



TANDEM

Empowering families
through technology

Annual Report 2020



VRIJE
UNIVERSITEIT
BRUSSEL



King Baudouin
Foundation
Working together for a better society



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

We are extremely grateful to the King Baudouin Foundation for their support to enable this innovative and potentially transformative project. We are also delighted that the Tuberous Sclerosis Association (UK) were willing to provide additional funding to support the technology development component of the project.

We have worked very hard in year 1 to get the project going, have been very encouraged by the dedication and hard work of all *TANDem* consortium members, and by the ongoing support and enthusiasm for the project from the global TSC community.



A handwritten signature in black ink, appearing to read 'P. de Vries'.

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

A handwritten signature in black ink, appearing to read 'A. Jansen'.

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



Prof. Petrus J de Vries and Prof. Anna Jansen



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’^[1, 2].

Project background

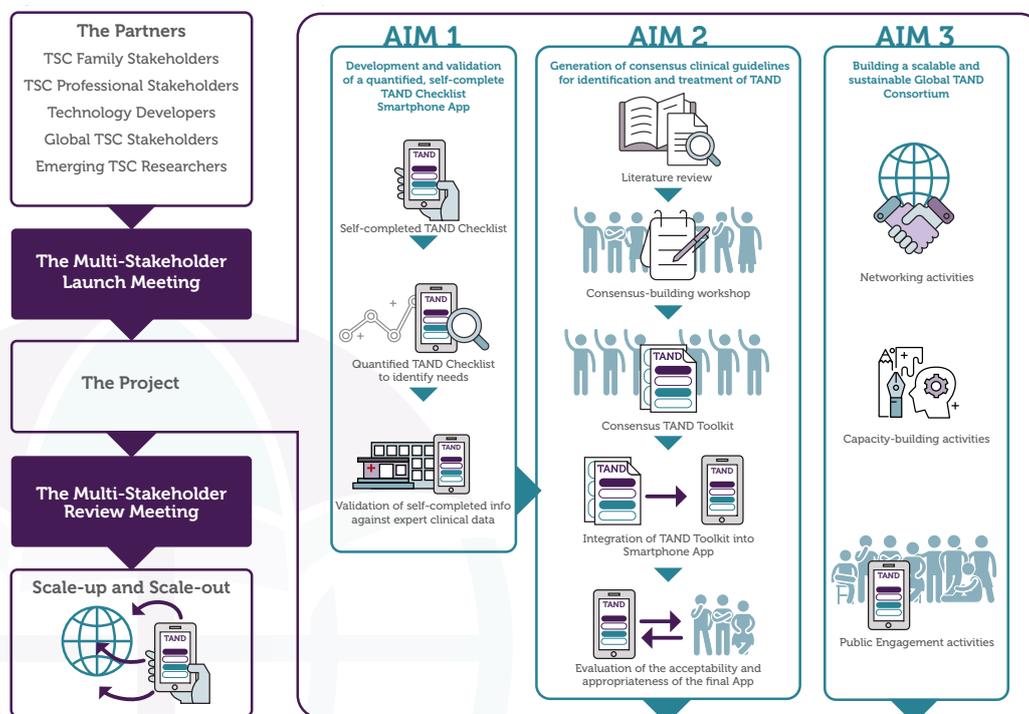
In 2012 we introduced the term ‘TAND’ and in 2015 created the TAND Checklist to reduce the ‘identification gap’^[3]. Research using the TAND Checklist showed that we could identify seven natural TAND Clusters that may be useful to reduce both the identification and treatment gaps for TAND further^[4, 5]. 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] Leclézio et al., (2018) *Pediatric Neurology*, 81: 38-44
- [5] de Vries et al., (2020) *Journal of Neurodevelopmental Disorders*, 12: 24

1 Introduction

Funding for the *TANDem* project was awarded on 4 April 2019 at a ceremony of the King Baudouin Foundation in the presence of Her Royal Highness Princess Astrid, Princess of Belgium.

Final contractual agreements were signed off between the University of Cape Town and the Dr & Mrs Charles Tournay-Dubuisson Fund, managed by the King Baudouin Foundation on 23 September 2019.

After contract negotiations the project officially started in November 2019.

This document represents interim report 1 as stipulated in the specific conditions of the grant.



The award ceremony. Petrus and An with Her Royal Highness Princess Astrid of Belgium



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2 Contract negotiations between the University of Cape Town and Vrije Universiteit Brussel

After completion of the contract agreement with the King Baudouin Foundation, we proceeded with development of a subcontract agreement between the University of Cape Town (UCT) and Vrije Universiteit Brussel (VUB).

The subcontract between UCT and VUB represents the legal document to describe the memorandum of understanding as required under specific conditions of the grant agreement. The subcontract outlines:

- a the work packages of each of the PI and co-PI sites
- b timelines and deadlines for the 4 years of the project
- c reporting between PI and co-PI sites and communication between sites
- d description of reporting procedures
- e agreement on internal distribution of funds
- f agreement on communication and publication
- g description of shared intellectual property

In addition to the legal agreement as outlined above, the PI, co-PI and *TANDem* consortium also co-created a number of different teams/groups with clearly defined roles and communication/integration tasks. These are outlined on pages 9-14.



3 Staffing and Human Resources

Two posts were advertised as part of the project – a PhD studentship and a postdoctoral project coordinator.

The original plan for the project was to have a PhD student in Belgium and a project coordinator in South Africa. We advertised in South Africa, Belgium and through TSC networks in the USA, UK and 28 TSCi countries. Even though there was some interest in the PhD post, we did not find a suitable candidate. However, we received a number of very strong applications for the project coordinator post and shortlisted 3 candidates (2 from Belgium, and one from the Netherlands).

After completing the interviews, we appointed **Dr Tosca-Marie Heunis** as postdoctoral project coordinator at VUB with a starting date of 1 March 2020. We identified an excellent postdoctoral researcher and sought permission from the King Baudouin Foundation to appoint a postdoctoral



researcher instead of a PhD student. This request was approved by the funder, and **Dr Stephanie Vanclooster** started on the project on 1 November 2019, based at VUB.

In June 2020, Prof. Jansen and Prof. de Vries performed 6-month performance reviews with both members of staff and made minor adjustments in their roles and tasks. Overall, both members of staff have performed well to date. The details of their roles and responsibilities are outlined on pages 9-14.



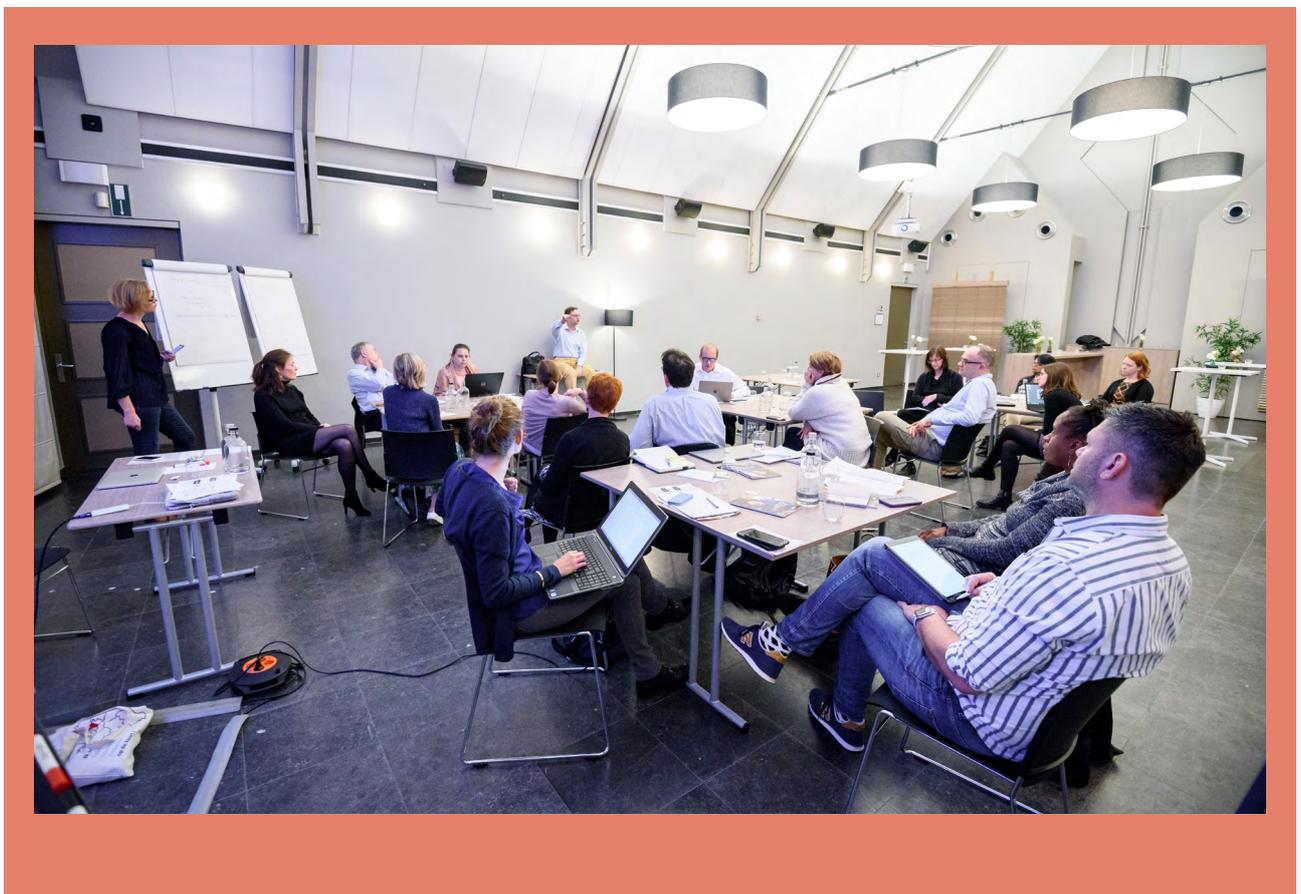
4 The Launch Meeting

As per the study protocol, the *TANDem* project had a launch meeting in November 2019 which took place at the Katholieke Universiteit Leuven (KUL) from 17–19 November 2019. The meeting was coordinated by Dr Vanclooster and hosted by Prof. Liesbeth De Waele (KUL).

The launch meeting included a range of introductory activities, small group and large group work to set out the goals, strategies and procedures for the project. With the exception of the project coordinator and the family representative from Japan, all members of the *TANDem* consortium were able to attend.

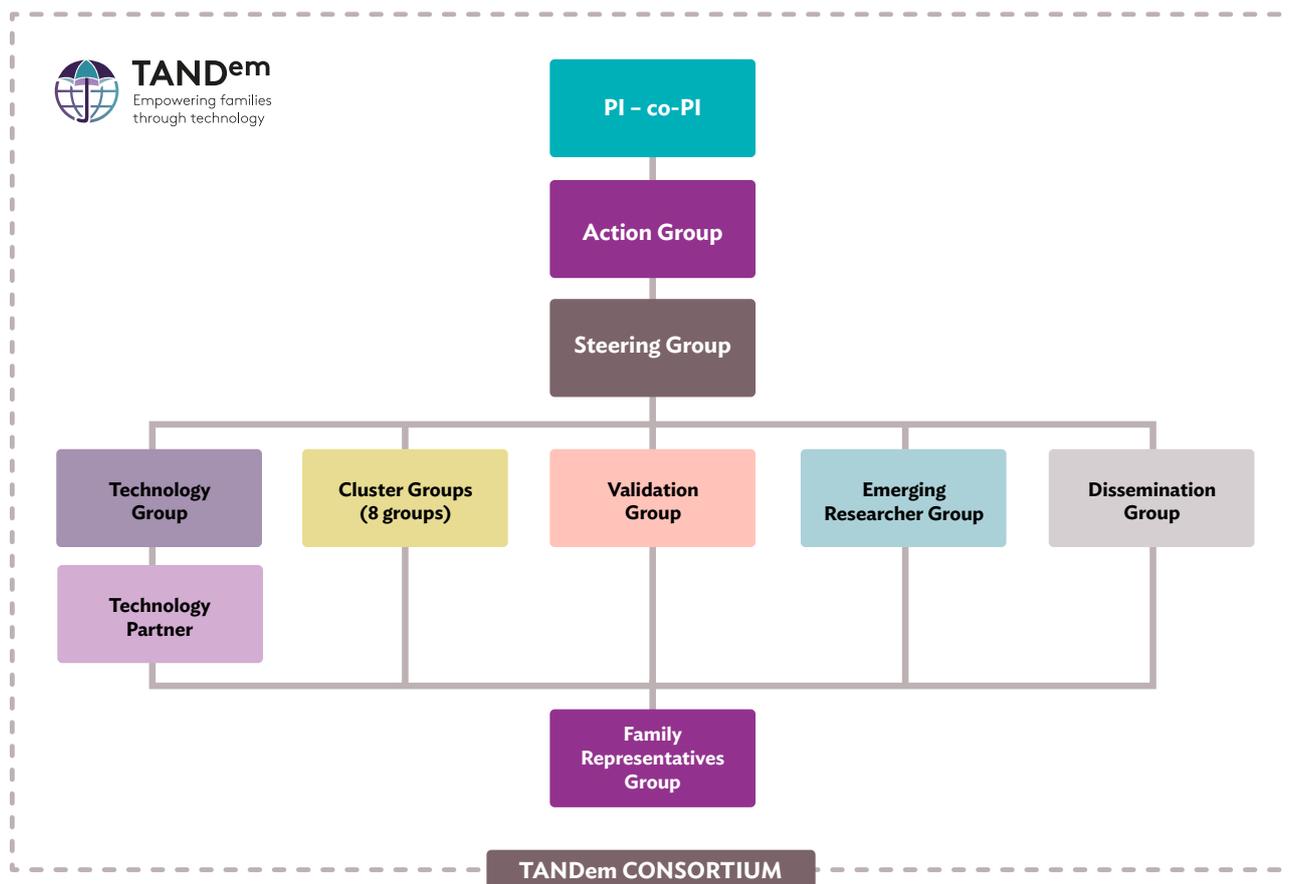


The launch meeting was a profoundly rewarding experience for all participants and provided an excellent opportunity to build a *TANDem* team spirit and structure for the consortium.



5 The *TANDem* consortium structure

The *TANDem* consortium and its group structures is shown in the figure below.



PI and co-PI

The consortium is led by the PI (Prof. de Vries) and co-PI (Prof. Jansen) who are responsible for the successful running and completion of the project.

The PI and co-PI are also responsible for all aspects of project oversight, financial management, HR management and ethical conduct of the *TANDem* project.

Action Group

The Action Group includes the PI, co-PI, the project coordinator and the postdoctoral researcher.

They are responsible for the day-to-day running of the project and for coordination between all groups in the project.

The Action Group has a weekly Zoom meeting to discuss project matters.

Steering Group

The Steering Group includes all members of the Action Group as well as:

Prof. Liesbeth De Waele (Leuven, Belgium)

Dr Chris Kingswood (London, UK)

Ms Shoba Srivastava (Mumbai, India).

Prof. De Waele is a co-lead of the project with Prof. Jansen. Dr Kingswood represents the Tuberous Sclerosis Association (UK) and is a family representative. Ms Srivastava is a family representative.

The Steering Group is responsible for oversight of activities in *TANDeM* and, in particular, provide a forum to bring a user/carer voice to the project.

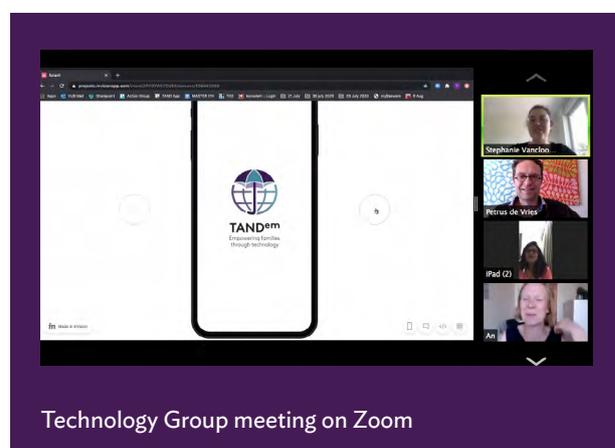
They meet monthly via Zoom.



Technology Group and the Technology Partner (Aim 1 of the *TANDeM* project)

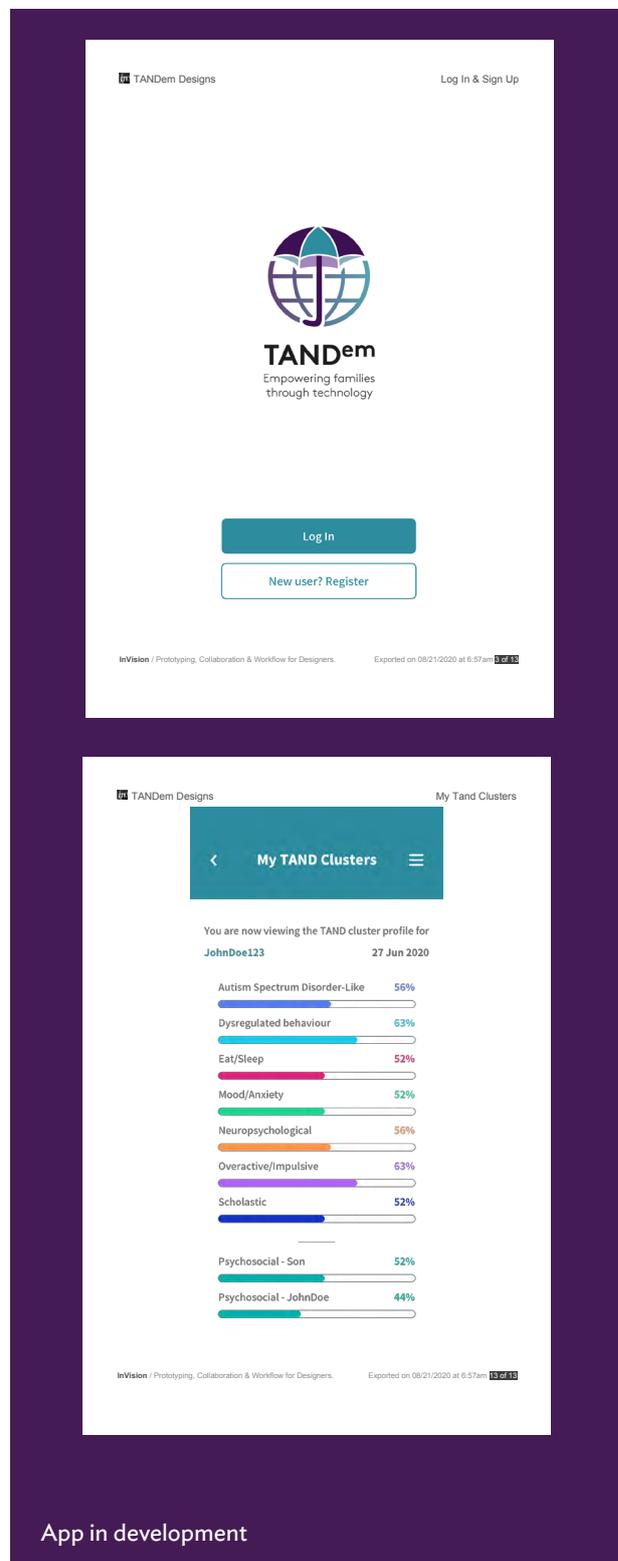
The Technology Group is led by Dr Tosca Heunis, the project coordinator. She is a qualified engineer with a PhD in signal processing of electroencephalography (EEG) for autism. Her work involved the analysis of resting state EEG signals as a potential biomarker for autism in children with and without Tuberous Sclerosis Complex (TSC). In addition, Dr Heunis worked as an app developer and solutions architect for a mobile app development company in South Africa, before moving to the Netherlands with her family. The Technology Group is responsible for all aspects related to app development within the *TANDeM* project. They meet on an ad hoc basis via Zoom.

After a significant search and comparison of several quotes, an app development company (ITHands) was identified and contracted for the project. They are based in the USA and India, and have a long track record of app development in collaboration with the non-profit sector. Contracts were completed between UCT and ITHands in May 2020. During the initial app design phase Dr Heunis and ITHands met twice



per week via Zoom. The final app wireframes and designs were signed off in August 2020 after which development of the TAND Toolkit app commenced. Dr Heunis now meets with ITHands once a week to discuss all app development queries and to perform interim iterative testing of the app and the app administration panel. She feeds back all technology development progress to the Action Group.

The current projected timeline is to have the minimum viable product for phase I of the app completed on target by the end of October 2020. Internal testing by the Technology Group then needs to be completed, after which data collection and validation of the TAND-SQ Checklist can commence. Development of phase I of the app involves user registration, capturing informed consent, user management, gathering information about their TSC, completing the TAND-SQ Checklist, displaying the TAND Cluster profile, and the capability to capture short surveys. Phase II of the app will incorporate the clinical consensus guidelines for each cluster profile. Development will commence once phase I of the app has been completed and the consensus guidelines have been finalised.



App in development

Cluster Groups (Aim 2 of the TANDem project)

The Cluster Groups are led by Dr Stephanie Vanclooster, the postdoctoral researcher. Eight cluster groups were created to lead in the development of consensus guidelines for the assessment and treatment of TSC. Each cluster group has a lead, a co-lead, and 1–3 additional members, with at least one family representative.

Cluster groups generated a basic template for drafting of their literature reviews and all first drafts were completed by the end of May 2020. After internal review by the Action Group, a modified structure was proposed and all cluster groups have restructured their chapters based on the revised format.

Between June and August 2020 each cluster group presented their chapter to the consortium. These cluster presentations happened once per week via Zoom. Each cluster chapter was reviewed by 2 or more reviewers (at least 1 family representative and 1 academic member of the consortium). Cluster meetings included a presentation of the cluster chapter (20min) followed by feedback from reviewers (20min) and open discussion about the chapter (20min).

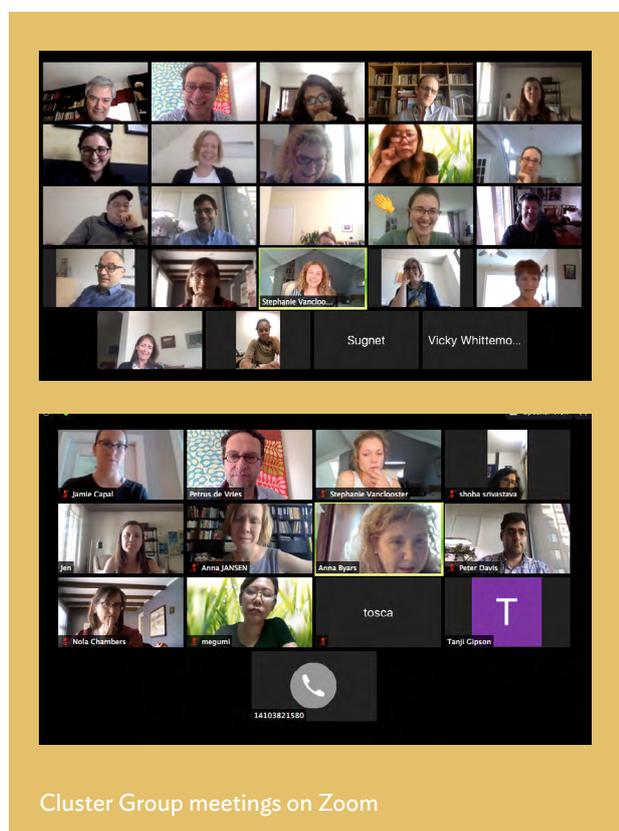
Cluster chapters are the basis for a) individual chapters in a TAND book for families and practitioners, b) a consensus clinical guideline manuscript for peer-reviewed publication, and c) the generation of the consensus clinical guidelines toolkit to be built into the TAND Toolkit app.

The activity surrounding the cluster work has been on target and has been very positive and productive to date. All chapters have been completed and reviewed and all clusters have submitted summary statements and recommendations that will be used for consensus building, described below.

Validation Group (Aim 1 of the TANDem project)

The Validation Group is responsible for the validation of the app-based TAND-SQ Checklist against expert clinical data. It includes the Steering Group plus representatives from the two validation sites – Boston (Prof. Mustafa Sahin and Dr Peter Davis) and Cincinnati (Prof. Darcy Krueger and Prof. Jamie Capal). Validation is scheduled to start in Quarter 1 of 2021.

At present the main activity is discussing IRB/Ethics regulations and requirements for this part of the project.



Cluster Group meetings on Zoom

Emerging Researchers Group (Aim 3 of the TANDem project)

Given that research mentoring and capacity building are goals of the TANDem project, a separate group was set up for self-identified emerging/early career researchers. This group meets quarterly via Zoom and uses the meeting as a forum to talk about career development, research and mentoring ideas.

Dissemination Group (Aim 3 of the TANDem project)

This group is responsible for communication and dissemination of information about TAND and the TANDem project. It is led by Prof. De Waele and includes the Action Group and other consortium members.

The Dissemination Group led the development of the TANDem logo and visual branding, and is currently developing a TANDem website for ongoing information sharing about TAND and the TANDem project.

A range of dissemination activities have already taken place over the last 12 months including:

- a a publication about the TANDem project in the Tuberous Sclerosis Alliance (USA) newsletter
- b a live-streamed Facebook presentation about the TANDem project (with >2,500 live viewers) in March 2020
- c two podcasts
- d participation in a Zoom webinar about COVID-19 and TAND in partnership with the Tuberous Sclerosis Association, UK



The TANDem project featured in the Tuberous Sclerosis Alliance (USA) newsletter

Family Representatives Group

The TANDem project was fundamentally set up as a participatory project with multilevel stakeholders. For this reason, it was important to ensure that people with TSC and families who live with TSC have a clear and strong voice at all levels of the project.

The Family Representatives Group therefore includes all TANDem members who have a lived experience with TSC. All of them wear multiple 'hats' as part of the project, either as scientists, educators, clinicians or as leaders in global non-profit organisations. Family representatives are part of all other groups in the project to ensure the project will deliver direct benefits to the TSC community.

TANDem consortium

All collaborators on the project are members of the TANDem consortium, which meets every 3 months via Zoom.

In the consortium meeting all groups report back to one another to ensure that there is a single forum for information sharing and planning.

The key goal of the last consortium meeting was to make a decision about the face-to-face consensus conference that had been scheduled to take place in London in November 2020 (on the two days preceding the International TSC conference). In light of the COVID-19 pandemic, the TSC conference was postponed to June 2021. After deliberations, a decision was made a) to hold a virtual consensus conference in November 2020, and b) to have a separate face-to-face TANDem consortium meeting in June 2021.



The TANDem consortium meeting on Zoom

The global map below shows all members of the consortium and their geographical locations.



6 Milestones and deliverables in relation to the *TANDem* protocol timelines

As outlined in the *TANDem* protocol, Year 1 included the first 3 of the project steps:

Step 1 (months 1–3):

Setting up the project and launch meeting.

We were able to complete the contractual paperwork, appointments and launch meeting. This step has allowed us to form the consortium, agree on work packages and teams, communication strategies and to develop the *TANDem* logo.

Step 2 (months 4–15):

Development and quantification of the *TANDem*-SQ Checklist and Smartphone app.

We have developed the *TANDem*-SQ, a self-report and quantified version of the *TANDem* Checklist, based on the original *TANDem*-L. The *TANDem*-SQ has been reviewed by the Steering Group and Family Representatives Group, typeset by our graphic designer and is currently under review by the consortium.

The *TANDem* Toolkit app is currently under development, as described above, with a scheduled phase I completion date of 30 October 2020. In November 2020, the Technology Group will conduct internal testing of the app. During this time the app developer will be available to fix any app-related bugs encountered. Data collection and validation is planned to commence early in 2021.

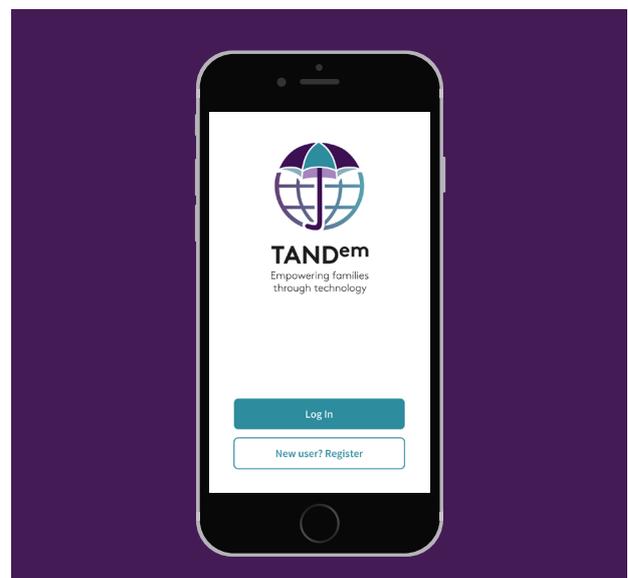
Step 3 (months 4–15):

Generation of consensus clinical guidelines for the identification and treatment of *TANDem*.

As outlined above, this process was led by the Cluster Groups, and the first set of cluster chapters have been written, reviewed and revised. Clusters have performed detailed reviews of the literature and have developed consensus within each cluster.

The next step is to develop consensus between clusters and within the consortium as a whole. This process has started and is outlined on pages 16 and 17.

In addition to the detailed targeted review within clusters, we have also started to conduct a comprehensive scoping review across all aspects of *TANDem* research performed to date. This process is being led by Dr Vanclooster, the postdoctoral researcher, and Dr Stacey Bissell, one of the cluster leads. Our aim is to complete the scoping review data analysis by November 2020, and for the manuscript to be ready for submission early in 2021.



7 The virtual consensus conference (November 2020)

Given that COVID-19 has prevented a face-to-face conference in November 2020, we are now preparing for a virtual consensus conference.

The conference will take place on 9, 10 and 11 November 2020, and will consist of three 4-hour Zoom sessions in total.

Session 1 (9 November 2020)
will focus on consensus building

Session 2 (10 November 2020)
will focus on the transition process from cluster chapters to the toolkit guidelines to be incorporated into the TAND Toolkit app

Session 3 (11 November 2020)
will focus on next step planning, including decision-making about impact activities scheduled for June 2021 in London, UK

In preparation for the virtual consensus-building, we have generated a remote procedure for this activity:

- a All summary statements and recommendations from the Cluster Groups have been assembled into a single document to be distributed to all *TANDeM* consortium members
- b Consortium members will rate each statement and recommendation using a Likert scale (strongly agree/agree/disagree/strongly disagree)
- c Consortium members will also rank their top 3 recommendations per cluster
- d All data will be collected using Google Forms and will be summarised to identify which items consensus has already been achieved for, and which items require further clarification and direct consensus discussions
- e A final round of ranking will be included in the virtual consensus meeting
- f The final list of consensus items will be used to draft the consensus manuscript for peer-reviewed publication
- g Top-ranked items will also be used to develop the TAND Toolkit for the app



8

Next steps for the *TANDem* project

Over the next 12 months (year 2 of the project), we will:

- a Complete the November consensus conference (virtual meeting)
- b Complete website development
- c Complete the scoping review
- d Finalise ethical submissions in all relevant centres
- e Complete development and internal testing of phase I of the app
- f Perform data collection and validation of the app-based *TAND-SQ*
- g Start drafting the toolkit to be incorporated into the TAND Toolkit app
- h Have a consortium meeting with impact activities in June 2021



9 The impact of the COVID-19 pandemic

In spite of the global devastation caused by the COVID-19 pandemic, the *TANDem* consortium has been very fortunate. Given that the project is a global one with a strong technology component, we have been able to continue with all project aims over the last 12 months.

Our only modification to the project so far has been the need to move the face-to-face consensus conference to a virtual conference, which will take place in November 2020, at the same time as the originally scheduled face-to-face conference.

We have also not had any major financial impact given that the consensus conference did not require any pre-payment. We have been very conscious of the impact of the pandemic on global economies and currency fluctuations. We therefore negotiated with the University of Cape Town to hold *TANDem* funds in a ‘transmission’ account in euros and to draw-down funds to UCT or VUB only as required. This has fortunately provided significant protection against currency fluctuations over the last 12 months.



10 Deviations from the project plan and/or contractual agreements

To date we have had 3 deviations from the project plan/contractual agreements, and all of these have been approved by the King Baudouin Foundation:

- 1 We appointed a postdoctoral researcher instead of a PhD student
- 2 We transferred budget from UCT to VUB for the project coordinator (who was scheduled to be appointed through UCT)
- 3 We changed our technology provider from a South African non-profit technology development company to ITHands (a USA/India-based technology development company)

Given that we have appointed both members of staff at VUB rather than one at UCT and one at VUB as originally budgeted, we are seeking approval from the King Baudouin Foundation to revise the project budget by moving the project-coordinator funding from the UCT budget to the VUB budget for years 2, 3 and 4 of the project. Once approved by the funder, we will proceed with contractual amendments to reflect this.



