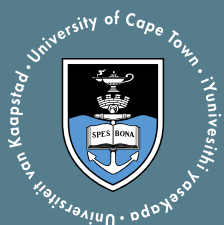
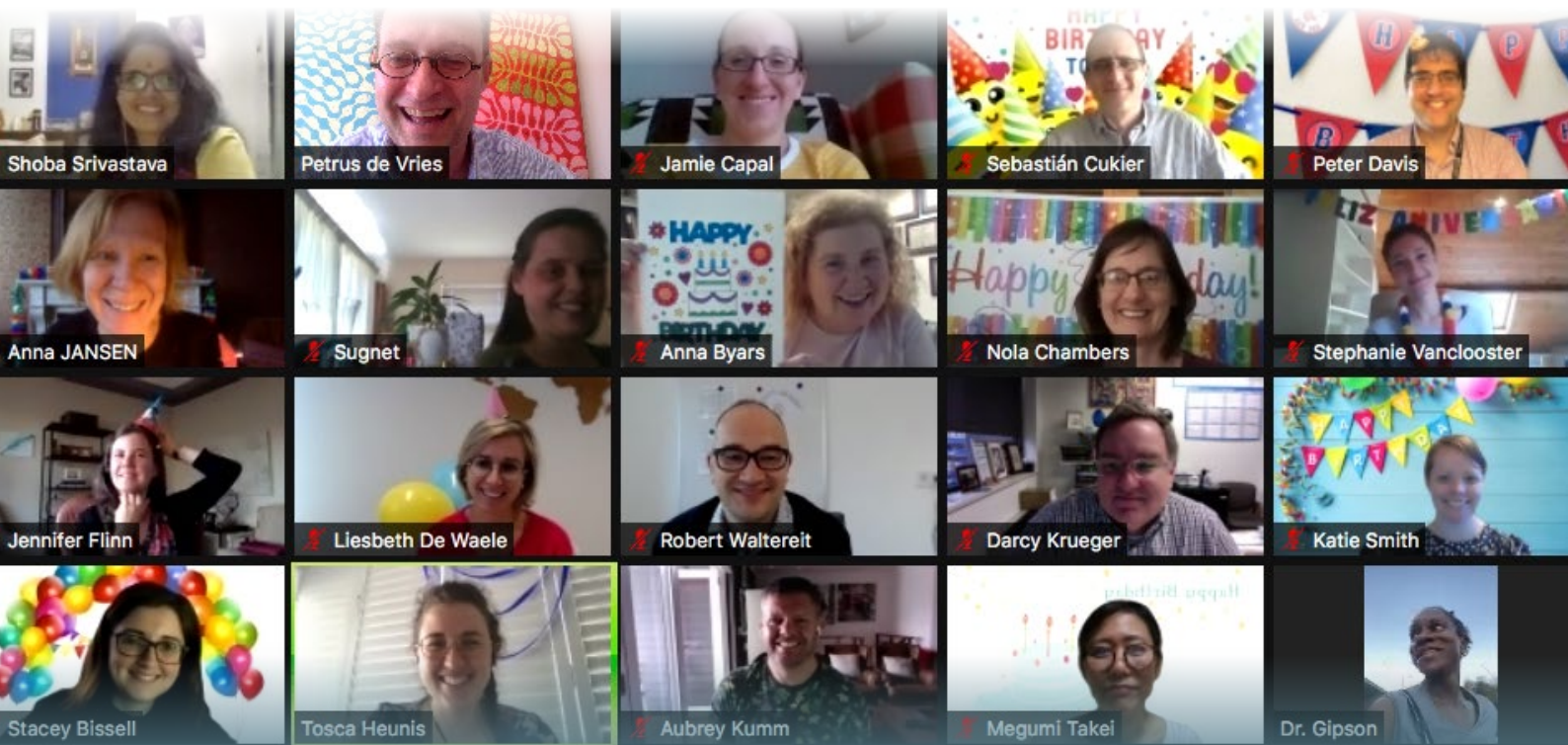




# TANDEM

Empowering families  
through technology

## Annual Report 2021 (YEAR 2)



VRIJE  
UNIVERSITEIT  
BRUSSEL



**PROJECT TITLE:**

Empowering families through technology: a mobile-health project to reduce the TAND identification and treatment gap (TANDeM)

**FUNDER:**

Fund Dr & Mrs Charles Tournay-Dubuisson, managed by the King Baudouin Foundation

**AGREEMENT NUMBER:**

2019-J1120010-213544

**PRINCIPAL INVESTIGATOR:**

Prof. Petrus J de Vries,  
University of Cape Town, South Africa

**CO-PI:**

Prof. Anna Jansen,  
Vrije Universiteit Brussel, Belgium

**GRANT PERIOD:**

4 years

**STARTING DATE OF THE PROJECT:**

1 November 2019

# Welcome from the TANDem PI and co-PI

Welcome to the report on year 2 of the TANDem project, generously supported by the King Baudouin Foundation in Belgium. Year 1 of the project was characterised by lots of excitement and setting up of the 4-year global project. As described in the 2020 annual report, we were fortunate to launch the project in November 2019 with in-person activities in Leuven before the COVID-19 pandemic hit early in 2020. In spite of the challenges of COVID-19 we were able to complete year 1 of the project very much on track.

Year 2 of TANDem was a full year of research in the context of COVID-19, and we had to find a range of creative strategies to keep the momentum and energy of the project going in the absence of any opportunities for in-person collaborative work. However, as you will see in this report, TAND consortium members have been remarkable in their resilience and ongoing commitment to the project and its greater goals. Despite many barriers, the project has achieved the majority of goals for year 2, and the ongoing support and enthusiasm from the global TSC community has remained strong.

We hope you will enjoy reading about this innovative and potentially transformative project and about all the year 2 achievements and deliverables of the project.



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**Prof. Petrus J de Vries**  
MBChB, FRCPsych, PhD  
PI (University of Cape Town)



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**Prof. Anna Jansen**  
MD, PhD  
co-PI (Vrije Universiteit Brussel)





# The TANDeM project in a nutshell

**Tuberous Sclerosis Complex (TSC)** is a rare genetic disorder that affects about 1–2 million people around the globe. People with TSC have a wide range of physical manifestations including growths in many organs of the body, including the brain. **TSC-Associated Neuropsychiatric Disorders (TAND)** represent the number one concern to families around the globe, yet they are highly under-identified and under-treated – we refer to these as an ‘identification gap’ and a ‘treatment gap’<sup>[1, 2]</sup>.

## Project background

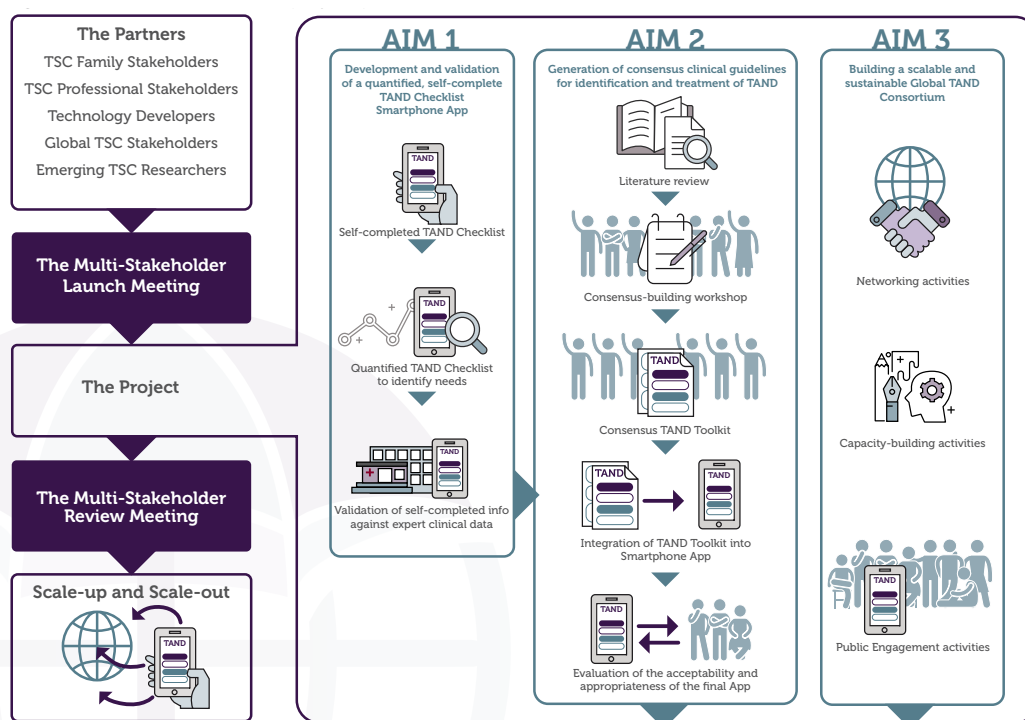
In 2012 we introduced the term ‘TAND’ and in 2015 created the **TAND Checklist** to reduce the ‘identification gap’<sup>[3]</sup>. Research using the TAND Checklist showed that we could identify seven natural TAND Clusters that may be useful to reduce both the identification and treatment gaps for TAND further<sup>[4, 5]</sup>. Following our earlier work, community-based participatory research with families and a range of TSC stakeholders identified three next steps for action:

- 1 Creation of a self-report and quantified version of the TAND Checklist
- 2 Creation of a digital tool such as an app for the TAND Checklist
- 3 Generation of evidence-based guidelines and a toolkit for next-step management of TAND Clusters

## TANDeM project aims

The TANDeM project was a direct result of the feedback from our TSC stakeholders, and has three aims:

- **AIM 1:** Development and validation of a quantified, self-report TAND Checklist (TAND-SQ), built as a mobile app
- **AIM 2:** Generation of consensus clinical guidelines for identification and treatment of TAND Clusters, to be incorporated as a toolkit into the app
- **AIM 3:** Establishment of a global TAND consortium through a range of networking, capacity-building and public engagement activities



## References:

- [1] de Vries et al., (2018) *American Journal of Medical Genetics*, 178C: 309–320
- [2] King Baudouin Foundation (2018) *Mind the Gap! Working together to set research priorities for Tuberous Sclerosis Complex*. Pub No 3555
- [3] de Vries et al., (2015) *Pediatric Neurology*, 52: 25–35
- [4] Leclezio et al., (2018) *Pediatric Neurology*, 81: 38–44
- [5] de Vries et al., (2020) *Journal of Neurodevelopmental Disorders*, 12: 24

# 1 Year 2 in the time of COVID-19

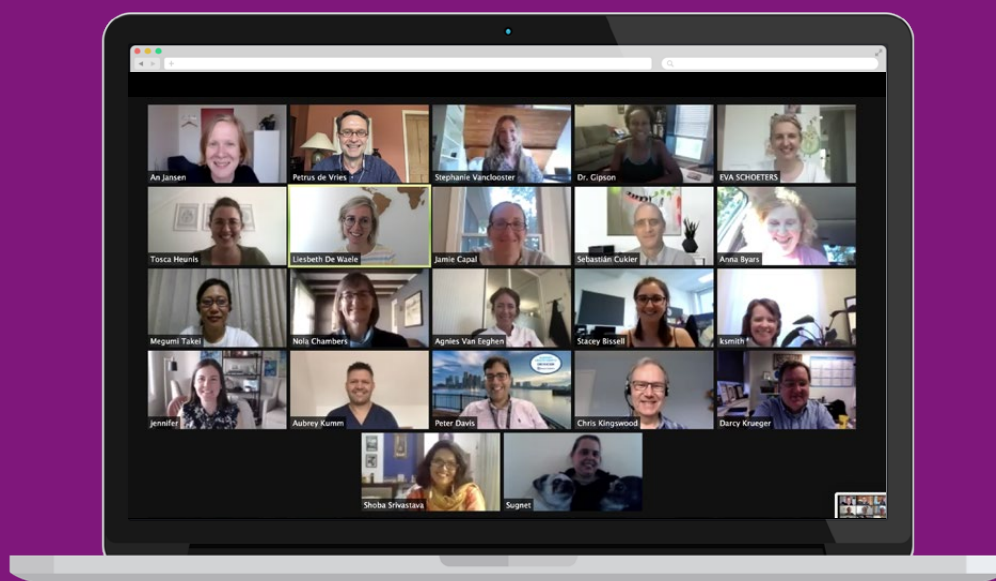
At the end of year 1 we set ourselves 8 next steps for the TAND<sup>em</sup> project.

The goals were:

- a Complete the Consensus Conference (scheduled as a virtual meeting in November 2020)
- b Complete development of the TAND Consortium website
- c Complete a scoping review of all TAND research to date
- d Finalise submissions to research ethics boards in all relevant research sites
- e Complete development and internal testing of the first phase of the TAND Toolkit App
- f Perform data collection and validation of the app-based TAND-SQ
- g Start development and design of the toolkit to be incorporated into the TAND Toolkit App
- h Have a Consortium meeting with impact activities in June 2021

This report outlines achievements in relation to these goals in year 2 of the TAND<sup>em</sup> project, and represents the formal report as stipulated in the specific conditions of the grant.

*“ I’m very curious to see how the app will be seen from the users’ point of view; how this tool will make their lives a little better.”*





## 2 The Virtual Consensus Conference (November 2020)

Given that COVID-19 prevented an in-person Consensus Conference, we switched to a virtual Consensus Conference, which took place from 9–11 November 2020.

In preparation, TAND Consortium members were asked to do the following:

- a Cluster groups prepared expert chapters summarising the current literature and evidence-base relevant to the cluster, and prepared summary statements and recommendations from the current literature and evidence-base
- b Summary statements and recommendations from all clusters were collated and shared with all consortium members to rate each statement and recommendation on a Likert scale (from strongly agree to strongly disagree)
- c Consortium members were also asked to rank their top 3 recommendations per cluster
- d All data were collected and summarised to identify items where consensus had already been reached, and to identify items that required further discussion and clarification

The Consensus Conference was divided into three sessions.

### Session 1: Consensus building (9 November 2020)

In this session all preparatory work was presented and items that required consensus discussions were raised. After discussions, a second round of ranking was performed electronically to identify the final list of consensus items. We agreed to generate three products from the consensus-building process:

- 1 A book for families and practitioners (most comprehensive)
- 2 Consensus clinical guidelines for TAND (summary of chapters)
- 3 A toolkit to be built into the TAND Toolkit App (practical and specific elements from the consensus guidelines)

### Session 2: TAND Toolkit development (10 November 2020)

This session kick-started discussions about the actual toolkit to develop for inclusion in the App. The consortium agreed on key principles for the TAND Toolkit, developed a core structure for toolkit elements, and agreed a process to start assembling elements to include or design for the toolkit.



### Session 3: Next step planning (11 November 2020)

During this session the consortium reviewed options for the June 2021 impact activity and agreed on other actions for year 2 of the project. We ended the Consensus Conference with a ‘three-word challenge’ where all consortium members were asked to summarise the key concepts of the project in three words.

“ It’s amazing to see how we went from the launch meeting, with ideas all over the place, to a tangible structure, only one year later. We did it in a year’s time, that’s impressive. It speaks of the expert level of this group.”

#### THREE WORD CHALLENGE

EARLY	BROAD/WIDE	REACT
PRACTICAL	EMPOWERING	GENERALISABLE
MONITOR	IDENTIFY	INTERVENE
IDENTIFY	INTERVENE	INFORM
EARLY	TARGETED	CONNECTED
IDENTIFICATION	INTERVENTION	IMPLEMENTATION
MONITORING	ACTION	HIERARCHY
EARLY	MARATHON	PROACTIVE
COMPREHENSIVE	UNIVERSAL	ACT
MONITORING	INTEGRATING	EMPOWERMENT
CARE	CONNECT	KNOWLEDGE
COMPLEX	ACT	EMPOWER
EMPOWERMENT	ACCESS	HELP
ESSENTIAL	SPECIALIST	SEEK
TICK	FIND	ACT
INFORM	SUPPORT	ENGAGE
LOW THRESHOLD	ACCESS	FIRST-LINE SUPPORT
LISTEN	LOOK	LEAP
PRAGMATIC	CONCISE	MULTILAYERED
SCREEN	ACT	REPEAT (MONITOR)

### 3 Launching the TAND Consortium website, YouTube and Twitter

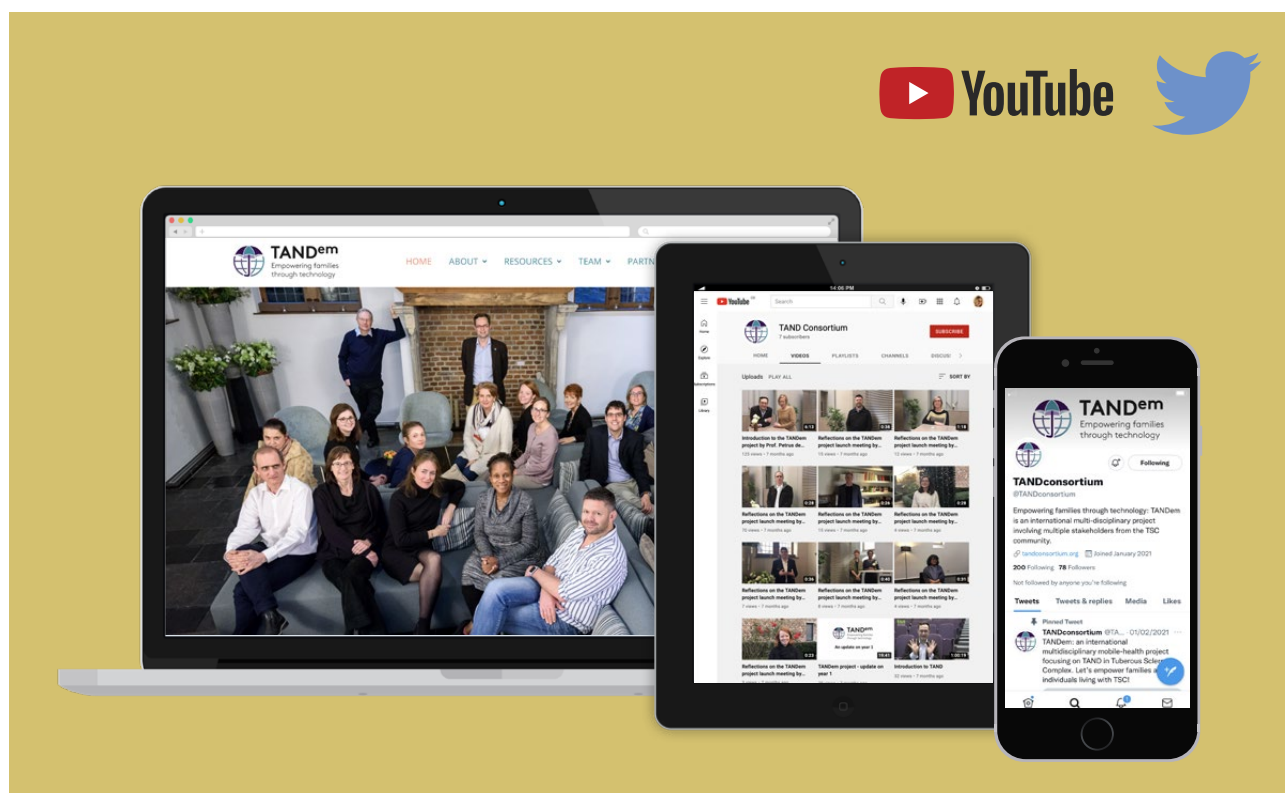
After many months of preparations, the TAND Consortium website, Twitter account and YouTube channel were launched on 1 February 2021.

The **website** was developed with the goal of serving as a 'living' resource about TAND for the global TSC- and TAND community, and includes not only project-related information, but also hosts all authorised translations of the TAND Checklist, relevant publications, talks and other TSC- and TAND-related resources. In addition, we created a page where families and people who live with TSC can upload their 'TAND tips' and suggestions to inform the TAND Toolkit development process. The website can be found at [www.tandconsortium.org](http://www.tandconsortium.org).

The **YouTube channel** was set up to host all relevant talks, webinars and video-based toolkit elements.

The **TAND Consortium Twitter account** was created to support dissemination of up to date TAND information and to increase the impact and reach of TANDem project activities.

*“It’s amazing how everything is coming together and keeps on growing. It’s all connected.”*





# 4 The Scoping Review

One of the goals of the TAND<sup>em</sup> project was to perform a scoping review of all TAND-related research that had ever been published in the peer-reviewed literature. The purpose of the review was to describe the landscape of TAND research to date, to identify key gaps in the TAND literature, and to make recommendations for future TAND research.

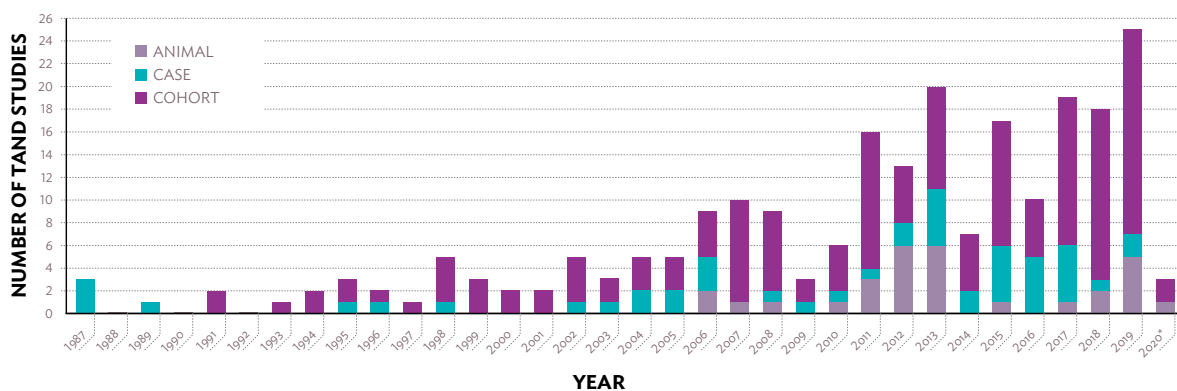
Dr Stacey Bissell (Birmingham, UK) and Dr Stephanie Vanclooster (Brussels, Belgium) led the huge task of screening 2,841 publications to identify 230 relevant ones. Ten research questions were examined. We were delighted to see a recent increase in TAND publications with more than half of all TAND research conducted after the coining of the term ‘TAND’ in 2012. The manuscript was submitted for peer-review in September 2021, and we hope that the findings and recommendations will inspire much further high-quality TAND research around the globe.

“ Even though there has been an increase in TAND research over the years, we found no studies of non-pharmacological interventions such as talking treatments for any of the TAND manifestations. This was a shocking finding, and a real wake-up call for the TAND research community. We have to do better! ”

## The Scoping Review Research Questions

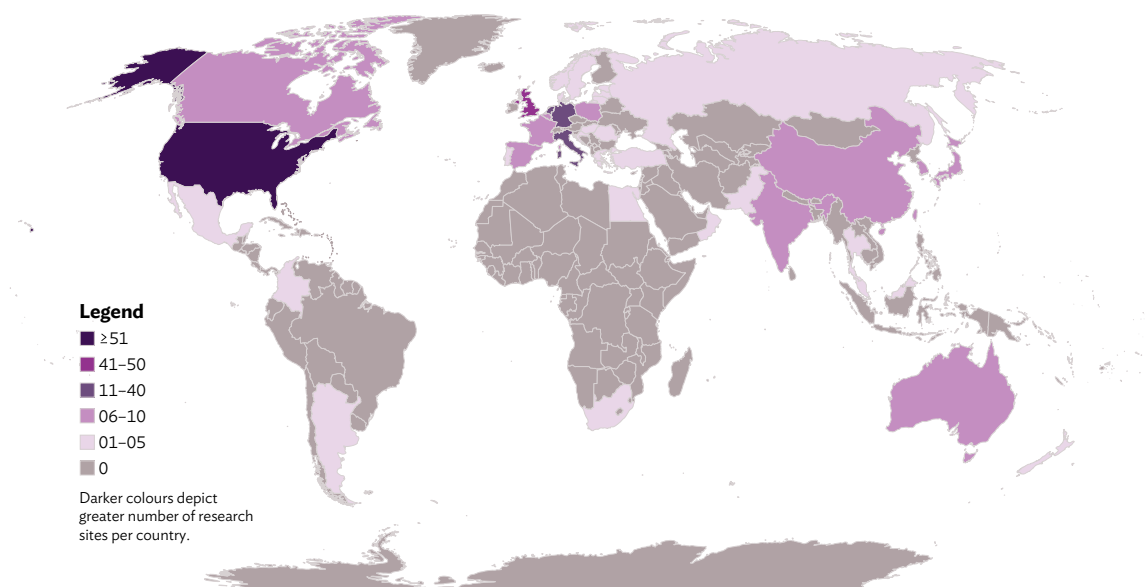
- 1 How much TAND research has been done over the years?
- 2 Where has TAND research been done in the world?
- 3 Which TSC age groups have been investigated?
- 4 What is the overall quality of existing TAND research?
- 5 Which TAND levels have been investigated?
- 6 Which research methods and measures have been used to investigate TAND?
- 7 How much qualitative and quantitative research has been conducted?
- 8 In human studies, how many intervention studies have been conducted?
- 9 Have remote technologies been utilised to study TAND?
- 10 Which TAND clusters have been studied?

## Number of TAND studies across years according to study type



\* = Search was completed in March 2020, and therefore does not represent full number of TAND studies published in 2020.

## World map depicting the geographical location of 341 individual research sites across 230 studies



# 5 Paperwork, paperwork, paperwork

One of the features of year 2 was the processing of vast amounts of paperwork. This included finalisation and signing of:

- a The ethics submissions in Cape Town, Brussels, Leuven, Boston, Cincinnati and by the TSC Alliance (USA)
- b The Data Transfer Agreement between all relevant institutions
- c Privacy Policy and Terms of Use of the TAND Toolkit App
- d Privacy Policy and Terms of Use of the TAND Consortium website
- e TAND Consortium Publication Policy
- f Consenting all TAND Consortium members

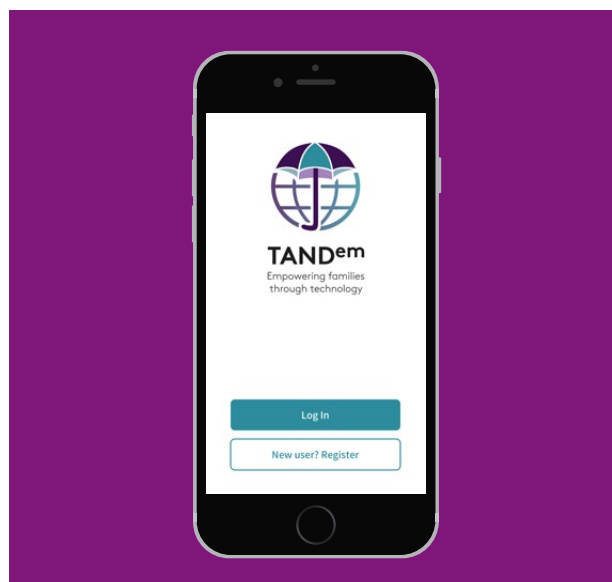
*“ I’m so glad to be part of this multidisciplinary group. I feel so supported. ”*



## 6 Development and internal testing of the TAND Toolkit App

Over the last year Dr Tosca Heunis (Brussels, Belgium) has continued to work very closely with ITHands, our app developers based in India. She has weekly meetings with them and has been performing interim iterative testing of the app and the data administration panel. The initial projected timeline for phase I of the app was delayed due to various factors, including technical development limitations, changes to the structure of the TAND-SQ, developing and incorporating the Electronic Informed Consent, Privacy Policy and Terms of Use documents, obtaining an Apple Developer Programme license, and the impact of COVID-19. The slowing down of the process in 2021 has fortunately allowed the team to improve a number of elements in the app that will improve user-friendliness in the long run.

The app will allow users to register in a secure way and to add a number of members to their 'TSC family' profile. Once registered, users will be able to capture a 'TSC story' (information about the TSC diagnosis), complete a self-report, quantified version of the TAND Checklist (to identify and quantify the severity of TAND difficulties experienced), view the cluster profile (that illustrates how different TAND clusters are affected), and to view the 'TAND toolkit'. The TAND toolkit will provide evidence-informed information about each cluster, including an introduction to the cluster, what should families seek (e.g. assessment, diagnosis, and treatment



by a professional), and what can families do for themselves (e.g. self-help, home-based actions, strategies and interventions). The final component of the TAND Toolkit app is the ability to do 'surveys' (to collect additional information from users about various aspects of TAND). Phase I of the app includes all development except for the toolkit, which forms part of phase II. The app can be used on Android and iOS mobile devices.

We plan to complete internal user acceptance testing (within the consortium) of phase I of the app on Android and iOS devices in October 2021.

*“ Seeing the first version of the app was the highlight for me. It has become something very real. ”*

# 7 The TAND-SQ: development, design, and pre-piloting

One of the exciting achievements of year 2 was the development, design, and pre-piloting of the self-report and quantified version of the TAND Checklist, referred to as the TAND-SQ. Through an iterative process, core elements from the original TAND Checklist (TAND-L) were revised and augmented to generate the self-complete version. A user-friendly quantification component was added to relevant items, and the draft checklist was reviewed by members of the consortium and a wider group of TAND stakeholders.

The formatting of the TAND-SQ went through five rounds of proofing (thanks to our talented and patient graphic designer, Deborah White from the *Department of Shapes and Colours* in the UK) and further review by the consortium members. Following finalisation of the paper version, all consortium members participated in a formal feasibility evaluation of the TAND-SQ. These results will be combined with the pre-piloting data of a small group of families and individuals with TSC in the USA.

**TAND-SQ**  
Self-report, Quantified TAND Checklist (2021)

Tuberous Sclerosis Complex (TSC) is associated with a range of neuropsychiatric disorders that we refer to as TAND (TSC-Associated Neuropsychiatric Disorders). All people with TSC are at risk of having some of these difficulties. Some people with TSC have very few, while others will have many of these difficulties. Each person with TSC will therefore have their own TAND profile, and this profile may change over time. This checklist was developed for individuals and families who live with TSC to complete for themselves with the goal of a) screening for TAND difficulties at home, b) to quantify these difficulties, and c) to help guide next steps for self-help and for further discussions with healthcare and other service providers.

**Let's get started**

Name of the person completing the TAND-SQ Checklist: \_\_\_\_\_

Date you completed the TAND-SQ Checklist: [ ]/[ ]/[ ]

Who is the TAND-SQ Checklist about? This checklist will refer to this person as [subject].

☐ Myself ☐ My son ☐ My daughter ☐ My partner ☐ My mother ☐ My father  
☐ My brother ☐ My sister ☐ My grandchild ☐ Other (please specify) \_\_\_\_\_

Name of the person [subject]: \_\_\_\_\_

Date of birth: [ ]/[ ]/[ ] Age: [ ] Sex: ☐ Male ☐ Female ☐ Other

Preferred personal pronouns: ☐ He/Him/His ☐ She/Her/ Hers ☐ They/Them/Theirs

**Instructions for use**

As you will know, the majority of people with TSC have some difficulty in learning, behaviour, mental health, specific aspects of their development and so on. The TAND-SQ Checklist was designed to help parents/ caregivers or individuals with TSC to check for these kinds of difficulties. The checklist should take about 20 - 30 minutes to complete. You will see a number of questions. Some may be directly relevant and some might not be relevant at all. Some of the items can be quantified (given a severity rating) based on how good or difficult things have been over the last month. Even if you can't remember everything, just answer as best as you can and please try to complete all items. At the end you will have the chance to write down any additional difficulties that were not captured.

Where you see the pencil sign we have created space for you to make short notes if that would be helpful to you.

If you are caring for someone with TSC, please start with question 1.  
If you have TSC and you are completing the TAND-SQ for yourself, please start with question 3.

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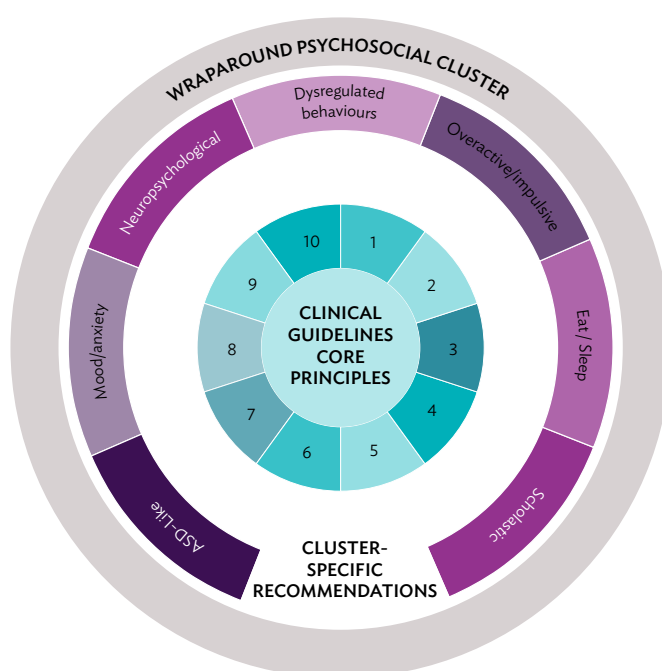
# 8 From consensus to TAND Toolkit

The TAND Toolkit development was kick-started at the November 2020 Consensus Conference. Consortium discussions led to the identification of the key purpose and principles of the TAND Toolkit, and generated options for potential components of the toolkit. In 2021 cluster teams were supported to start thinking about toolkit components.

Further teamwork and discussions at the June 2021 consortium meeting helped to create an overall structure for toolkit elements which will include introductory videos about each cluster, and sections on ‘what to seek’ and ‘what to do’. Creative toolkit design sessions were scheduled from September – October 2021.

“ I’m looking forward to see the toolkit becoming a real living tool. It will mean so much to families who could use all the help they can get. ”

TAND consensus diagram



Consensus Clinical Guidelines have:

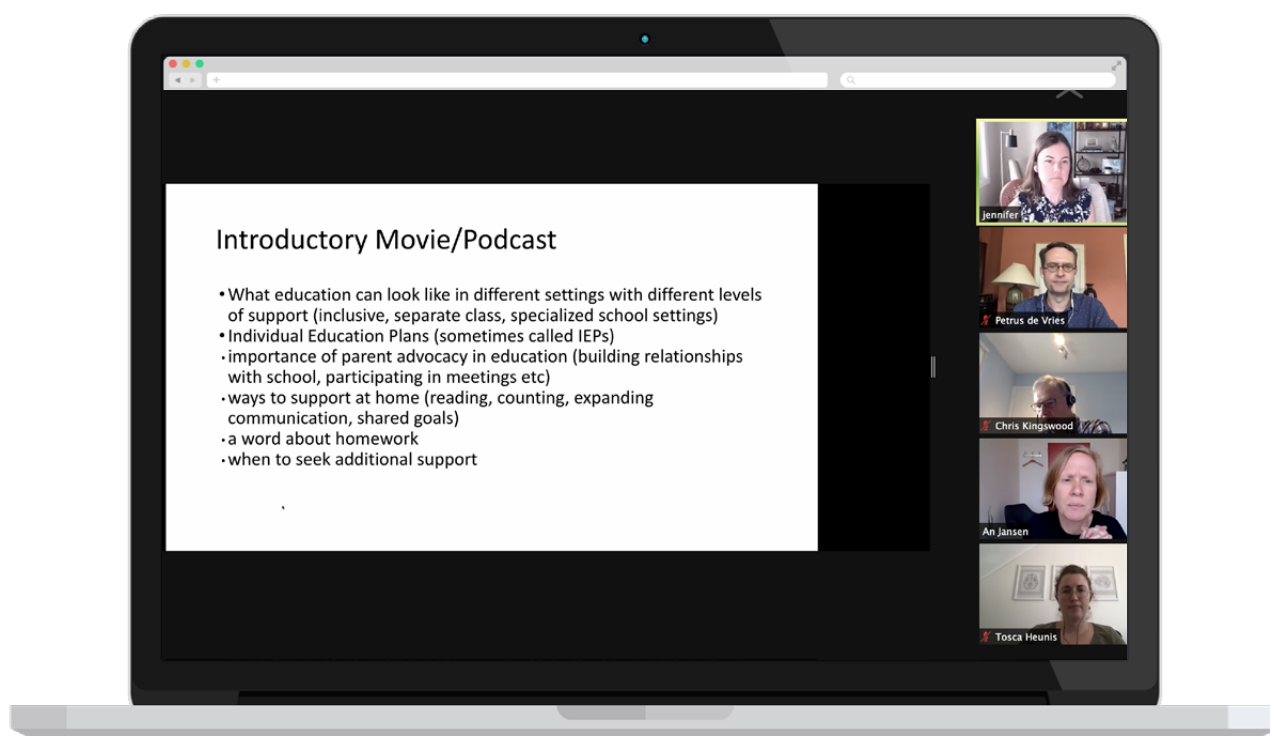
- Ten core principles
- Recommendations specific to the 7 clusters
- Recommendations for a ‘wraparound’ psychosocial cluster

## Purpose and principles of the TAND Toolkit

- First aid to families
- Personalised
- Tailored information targeted at TSC
- Key resources
- Usable
- Strategies
- Practical
- Short, simple and generalisable
- Universal and locally implementable
- Open-access and free

## Potential components of the TAND Toolkit

- Short videos about concepts
- Short demonstration videos
- Active learning sheets
- Infographics
- Collated links to resources
- FAQs including who does what around the world?
- Healthy habits



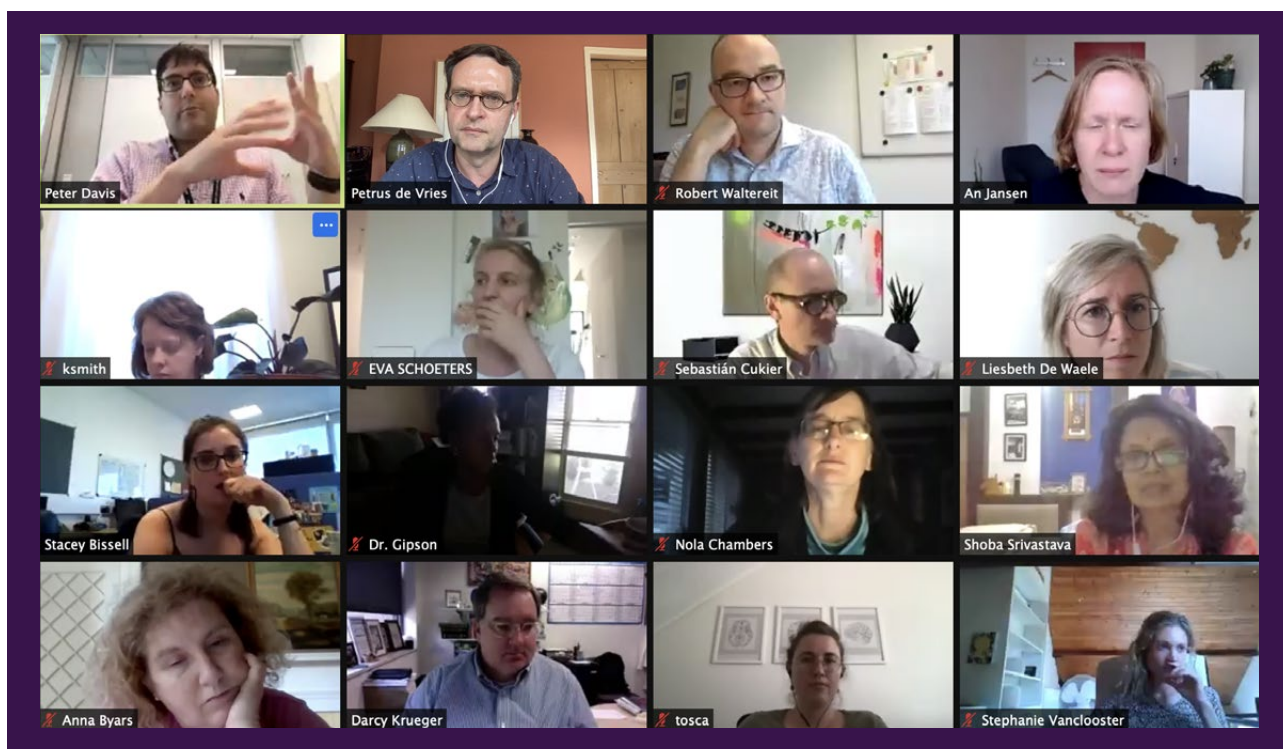
# 9 Consortium Meeting 2021

The original goal of the June 2021 Consortium Meeting was to hold an in-person event in London on the day before the International TSC Research Conference which was scheduled for 17–19 June 2021. As a result of the COVID-19 pandemic, the TSC conference was switched to a virtual meeting, and the TAND Consortium decided also to have our consortium meeting via Zoom.

The goals for the 2021 consortium meeting were to:

- a Provide updates on project goals and activities
- b Work on the TAND Toolkit
- c Plan actions and next steps for the remainder of year 2 and into year 3
- d Discuss potential activities in 2022 (year 3 of the project)

“ *Seeing our recommendations coming out in the near future, that will be great. Such a support to so many families.* ”



# 10 Impact and dissemination activities

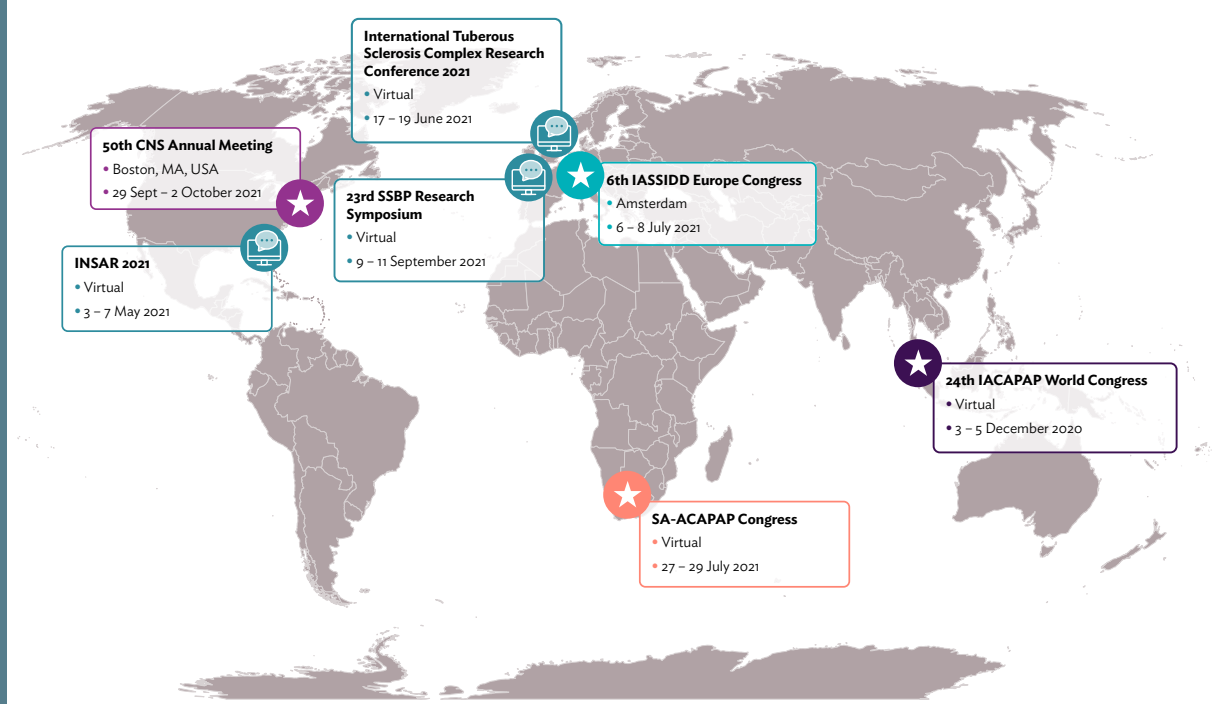
Even though our original grant outline scheduled impact and dissemination activities only for year 4 of the project, the COVID-19 pandemic allowed us to refocus and implement a range of impact and dissemination activities already in year 2. The dissemination team, led by Prof. Liesbeth De Waele (Leuven, Belgium), coordinated a broad range of impact and dissemination activities.

*“ I’m surprised that our group works so perfectly, everyone with a different background. It’s nice to be part of such a broad community worldwide. ”*

Dissemination activities included:

- Submission of TANDem abstracts to a range of conferences and audiences across the world
- Keynote presentations at international conferences
- A dedicated session on TANDem at the International TSC Research Conference
- Dissemination activities to the TSC community in South Africa, USA, Germany, UK, Netherlands and Australia
- Emerging researcher presentations of posters and talks at various conferences
- Registration of Ms Shoba Srivastava (Mumbai, India) as PhD student at the University of Cape Town for a project on TAND in India

## Abstracts all over the globe



## TANDeM Dissemination activities



Conversations about Tuberous Sclerosis Complex  
Saturday 15 May 2021  
15:30 – 17:00 South African Time

**TSC Global Awareness Day**  
May 15

**TSSA**



Speakers: Alexis Minnaar  
Prof. Anna Jansen  
Prof. Petrus de Vries

To register, please email [rehana.iffendi@uct.ac.za](mailto:rehana.iffendi@uct.ac.za)  
(Please put "TSSA" in the subject heading of your email)  
Once your email has been received, a Zoom link will be sent to you.

**INSAR 2021 VIRTUAL**  
**MAY 3 - 7, 2021**



## TSC Talks! In the Hot Seat with Professor Petrus de Vries & Alexis Minnaar; A Discussion on TSC Assoc. Neuropsychiatric Disorders, aka~TAND

TSC Talks!





# 11 Next steps for 2022

Over the next 12 months (year 3 of the project), we will:

- a Complete pre-piloting of the paper version of the TAND-SQ
- b Publish the TAND-SQ in the peer-reviewed literature and make it available through the TAND Consortium website
- c Complete phase I app development
- d Collect TAND-SQ data via the app and via the TSC Alliance portal
- e Complete evaluation of the technical feasibility of the app
- f Complete validation of TAND-SQ data in relation to expert data (Boston/Cincinnati) and real-life clinical data (TSC Alliance)
- g Complete development and design of the TAND Toolkit materials
- h Incorporate the toolkit into the app (phase II of app development)
- i Perform evaluation of the feasibility of the complete TAND Toolkit app (Belgium, USA)
- j Publish a range of peer-reviewed articles related to the project
- k Participate in the 2022 World TSC Conference (USA), including TANDem activities with the TSC community
- l Participate in other dissemination activities



