childhood trauma impacting on individual stress system dynamics in persons with major depressive disorder?"



My project measures emotional, behavioural and physiological stress responses in daily life over time in persons with major depressive disorder. The impact of childhood trauma exposure (present in about 50% of all depressed patients) on differential stress system dynamics will be evaluated. I will also examine if we can better understand individual variation in stress-related symptomatology via multimodal interactions of different stress system components.

Magdalena Sikora, PhD student, University of Twente

"How to support the selection process of wearable devices for monitoring the physiological stress response in daily life?"



Considering the rapid developments in the field of wearables and the high number of new devices coming into the market, selecting the best wearable for monitoring the physiological stress response in daily life remains challenging. It is therefore my aim to develop and continuously maintain a database with wearables which will allow researchers to browse, compare and select the most suitable device for their study. Next to technical information on the device, the database will include other research-relevant information, such as validity, usability or information on access to raw data. The database will be available online as a selection tool.

Artemis Stefani, Postdoctoral researcher, VU Amsterdam

"What is the best possible and most reproducible pipeline for stress wearable validation?"



The measurement of stress in daily life requires tools that accurately and reliably quantify physiological responses. Commercial wearables that are used to measure stress in ambulatory settings are often not sufficiently validated. The current validation landscape of consumer and research wearables is highly variable, so a common framework for stress wearables evaluation is needed. My project aims to develop a rapid and extensive pipeline for wearable validation both inside and outside the lab compared to a gold standard. The conceptualization of the validation pipeline will provide a common framework for validation which can be applied to different wearables. As a first step, my work starts with reviewing the available tools measuring executive functioning and related cognitive processes in daily life and to identify potentially promising tools that will undergo further development or validation in the future.

Anaïs Thijssen, PhD student, Amsterdam UMC

"What is the genetic basis of symptom-level depression heterogeneity?"

My study explores the genetic basis of different depression symptoms. We aim to further investigate the potential genetic relationships between depressive symptoms and broader psychiatric constructs, i.e., whether genetic influences for other psychiatric disorders "colour" the expression of depression. Another question is whether different depressive symptoms are a manifestation of quantitative or qualitative genetic differences, i.e., are some symptoms associated with more genetic risk or with different genetic risk. To be able to answer these questions we will develop new visualization tools based on genetic distances between subgroups. Analyses can also be applied to test the genetic basis for broader mental or even cardiometabolic disorders.

Bülent Ündes, PhD student, VU Amsterdam

"Can we detect and predict stress episodes using advanced deep learning techniques from real-time ECG Data?"



This study aims to harness the potential of modern deep learning approaches to real-time detection and prediction of stress episodes. Our methodology involves leveraging data from a comprehensive and controlled laboratory study featuring diverse mental stressors. To enhance the interpretability and efficiency of our model, we integrate techniques from both explainability and efficiency research. By combining cutting-edge deep learning methods with a rich dataset, we strive to contribute to the development of a robust and effective tool for identifying and predicting mental stress in daily life scenarios.

Sjors van de Ven, PhD student, VU Amsterdam

"How can physiological measures be refined to advance the methodology of ambulatory stress detection?"



Heart rate measurements in naturalistic settings are often confounded by the physiological impact of physical activity. Correcting heart rate for physical activity helps isolate fluctuations due to mental stress and gives an indicator that is associated with perceived stress and salivary cortisol. This study explores methods to improve the estimation of the impact of physical activity using accelerometers, validated across a range of postures and activity types in a laboratory setting. As a proof-of-principle, we assess if corrected heart rate is selectively increased during psychologically stressful conditions. The overall objective is to enhance ambulatory stress detection methodology through improved physiological measures.

Lianne de Vries, Postdoctoral researcher, Erasmus MC

"How can we prevent mental health problems via resilience or well-being?"

The prevalence of mental health problems among youth is rising. In my research, I focus on preventing mental health problems via resilience and well-being. Using ecological momentary assessment (EMA), we aim to earlier identify mental health issues and optimize/develop digital preventive tools, such as smartphone apps. Additionally, I aim to improve the measurement of resilience in daily life and investigate its relationship with mental health and well-being. I also set up a large-scale EMA study in the Netherlands Twin Registry with eight daily surveys and passive sensing in ~1000 participants, to gain insights into realtime influences on daily affective well-being.

Yong Zhang, PhD student, University of Groningen

"How can we improve the methodology of intensive longitudinal research?"

As daily life research using ambulatory assessments becomes increasingly popular, we are entering a new territory where many methodological questions are not yet tackled sufficiently. What, when, and how should the measurements be? How should we properly model the endogenous temporal dynamics of individuals while making sure exogenous contextual variables receive enough attention? The high complexity of intensive longitudinal data makes any rule-of-thumb style thinking unfeasible when dealing with such questions. My research thus focuses on answering these questions with simulation-based methods and developing tools that can be used by future researchers in their own research scenarios.

Noa van Zwieten, PhD student, Amsterdam UMC

"Can 2-week ambulatory data on physical activity and on negative and positive affect discriminate persons with different psychiatric status (having versus not having a depressive and/or anxiety disorder)?"



This study is using data from the NESDA cohort to explore the temporal associations between actigraphy-assessed physical activity and EMA-assessed positive and negative affect in a sample comprised of individuals with depressive and/or anxiety disorders diagnosis, subthreshold depressive and/or anxiety symptoms, and asymptomatic individuals. My first aim is to examine how these associations differ between persons with current disorders, subthreshold disorders and asymptomatic individuals, using a confirmatory subgroup approach. The secondary aim is to identify data-driven subgroups based on similar patterns of within-person associations over time. Data-driven subgroups are compared to the confirmatory subgroups and each another regarding patient, sociodemographic, psychiatric clinical and daily characteristics.



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