Boosting Societal Adaptation and Mental Health in a Rapidly Digitalizing Post-Pandemic Europe: BootStRaP

Deliverable D1.2

Phase 1 Protocol

WP1 – Recruitment and Retention

Task 1.1 – Ethics and Legal Issues

Short title: BootStRaP

Version number: 1.2

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Dragon Game app	17/05/2024	Anita Meinke Megan Smith	University of Zurich University of Hertfordshire	Addition of the Dragon Game app
Voucher delivery	19/09/2024	Megan Smith	University of Hertfordshire	Voucher is not delivered via the BootstrApp

Statement of originality:

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation, or both.

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General Information

This document provides details regarding the setting up of, conduct, analysis and dissemination of the European Health and Digital Executive Agency (HADEA) funded study (Project: 10108238; Boosting Societal Adaptation and Mental Health in a Rapidly Digitalizing, Post-Pandemic Europe).

The University of Hertfordshire will sponsor this trial. The below listed organisations are the collaborators of the study. As such, a collaboration agreement will be signed by the parties, specifying responsibilities and financial arrangements.

Chief Investigator	Prof. Naomi Fineberg
Study Coordinator	Natalie Hall
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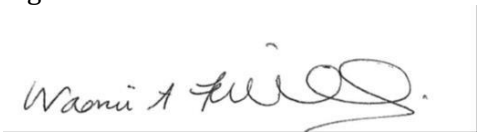
Signature Page

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator (CI) agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Good Clinical Practice (GCP) guidelines, the Sponsor's (and any other relevant) Standard Operating Procedures (SOPs), and other regulatory requirements as amended.

We agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

We also confirm that we will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest, accurate and transparent account of the study will be given; and that any discrepancies and serious breaches of GCP from the study as planned in this protocol will be explained.

Name:	Role: Chief Investigator	Signature:
Naomi Fineberg		 Date: 12/04/2024

Glossary of Abbreviations and Key Terminology

Abbreviations and definitions:

ACSID	Assessment of Criteria for Specific Internet-use Disorders
BFI-10	10-item version of the Big-Five-Inventory
BootStRaP	Boosting Societal Adaption and Mental Health in a Rapidly Digitalizing, Post-Pandemic Europe
CHI-T	Cambridge–Chicago Compulsivity Trait Scale
CI	Chief Investigator
CRF	Case Report Form
CSS	Cyberchondria Severity Scale
DASS-21	Depression Anxiety Stress Scale
DEC	dissemination, communication and exploitation
DPA 2018	Data Protection Act 2018
EAB	Ethics Advisory Board
EGCS	Experience of Gratification and Compensation Scale
EQ-5D-Y	European Quality of Life 5 Dimensions
EU	European Union
EYMH	Euro Youth Mental Health
FAIR	findable, accessible, interoperable, reusable
FAS	Family affluence scale
FOMO	Fear of Missing Out
GA	General Assembly
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
HADEA	European Health and Digital Executive Agency
HRQoL	Health-Related Quality of Life
I-PACE	Interaction of Person-Affect-Cognition-Execution
IAB	Impact Advisory Board
ICF	Informed Consent Form
IDC	Inter Disciplinary Center
ISAAQ-10	Internet Severity and Activities Addiction Questionnaire – 10 item version
ISAAQ-A	Internet Severity and Activities Addiction Questionnaire - Activities
ISAAQ- ED	Internet Severity and Activities Addiction Questionnaire – Eating Disorder
IUES	Internet Use Expectancies Scale
NIAAA	National Institute on Alcohol Abuse and Alcoholism
OS	Operating System
PaedS	Paediatric Self-Stigmatization Scale
PI	Principal Investigator
PIUQ	Problematic Internet Use Questionnaire
PPI	patient-public involvement
PQ-LES-Q	Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire
PUI	Problematic Use of the Internet
QA	Quality Assurance
QALYs	Quality Adjusted Life Years
QC	Quality Control

QMS	Quality Management System
Participant	An individual who takes part in a study
PO	Project Office
REC	Research Ethics Committee
RedCap	Research Electronic Data Capture
S-CIUS	Short-Compulsive Internet Use Scale
SAB	Scientific Advisory Board
SC	Steering Committee
SDQ	Strengths and Difficulties Questionnaire
SERI	Swiss State Secretariat for Education Research and Innovation
SOCS	Short Obsessive Compulsive Disorder Screener
SOP	Standard Operating Procedure
SST	Stop-Signal-Task
TSC	Trial Steering Committee
UK	United Kingdom
UKRI	Research and Innovation Fund, Innovate UK program
UPPS-P	Urgency – Premeditation - Perseverance - Sensation Seeking - Positive Urgency
WP	Work Package

Study Summary

Full title	Boosting Societal Adaption and Mental Health in a Rapidly Digitalizing, Post-Pandemic Europe
Short title/Acronym	BootStRaP
Protocol Version Number and Date	Version 1.1 16/05/2024
Start Date	When all approvals have been received (REC and R&D)
End Date	01/09/2025
Study Duration	12 Months
Study Design	Naturalistic Cohort Study
Sponsor/Co-sponsors	The University of Hertfordshire
Chief Investigator(s)	Prof. Naomi Fineberg
Funder	European Union, European Health and Digital Executive Agency (HADEA), Research and Innovation Fund, Innovate UK program (UKRI), Swiss Confederation, State Secretariat for Education Research and Innovation (SERI)
REC Number	LMS/SF/UH/05626
Study Objective(s)	To determine the multifactorial determinants of healthy vs. unhealthy internet usage among European adolescents aged 12-16 years. To determine the health economic impact of Problematic Use of the Internet (PUI) for European citizens
Planned Sample Size	3,600 (approximately 400 young people at each site)
Participants	Young adolescents aged 12-16
Intervention	Not applicable.
Follow up duration	The primary endpoint is assessed monthly during a six month period. Additional variables quantifying PUI are recorded at Baseline and six months after baseline.
Outcomes	The primary endpoint quantifying PUI is the short compulsive internet use scale (S-CIUS) (Besser et al., 2017; Pérez-Sáenz et al., 2023). In addition, PUI symptoms will be quantified by the PIUQ (Demetrovics et al., 2008) and the ISAAQ (Omrawo et al., 2023).

1. Introduction

1.1. Study rationale

Problematic use of the internet (PUI) is a public health concern in an era of digital technology where young people become familiar with computers, mobile devices and the Internet at very early ages. Although young people's internet use has many functional and enriching aspects, some adolescents may develop unhealthy patterns of internet use and may experience associated health issues which develop early in life and once present tend to endure (Brand et al., 2019; Gjoneska et al., 2022).

1.1.1. Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study.

The epidemiology of PUI is still unclear and prevalence rates differ strongly with a variety of assessment methods. Prevalence also differs among PUI subtypes with low/lower-middle income countries showing a higher burden (Meng et al., 2022). In a recent study of European school children, rates of PUI reached as high as 30% (Mohler-Kuo et al., 2021).

Besides socio-economic determinants of risk for developing PUI, in children and adolescents there may also be risk determinants that lie in the personality constitution, including regulation of cognition and executive function (see Figure 1). The Interaction of Person-Affect-Cognition-Execution (I-PACE) model, developed by members of our Consortium (Brand et al., 2019), defines a range of different vulnerability factors driving risk of PUI, their interactions and the consequences for mental health. The central assumption is that PUI develops through the interaction between an individual, their mental and physical state, cognitive processing and specific aspects of the digital environment.

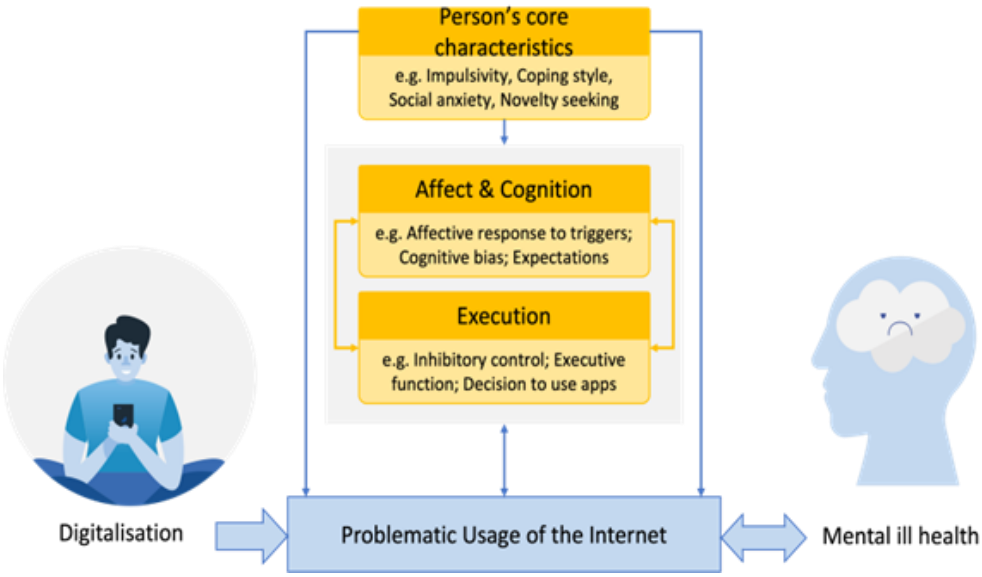


Figure 1: The mediating role of persons' characteristics between digitalisation and mental health

As the issue of causality is highly relevant for deriving appropriate interventions, we aim to identify individual risk and resilience factors. According to current models, vulnerability to PUI is linked to a broad range of individual and relational and societal factors (see logic model, Figure 2) that centre around fundamental difficulties in executive processing linked to 'self control' that may feasibly be detected in 'at risk' individuals. Self-control in relation to internet use can, in turn, be decomposed into (at least) two complementary and potentially interlinked latent phenotypes involving A) affect (emotion) regulation, controlling sensitivity to positive and negative reinforcement driving the pathway toward addiction (Brand et al., 2019) and B) inhibitory executive control restraining impulsive/compulsive urges to repetitively engage acting as a counterpart to the driving pathways (Brand et al., 2019).

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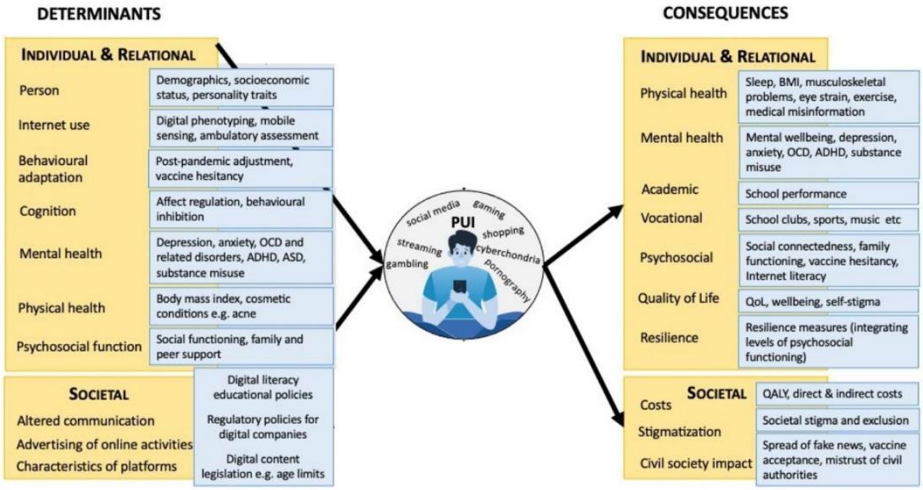

Figure 2: The logic model of PUI (based on (Brand, 2022; Brand et al., 2019b).

Convergent evidence suggests these two phenotypes might be linked to specific cognitive determinants that enhance the risk for developing PUI (Figure 2). As such, PUI driven by low affect regulation capacity might be learned through positive (experiencing reward and pleasure) and negative (experiencing less stress and negative mood) reinforcement where the Internet is used to "feel better/less bad". Another phenotype of PUI might be associated with excessive urge-driven or habitual behaviours that cannot be controlled and persist, possibly in a stereotyped way, despite knowledge that they are unnecessary or in the face of negative consequences, where the internet is used because of a sense of "must do", rather like compulsive disorders such as obsessive-compulsive and related disorders (Brand et al., 2019; Whiteside et al., 2004). The significance of this premise is that this proposed central mechanism applies not only to those 'at risk', but also across the well-being spectrum. Critical latent cognitive- control domains are proposed to develop differently across individuals with (at-risk for) PUI during adolescence, representing measurable targets for assessment of individual risk as well as a basis for individualized intervention (Brand, 2022; Fineberg et al., 2022).

Therefore, we hypothesize that it is of importance not only to determine the degree of risk/resilience in relation to PUI in general but also to differentiate the form of PUI, based on the presence of motivational drivers ("feels better" and "must do"), as a platform for designing and delivering prevention and

intervention options that target the drivers of problematic internet use at the level of the individual for greater efficacy.

In addition to the assessment of risk determinants of PUI, we assess the cost and burden of PUI, in order to provide reliable estimates as to how harmful PUI actually is to young people and in which specific ways it effects their well-being, and as a platform for the health economic assessment of the cost effectiveness of such interventions.

1.1.2. Level of evidence related to the mechanism of action.

The study does not include a 'treatment' intervention but will assess individual risk and resilience factors that distinguish phenotypes of PUI and will investigate which individuals may benefit best from specific interventions (which will be tested in a future study).

Based on extant theoretical models (Figure. 2), as well as our own data collected in preparation for this research (partial correlations significant against PUI scores with medium or larger effect size, each $p<.001$ ($N=640$)), risk phenotypes of PUI exist. These are underpinned by diminished self-regulatory abilities, which can be divided into effect regulation and executive control and which constitute two largely dissociable underpinning mechanisms (and thus intervention targets).

To address these affective and cognitive determinants of PUI, we will recruit a large cohort of young people (Cohort 1). We will assess measures in Cohort 1 that screen for executive control capacities, impulsive tendencies, compulsive traits and symptoms (Fineberg et al., 2022), mood disposition, affect-regulation and reward-based learning. Including measures that might be associated with both diminished affect regulation and diminished executive inhibitory control will allow us to cover various possible forms of PUI and reliably screen for high vs. low risk of developing PUI.

In order to conduct our neurocognitive assessment of affect regulation and executive inhibitory control, we use BrainPAC software (*Project - The BrainPark Assessment of Cognition (BrainPAC) Project | BrainPark*, n.d.). BrainPAC is a neuroscience-informed, accessible, engaging, and purpose-built tool to assess neurocognitive functions that drive many forms of addictive behaviours including PUI guided by the National Institute of Mental Health Research Domain Criteria and supported by international expert (DELPHI) validation (Albertella et al., 2020; Yücel et al., 2019, 2021). Several BrainPAC tasks have recently been shown to predict PUI (Albertella et al., 2017; Le Pelley et al., 2015). For example, greater reward- related attentional capture in the Value-Modulated Attentional Capture (VMAC) task ($p < 0.01$) was independently associated with a measure of PUI (JEG-IAT-10 score) while controlling for age, gender and stress (data in preparation for publication). Also, VMAC predicted PUI longitudinally, during the 2020-21 COVID-19 lockdown. Specifically, we found that this task moderated the effects of COVID stressors on PUI at follow-up ($p < .028$; $N = 246$) such that only those individuals who showed high attentional capture by reward cues and were exposed to COVID stressors went on to show greater PUI at follow-up. Individuals who were exposed to the same number of COVID stressors but who did not show attentional capture by reward cues did not show increased PUI at follow-up, indicating that low attentional capture by reward cues may be protective against stress-related increases in PUI (data in preparation for publication). Similarly, also, scores on the Stop-Signal Task (SST) (Verbruggen et al., 2019) have been shown to be enhanced in individuals with PUI (Ioannidis et al., 2019), indicative of lower inhibitory cognitive control associated with an unregulated and possibly harmful use of the Internet.

Therefore, we decided to include the VMAC and a BrainPAC-enhanced version of the SST into our assessment battery in order to screen for decreased inhibitory control in respective individuals.

Besides the neurocognitive assessments of affect regulation and executive inhibitory control, self-report measures of mood disposition and affect regulation (e.g., DASS-21, SDQ, IUES, EGCS) and compulsivity (e.g., SOCDS, CHIT) have repeatedly been shown to be associated with PUI (Brand et al., 2019; Chamberlain et al., 2017), and so we will also include these measures.

Importantly, passive mobile sensing of behaviour patterns such as physical activity levels, sleep patterns and internet use patterns provides essential objective measurement, less prone to confounds than hitherto, which could be of great value for assessing PUI (Carmi et al., 2022; Montag et al., 2019; Montag & Rumpf, 2021). Therefore, we also apply mobile sensing methods to supplement our innovative cognitive test batteries (BrainPAC), assessing key affective and executive (including inhibitory executive control) functions.
We additionally assess the cost and burden of PUI among adolescents in Cohort 1. These analyses are based on measures of Quality of Life. Despite the multitude of available quality of life instruments, concerns have been raised regarding the content validity of these instruments, and hence suitability for use in mental health in general and adolescent mental health in particular. While the EQ-5D (Wille et al., 2010) is probably the most widely validated scale for measuring Health-Related Quality of Life (HRQoL) across Europe, current cost–utility computations (mostly based on the EQ-5D and SF-36) favour physical health over mental health and rely on adult 'weights' for child and adolescent quality of life. This provides an opportunity for BootStRaP to develop our own weights considering the large scope of the project (sample size) but also cross-country validity (based on the sampling strategy). It is for this reason that we propose two HRQoL scales - the Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q) (Endicott et al., 2006), which is probably the most appropriate as it captures domains of relevance for adolescents and is sensitive to the kinds of factors that are most likely important in this study, which will be used as the main utility scale, and the EQ-5D-Y, which is crucially very short (2 mins application) and easy to apply (also has a visual analogue version), which we will apply as a secondary outcome. Most other scales used in the assessment protocol (see section 6.1.1., Table 1) have been used in previous studies and are considered reliable and valid.

2. Aims and Objectives

2.1. Study objectives

The *joint primary objectives* are to

- Determine the multifactorial determinants of healthy vs. unhealthy internet usage among European adolescents aged 12-16 years and **develop algorithms for quantifying individual risk of PUI**. The algorithms will be developed applying both classical and modern machine learning techniques. The primary endpoint quantifying PUI is the **short compulsive internet use scale (S-CIUS)** (Besser et al., 2017; Pérez-Sáenz et al., 2023). In addition, PUI symptoms will be quantified by the PIUQ (Demetrovics et al., 2008), the ISAAQ (Omrawo et al., 2023) and the ACSID-5 (Müller et al., 2022). (at baseline and t2).
- Use these algorithms to develop a **new, user friendly, digital platform** supported on a smartphone app (BootstrApp) that would **enable early detection of adolescents 'at risk' of PUI before it is apparent,** as a prototype method for early targeted intervention.

- Determine the **health economic impact of PUI for European adolescents**. Health economic impact will be reported as cost and burden of PUI in European adolescents.

The *secondary objectives* are:

- Investigate the logic model which underlies this study. The model is illustrated in Figure 2. The logic model describes preceding factors and consequences of PUI. We will generate and test structural equation models which are informed by the logic model.
- Explore further associations among the different constructs. For example, those at risk and not at risk will be compared, associations with well-being will be analyzed for its clinical importance, and with different forms of PUI (cyberchondria, social media use etc.), as assessed by the ISAAQ-A (Omrawo et al., 2023).

The data set is made available to BootStRaP researchers for further secondary analyses. Researchers who want to conduct secondary analyses will submit a proposal describing their question and intended analysis to the steering committee of the BootStRaP project. In general, proposals are acceptable if they do not threaten the scientific integrity of the BootStRaP project, as confirmed by the steering committee. In addition, local teams will seek research ethics approval where required by their local ethics committee. After the main study results have been published, the anonymized data set will be made available to other researchers according to FAIR principles (outlined in the Data Management Plan).

3. Methods

3.1. Study Design

This is a naturalistic cohort study aiming to develop an algorithm for predicting risk to develop PUI. This algorithm will inform subsequent phases and studies within the BootStRaP project.

The study is conducted across 9 study centers in different European countries, which will recruit adolescents via schools. On average 3 different schools will be included per center (400 students, 3600 in total) (Table 2). A heterogeneous general population-based sample of study participants ageing from 12 to 16 years, mixed gender, from diverse socioeconomic backgrounds and rural and urban environments will be recruited to cover the entire well-being spectrum.

An overview of the study and all assessments is provided in Table 1. For a period of 6 months, participating students will be prospectively assessed by having a specifically developed mobile app – the BootstrApp - installed on their smartphone, which will prompt the students to complete questionnaire assessments. There will be three survey-based main assessments (T1-T2, 1h per assessment, spaced by 3 Months). Short additional questionnaires will be integrated at defined timepoints throughout the study. This includes four additional assessments of the (S-CIUS) (Besser et al., 2017; Pérez-Sáenz et al., 2023), to provide monthly information on PUI, two 7-day periods (after T1 and T2) of daily information on activities on the internet and affect, and two items on mood and patience that will be queried every eight days (Table 1). Further passive mobile sensing data will be collected by the smartphone app itself (e.g. actual time and frequency using the smartphone per day). A six-month assessment period is known to be long enough for a significant increase in unhealthy internet use to emerge; in one large study of previously healthy internet users, 14% or 4.1% developed either problematic or pathological use, respectively, over 6 months (Chen et al., 2014). To predict risk for developing PUI from multisource big

data we use a Machine Learning approach rigorously underpinned by psychological theory (Montag & Rumpf, 2021).

***Table 1**- Schedule of procedures and assessments*

	Enrollment	**Assessments**					
	T1			**T1a**			**T2**
Procedure/ Variable	**Baseline**	**+1M**	**+2M**	**+3M**	**+4M**	**+5M**	**+6M**
Initial parent letter + study information pack	**x**						
Information session for parents *	**x**						
Reminder letter for Parents	**x**						
Information session for young people in class	**x**						
Informed consent and assent	**x**						
Demographics							
Sex	**x**						
Gender	**x**						
Age	**x**						
Year group at school	**x**						
PUI[a] and clinical variables							
S-CIUS[b]	**x**	**x**	**x**	**x**	**x**	**x**	**x**
PIUQ [c]	**x**						**x**
ISAAQ-A[d]	**x**						**x**
ISAAQ-10[e]	**x**						**x**
ISAAQ- ED[f]	**x**						**x**

ACSID-5[g]	x							x
DASS-21[h]	x							x
Alcohol items	x							x
PaedS[i]	x							x
Browser activity	x							x
Cognitive control								
BrainPac SST[j]	x							X
Question on patience [#]	→		→	→		→	→	→	→
Clinical variables								
SOCS[k]	x							x
SDQ[l]	x							x
CSS[m]	x							x
Affect regulation								
BrainPac VMAC[n]	x							x
Question on mood [#]	→		→	→		→	→	→	→
Persons' characteristics								
BFI-10[o]					x			
UPPS-P[p]					x			
Compulsivity and physical health								
CHI-T[q]					x			
Height and Weight					x			

Favorite sports interest		**x**
Internet use expectancies, Internet-use experiences, FOMO[r]		
IUES[s]		**x**
EGCS[t]		**x**
FoMO[u]		**x**
School performance, family background, smartphone restriction, vaccine hesitancy		
School marks		**x**
Family background		**x**
Socioeconomic status (FAS[v])		**x**
Vaccine Hesitancy Scale		**x**
Misinformation		**x**
Restriction		**x**
Mobile sensing[+]		
	→	
Assessment of cost and burden of PUI		
PQ-LES-Q[w]	**x**	**x**
EQ-5D-Y[x]	**x**	**x**
Ambulatory Assessment		

	x	x

*Note. * Participation of parents can be mandatory or voluntary based on local requirements. # Assessed every eight days. + Continuous recording.*

[a] *Problematic Use of the Internet*

[b] *Short-Compulsive Internet Use Scale*

[c] *Problematic Internet Use Questionnaire*

[d] *Internet Severity and Activities Addiction Questionnaire* - Activities

[e] *Internet Severity and Activities Addiction Questionnaire* – 10 item version

[f] *Internet Severity and Activities Addiction Questionnaire* – Eating Disorder

[g] *Assessment of Criteria for Specific Internet-use Disorders*

[h] *Depression Anxiety Stress Scale*

[i] *Paediatric Self-Stigmatization Scale*

[j] *BrainPac Stop-Signal-Task* (SST)

[k] Short *Obsessive Compulsive Disorder Screener*

[l] *Strengths and Difficulties Questionnaire*

[m] *Cyberchondria Severity Scale*

[n] *BrainPac- enhanced Value-Modulated Attentional Capture*

[o] short 10-item version of the *Big-Five-Inventory*

[p] *Urgency – Premeditation - Perseverance - Sensation Seeking - Positive Urgency*

[q] *Cambridge–Chicago Compulsivity Trait Scale*

[r] *Fear of Missing Out*

[s] *Internet Use Expectancies Scale*

[t] *Experience of Gratification and Compensation Scale*

[u] *Fear of Missing Out Scale*

[v] *Family affluence scale III*

[w] *Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire*

[x] *European Quality of Life 5 Dimensions*

3.2. Study Setting

There are 9 collaborating European academic organisations as part of the BooStRaP project (Table 2). The collaborating academic organisations have been chosen their established track record in recruiting large cohorts of adolescents in mental health research and active research partnerships with local schools (Duarte et al., 2022; Flamarique et al., 2016; García-Moya et al., 2015; Lindenberg et al., 2022; Van Oort et al., 2009; Werling et al., 2021). Each of these academic organisations will identify several schools willing to take part. These designated schools will act as the recruitment sites for the study.

Recruitment of study participants takes place in the school setting approximately in September, the exact study start depends on the recruitment center and the beginning of the school year. To maximize retention, assessment batteries may be completed according to individual preference either at school or at home, in one session or up to 4 sessions across several days. All data collection is done via the BootstrApp and the Dragon Game app and is pseudonymized. Push notifications will guide participants through the data collection.

The Sponsor is the University of Hertfordshire, an academic institution based in the United Kingdom. The study is centrally organized and based on a shared study protocol, but consent and recruitment procedures are adapted to local requirements where needed.

3.3. Study Participants

3.3.1. Description of target group

The study's aim is to detect early risk for problematic internet use and in consecutive projects prevent the development of addictive usage patterns across the whole well-being spectrum, rather than to treat an already developed pathological use. The whole adolescent population is therefore included rather than specific subgroups. The study population will consist of young adolescents of all genders and between 12 and 16 years, recruited from schools with different socioeconomic backgrounds and from rural and urban areas. We strive to include young people from low/middle income families who might be especially vulnerable for PUI. By definition, the BootStRaP study is designed to evaluate and moderate online behaviour among young people using mobile devices. Therefore, it is a necessary condition, that young people involved have routine and exclusive access to a mobile device to be able to take part in the study.

The eligibility criteria are:

- Age between 12 and 16 years
- Routine access to a mobile device
- Student at a school involved in the study

3.3.2. Approaching study participants

Local research teams have already established contact with many schools interested in the project, as student ambassadors (see section 9) have been involved in reviewing study materials. The recruitment plan (Table 2) guides the selection of schools for participation. Within these schools, different classes are invited to participate, and all students of these classes are potential study participants. The parents of invited classes are informed before their child's information session and asked to provide consent, as detailed in section 4.3. Together with the designated BootStRaP Ambassadors (teacher and/or student, see section 9), local researchers then meet the students during class time to introduce and explain the

study, answer the students' questions, and obtain assent. It will be made clear there is no school pressure to participate.

3.3.3. Sample size, basic assumptions

This study is the first in a series of three studies building upon each other, which will be conducted within the BootStRaP project. Therefore, considerations regarding sample size and power estimates include the prospect of interventions introduced in subsequent studies. As yet there is little evidence of the effectiveness of this kind of intervention of problematic internet use (specifically as measured by the PIUQ), we assume alpha=0.05, 1-beta=0.8, with clustering by class (assumed to be n = 30), and a small effect size d=0.3, giving a required sample size n=176 per group. Further we assume 70% completion, and that 30% of children are high risk, providing samples of n=838 per group. We assume 2 groups (Type A [i.e., affect regulation phenotype] and B [i.e., inhibitory executive control phenotype]) and a control group for estimation and the total required sample size is therefore 3*838 = 2514, or 280 per study site. If a centre underperforms, others will increase recruitment to target.

4. Study Procedures

4.1. Study Setup

Ethical approvals will be obtained from each of the 9 collaborating academic organisations. The University of Hertfordshire, as the lead academic organisation, will provide a template set of study related documentation (e.g., study protocol, participant information sheets, informed consent and assent forms) that can be localised to meet the needs of local ethics committees. The study will be registered on CORDIS.

The BootStRaP study team has been established and BootStRaP ambassadors (teachers and students) will be recruited at each site. All study sites will be trained on the study related processes and procedures, and Good Clinical Practice (GCP) training will be performed where required. A project office (PO), steering committee, general assembly and three advisory boards (scientific, ethics and impact) have been formed. Ongoing monitoring of study processes and procedures will be undertaken on a regular basis by an independent monitor reporting to the PO and steering committee.

The BootstrApp used to provide questionnaires and collect information on mobile phone use is currently under development and will be ready and tested in mid-2024, as will the Dragon Game app which will be used to administer the BrainPAC tasks. A data storage system to store all assessments collected by the BootstrApp will be set up by the Ulm University (UULM). A project website (Net and Me – BOOTSTRAPP (internetandme.eu)) has been developed which will be used to present information on this and other studies in the BootStRaP project.

4.2. Recruitment

We will identify a small number of schools via existing academic relationships in each of the 9 collaborating countries who will act as recruitment centres. At each of these schools, we will designate teachers (at least one) and students (at least one, ideally more) to act as BootStRaP Ambassadors for the duration of the project. These BootStRaP Ambassador teachers and their continuous integration into BootStRaP meetings will ensure the involvement and retention of students in the study.

If a student organisation is available in schools, we will where possible also work with them to motivate student participation. We will also negotiate the most acceptable local incentives for aiding recruitment and retention among students (e.g., lotteries, competitions, honoraria, which may differ across centres), and optimal local methods for accessing potential participants in designated school classes.

Together with the designated BootStRaP Ambassadors (teacher and/or student), local researchers will meet the students as a class, introduce and explain the study and demonstrate the BootstrApp, which is uploaded onto students' smartphones for the duration of the study. Students have an opportunity to ask questions about the study.

Parents or guardians will also be given a parent or guardian information pack and the opportunity to attend at least one information session where they can ask any questions.

Eligible students will need to have received parent or guardian consent before providing their own assent. There will be a holding page present on the BootstrApp to prevent students starting the study before the information session has been delivered. Once students have attended the information session (delivered face-to-face, hybrid, or by video recording – school dependent) and provided assent, they will be given a code to enter the active assessment section of the BootstrApp and begin the study.

Study Campaign:

We will also run a national and international publicity campaign (supported by university press offices) in which delegates from candidate schools in each recruitment region will be invited to participate, to generate interest and enthusiasm in our European project among local schools.

Our research team will follow-up and regularly communicate with schools that are potentially interested to discuss the protocol to encourage participants. Our consortium has vast experience in interacting with the news, media and nurturing relationships with headteachers and staff of selected schools and in recruiting adolescents for interventional studies.

Table 2 – BootStRaP Recruitment Plan

Study centers/ country	**No. and types of participating school selective/ nonselective, urban/rural, mixed/single gender**	**Proposed size of total school sample**
University of Porto (UPORTO), Portugal	4 schools; nonselective; 2 schools in urban area;2 schools in rural area; all schools mixed gender	400 participants PA
Fundación para la Investigación Biomédica del Hospital Gregorio Marañón (FIBHGM), Spain	4-5 schools (more can be added if needed), mostly urban (rural areas could be added), mixed gender, different academic status. Years 1-4 at secondary schools (age 12-16)	400 participants PA
University of Hertfordshire, United Kingdom	6 schools: 2 per year for 3 years. Drawn from different parts of Hertfordshire, with pockets of high deprivation and ethnic diversity; selective/non-selective; urban/rural mix. 5/6 schools mixed gender aged 11-18 years. Academy status, nonselective	<=500participants PA

University of Heidelberg, Germany	Grades 6-10, (age: 11-18); 50% high-level, 30% medium-level, 20% low-level; urban (50%) and rural (50%)	350 participants PA*
University of Zurich, Switzerland	2-4 Secondary schools (12-15 years, medium level), 1-2 high schools (12-18 years, high-level,), 1-2 occupational schools (low/medium). Mixed gender, rural and urban	400 per participants PA
ELTE Eötvös Loránd Univsersity, Hungary	Age-appropriate selective sample of students from grades 6- 9 (12-16 yrs) in 4-5 schools. 3-4 urban, 1-2 rural. Mixed gender.	400 participants PA
Lithuanian University of Health Sciences, Lithuania	Selective sample of 4-5 schools. 3-4 urban, 1-2 rural. Mixed gender.	400 participants PA
Vrije Universiteit Amsterdam, Netherlands	Selective sample of hopefully 4-5 schools, perhaps more are needed (6-8): mostly urban, partly more rural areas, mixed gender, most likely also mixed ethnicity, different educational levels, with most from “mediate/high level". Classes in years 1-3 at secondary schools (ages 12-16 yrs)	400 participants PA
Centre Hospitalier Universitaire de Montpellier (CHUM), France	Selective sample of 4-5 schools. 3-4 urban, 1-2 rural. Mixed gender. Grades 7 – 11 (age 12 – 16/17 YO)	400 participants PA

4.3. Informed Consent

Active consent will be obtained prior to participation by assent from the child and parent or guardian consent for the child’s participation.

Although in several countries some of the young people will be old enough to provide informed consent for themselves, as all children will be recruited through schools, we will keep the process the same for all. Parents or guardians will be asked to provide consent (on behalf of the child) followed by child assent to take part in the study. Parent or guardian consent will be collected either on paper or electronically via the school’s preferred process. Assent will take place online directly in the BootstrApp. If required, child consent will be collected additionally on paper, depending on local requirements. The process is explained below, and Figure 3 provides a summary.

1. *Parent or Guardian Information Session*

All parents or guardians of children aged 12-16 years at the designated schools will be sent an information pack including: a letter inviting them to attend a dedicated information session, a copy of the approved participant information sheet for parents, their informed consent form (ICF), the approved young person information sheet and instructions on how to download the BootstrApp and the Dragon Game app.

This information pack will also be available to take home/be resent after the information session if needed and will be sent either in paper or electronic format, depending on local requirements and the school's communication policy. Parents or guardians will be invited to attend at least one information session run at the school delivered by the research team with support from the School's BootStRaP ambassadors (teacher and/or student).

This session will include adequate opportunity for the parent or guardian to ask any questions necessary and have them answered by the research team. Parents or guardians will be given information on how to contact the study team if they have further questions after the session. The timing and organization of these sessions will be defined by the local research teams together with schools.

2. *Parent or Guardian Consent*

Information on how to provide consent will be provided within the parent or guardian information pack. Once the parent or guardian is informed, we will ask them to provide consent for their child's participation in the study by completing an ICF. A parent or guardian will be required to give consent for their child's participation ahead of their child's assent to take part. If they do not wish their child to participate, they may fill in a box on the consent form registering this decision.

We understand that schools work differently and will work with the school to tailor the process to meet their preference and policies but also ensure processes are meeting local governance requirements. We will offer the choice of the following processes to gain parent or guardian consent for their child's participation:

> **Option 1**: Paper consent: Parents or guardians will receive their ICF in paper format and will be required to agree to the statements and sign with a wet signature.
>
> **Option 2:** Electronic consent via email: Schools will send parents the consent form along with the parent pack via email as an attachment. Parents or guardians can then agree to the statements and sign electronically on the form.
>
> **Option 3:** Electronic consent via database developed by local site: If requested, a database will be created purely for the collection of consent. The recruitment centres using that option create their own database held on their university servers. Parents or guardians will receive a link taking them directly to the electronic consent form where they will agree to the statements and sign electronically.

Ahead of the information session held at the school for the children, parents or guardians will be sent a letter reminding them to complete the consent form and support the download of the BootstrApp and the Dragon Game app on to their child's phone. If consent is on paper, they will also be reminded to send with their child to their information session at school.

3. *Downloading of the BootstrApp*

Parents or guardians will be asked to assist their child to download the BootstrApp and the Dragon Game app onto their mobile phone, using the download instructions provided in the parent pack, if they are happy for their child to take part.

They will need to enter the access code provided to them in their parents or guardians information pack into the BootstrApp. This code is required to ensure that the BootstrApp will be available to the child

when they attend their own information session at the school, as they will be using the BootstrApp to give their assent. The BoostrApp is available for all those with access to an App Store (Apple or Android) but only those with the given code will be able to access the app following the download and installation. This is to prevent those who are not students at the involved schools from taking part in the study.

Parents or guardians will be informed that once this BootstrApp is downloaded and installed onto their phones, their children will be able to access the participant information for students but a "holding page" will prevent them from going any further until they attend their own information session and give assent. Parents will be asked to encourage their children to read this material in advance of the student information session, should they wish to, but this is not essential as the same information will also be covered in the student information session.

4. Child Information Session

All children within the designated age range will be invited to attend a student information session (either in person or virtual) run by the research team along with the school ambassadors at their school. The session will run in group format and the number of potential participants in each group will be determined by the school and will ensure adequate opportunity for all potential participants to ask questions.

During the session the study will be explained to the children, the BootstrApp will be demonstrated, and the researcher will review the consent forms and identify those children whose parents or guardians have given consent.

5. Child Assent Provided on the BootstrApp

The research staff will check the parent or guardian ICF has been provided. In recruitment centres which require a child paper assent form, these forms will be checked together with the parent's forms. For those that have received parent or guardian consent, a unique parent identifier will be appended to the consent form and the child will be supported to enter this onto the BootstrApp. This is to ensure the child's identity could be found in case of need, such as premature withdrawal and to show that the child has received parent or guardian consent. In the case of children whose parents do not wish them to participate, it will be made clear at the student information session that they will not be able to proceed.

The child will then be asked to make sure they have read through the study information before giving their assent via the BootstrApp. The child information will be provided on the BootstrApp but hard copy information sheets will be available to children if preferred.

Children who would like to take part will then be able to provide assent to take part via the BootstrApp by agreeing to the statements presented to them (as shown in the accompanying consent form documentation). This will also be required, in the case children are required to provide assent on paper in line with local requirements.

To commence the study, students will be required to enter a study start code into the BootstrApp. This study start code is school specific and will allow whole cohorts to begin at the same time. Once this study start code has been entered, the child is enrolled in the study and will enter a 6-month assessment phase.

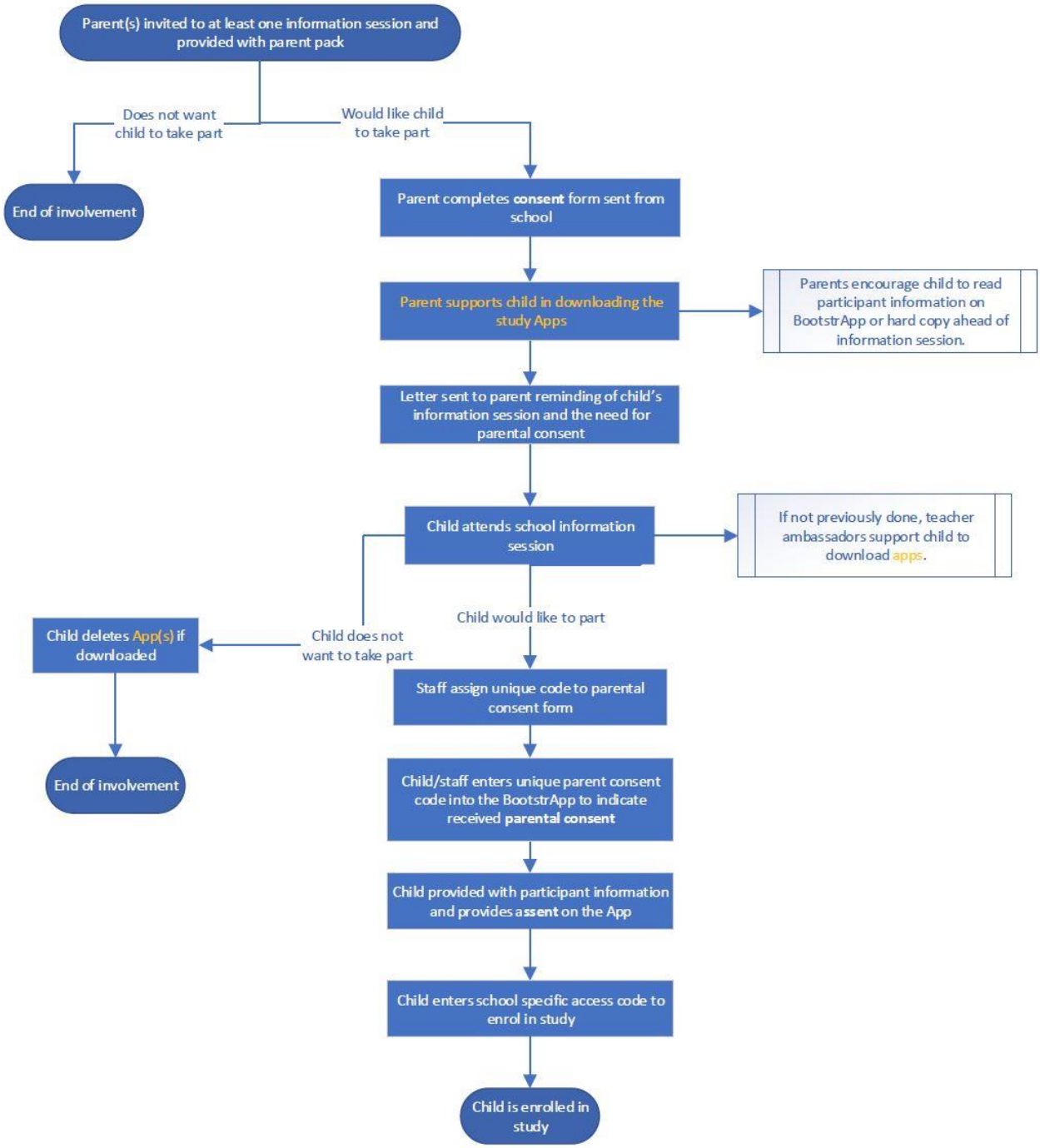

Figure 3: Consent process flow chart.

4.4. Withdrawal and discontinuation

Participation in this study is voluntary and study participants who wish to discontinue can opt out at any time without giving a reason. Participants can cancel their study participation in the "Cancel Participation" submenu inside the BootstrApp or by deleting the apps. The submenu includes a description of the implications of withdrawing from the study and a designated button to withdraw. Signing off the study results in an immediate stop of all data collection. Due to anonymization of data for Machine Learning and the data backup strategy, already transmitted data cannot be deleted, and this will be made clear in the participant information. Further processing will either take place pseudonymously (only for BootStRaP partners that have signed the Data Sharing Agreement) or anonymously (everyone else). The young people are informed before consenting on how they can withdraw, and that the deletion of data up to the point of withdrawal will not be possible.

4.5. Baseline

To initiate the study, the researchers meet the students together with the school ambassadors in class in dedicated information sessions, as outlined in the informed consent process (4.3). This meeting is announced to students and parents in advance. During the meeting, the researchers provide a detailed description and explanation of the study and encourage students to ask questions, if anything should be unclear. For students to provide assent and start participating, the parents must have provided consent in advance. After parental consent and assent and the information session at school, a unique code for each school must be entered to unlock the data collection. Afterwards the automated data collection via the app starts. For a list of the questionnaires at the first assessment block T1 see Table 1. Depending on local agreements with schools, time in class can be dedicated to completing the assessments or students will complete the assessments in their own time at home. To maximize retention, assessment batteries may be completed according to individual preference either in one session or up to 4*15 min blocks across several days.

4.6. Intervention

This is a naturalistic cohort study and does not include a treatment or intervention.

4.7. Follow up Procedures

BootstrApp will guide study participants through assessment blocks, granting access to information about upcoming assessments directly on its home screen. Automatic push notifications will be sent to prompt completion of upcoming questionnaires. Automated reminders will be dispatched through the app to ensure timely participation. Depending on individual agreements with schools, the young people can have the possibility to complete their assessments in class and local researchers can arrange visits in class or schools together with school ambassadors, to increase motivation and reinforce awareness of the upcoming assessment. The complete schedule of assessments including baseline and subsequent assessments is presented in Table 1.

4.8. Benefits

4.8.1. Benefits for schools

Participating schools become part of international research on PUI and can influence how the study is conducted (see section 9). They will get access to a network of PUI experts and will get featured on the

project website if they choose. In addition, schools can receive anonymous feedback if they wish. Educational input (e.g. Informative presentations for students or parents) can be offered by the recruitment centers depending on the interest of schools. School ambassadors will be involved in designing feedback and educational inputs for schools. Materials for developing educational input are already available on the BootStRaP website Net and Me – BOOTSTRAP (internetandme.eu). Any feedback or educational inputs are only provided after completion of the data collection, to avoid biasing the study results.

4.8.2. Benefits for study participants

As outlined, much emphasis will be placed on ensuring ongoing engagement with the young people involved, and participants who complete a minimum dataset will receive a certificate of completion and a payment compensation at the end of the 6-month assessment phase as a token of gratitude for their time and effort. Recruitment centres decide individually whether they provide the compensation in form of a voucher or a prize draw. Approximately 10 Euro per participant are available. The recruitment centres decide individually on the type of voucher.

In addition, study participants are offered feedback on their collected data after study completion in BootstrApp if they choose. This feedback will only be accessible after study completion, to avoid biasing the study results. The young people will be able to choose whether they would like to see feedback on their own data only, or additionally in comparison to the other participants as a whole. Feedback variables will include online activity such as screen time and the most used Apps, and some questionnaire results. Focus groups with young people at UULM and the study ambassadors (see section 9) were consulted for choosing the feedback variables.

4.9. End of Study

The end of study is defined as the time point when all participants have completed all scheduled assessments and all questionnaires/data items have been completed or the time frame to complete assessments is over for the last enrolled study participant. The study centers will be notified by the team at UULM.

Declaration of end of study forms will be completed and sent to each local Ethics Committee in line with their timelines and regulations e.g. within 90 days of the end of study where appropriate.

5. Safety

Study participants are a community sample and therefore generally healthy young people, not patients. The study is observational by nature and does not include a treatment intervention. The study assessments are survey based, not expected to cause distress and mostly take the form of validated questionnaires. The study participants are informed that they can withdraw at any time without giving a reason. Should participants experience emotional distress, the study app includes a dedicated submenu that signposts young people who may require assistance on where to seek help via school based, local or national mental health support services. The presentation of signposting content is developed together with young people at UULM. Easy accessibility and user friendliness for young people are high priorities and are assured by youth involvement activities (see section 9). It will be made clear in the participant information that no clinical interventions will be provided by the study team.

6. Data Collection, Management and Analysis

6.1. Data Collection

The study is a naturalistic cohort study with a 6-month prospective assessment period. The data is recorded automatically via a smartphone app, BootstrApp, which is developed for this study. Additional data is collected via the Dragon Game app, which includes the cognitive assessment tasks for affect regulation and inhibitory executive control. Apart from installation, the participants will only need to interact with the BootstrApp directly, as the BootstrApp will guide all data collection and forward the participants automatically to the Dragon Game app for the cognitive assessments. As a crucial part of data collection, no name or contact data are collected within the apps.

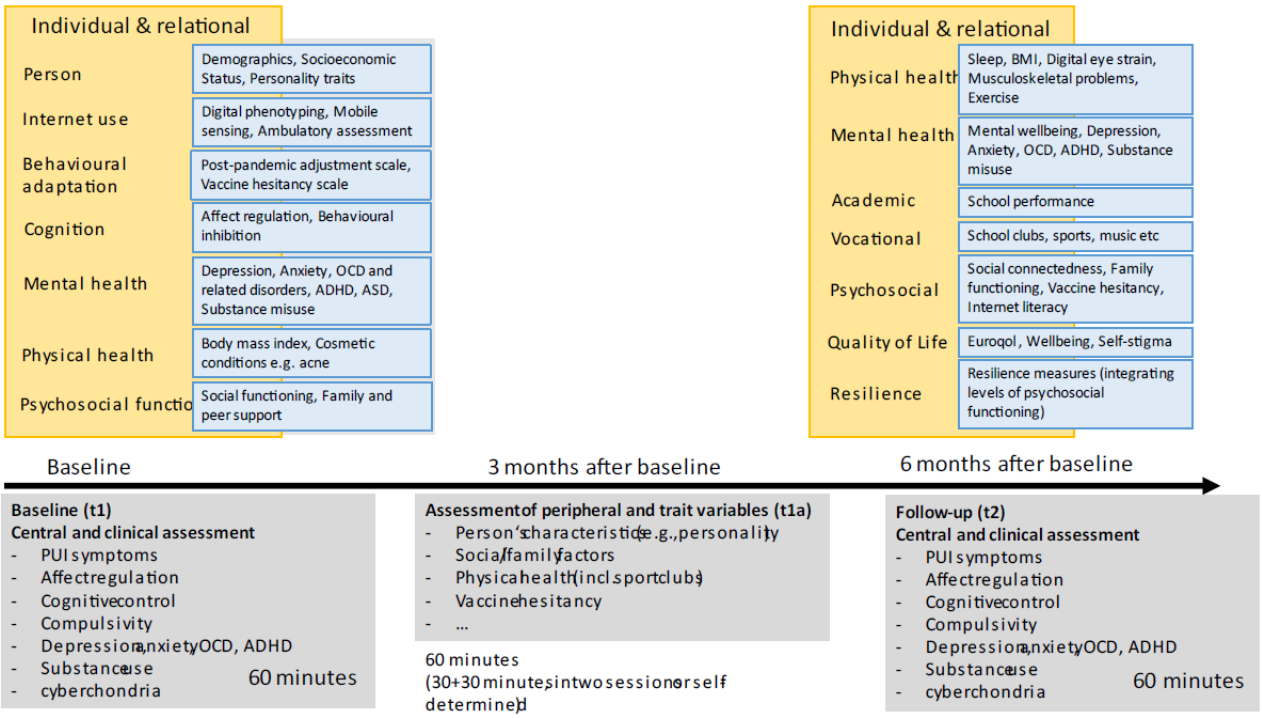

Figure 4: Key determinants (on the left) that are translated into the baseline assessment (t1)

The questionnaires and paradigms are applied in their respective translation (i.e., Dutch, English, French, German, Hungarian, Lithuanian, Portuguese, and Spanish). If not available in a certain language, instruments are translated by two independent researchers, back-translated into English, and validated by an expert panel with expertise in mental health research from University of Hertfordshire. The assessed variables reflect key determinants described in the logic model (Figure 4). Where necessary, permission to use is obtained and license agreements are arranged with the respective copyright holders of the instruments.

6.1.1. Assessment tools

Demographic information.

Questions on demographic information at T1 include age and year group at school as open text field questions. The study start code (see section 4.3) encodes participant's school and country of residence. Sex and gender information is collected using the two-step method as presented in Table 3.

Table 3. Demographic information (measured at baseline)

Were you born as a boy or a girl? >>We mean here how your parents registered you with the municipality.<<
as a boy
as a girl
prefer not to say
not sure
What do you feel you are? >>Your feelings may be different from how you were born.<<
a boy
a girl
between a boy and a girl
both a boy and a girl
neither a boy or a girl
prefer not to say
not sure

Core Determinants and Outcomes - measured at baseline + 6 months after baseline.

PUI variables

The ***Compulsive Internet Use Scale*** (CIUS) (Meerkerk et al., 2009) will be used in its 5-item short version (S-CIUS) (Besser et al., 2017) and is the primary outcome measure in this study and assesses severity of compulsive internet use.

The ***Problematic Internet Use Questionnaire*** (PIUQ) (Demetrovics et al., 2008) will be used in a shorter version (PIUQ-9) (Laconi et al., 2019).

The ***Internet Severity and Activities Addiction Questionnaire*** versions ISAAQ-10 (Ioannidis et al., 2023), ISAAQ-A (Omrawo et al., 2023) and ISAAQ-ED (Ioannidis & Chamberlain, 2020) will be used as other measures for PUI. While the ISAAQ-10 (Ioannidis et al., 2023) provides a measure of the extent of internet use, the ISAAQ-A (Omrawo et al., 2023) assesses which kinds of activities are done on the internet. Psychometric properties of scales have been evaluated and confirmed (Ioannidis et al., 2023; Omrawo et al., 2023). The ISAAQ-ED (Ioannidis et al., 2021; Ioannidis & Chamberlain, 2021)is specific to PUI in the context of eating disorder and psychometric properties are currently being evaluated.

A short version of the ***Assessment of Criteria for Specific Internet-use Disorders (***ACSID-11; (Müller et al., 2022)), the ACSID-5 will be used to measure the extent of symptom severity for the most prominent forms of problematic internet use behaviors (i.e., gaming, gambling, social networking, buying-shopping, pornography use) (Müller et al., 2022).

In addition, participants are asked about their ***Browser Activity*** "*What do you usually do when you're on the internet using your browser?*" in an open text question format.

Clinical variables

The 21 Item version (DASS-21) (Lovibond & Lovibond, 1995a; Szabó, 2010) of the ***Depression Anxiety Stress Scale*** (Lovibond & Lovibond, 1995b) used to assess symptoms of depression, anxiety, and levels of stress.

The ***Paediatric Self-Stigmatization Scale*** (PaedS) (Kaushik et al., 2017) measures self-stigma in children.

The Short ***Obsessive Compulsive Disorder Screener*** (SOCS) (Piqueras et al., 2015; Uher et al., 2007) will be used as self-report measure for obsessive compulsive disorder symptoms.

The ***Strengths and Difficulties Questionnaire*** (SDQ) (Goodman, 2001) will be used to assess emotional and behavioral difficulties.

The ***Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire*** (PQ-LES-Q) (Endicott et al., 2006) will be used as a measure for the clinical status of children and adolescents.

The ***EQ-5D-Y*** (Wille et al., 2010) will be used as a child-friendly measure of general health status and as behavioural risk factor surveillance.

The ***Cyberchondria Severity Scale*** (CSS) (McElroy & Shevlin, 2014) will be used in its 12-item short version (CSS-12) (McElroy et al., 2019) to assess a form of anxiety where online health research causes distress to the searching individual.

In line with the National Institute on Alcohol Abuse and Alcoholism (NIAAA), two items are proposed that can reliably detect ***early risk in adolescents' alcohol consumption***. They vary slightly in their wording and their order according to middle and high school. One question asks for the friends' drinking behaviors (e.g., "Do you have any friends who drank beer, wine, or any drink containing alcohol in the past year?") and a second question asks for their own drinking behavior (e.g., "How about you – in the past year, on how many days have you had more than a few sips of beer, wine, or any drink containing alcohol?" Details of risk assessment are explained in the associated YouthGuide (National Institute on Alcohol Abuse and Alcoholism, n.d.).

Cognitive Variables**Affect regulation.** The ***BrainPAC*** (*Project - The BrainPark Assessment of Cognition (BrainPAC) Project | BrainPark*, n.d.) ***enhanced value-modulated attentional capture*** (VMAC) task (see Figure 5) measures the tendency to develop reward-related attentional biases (Le Pelley et al., 2015), akin to sign-tracking in animals (Hearst & Jenkins, 1974) which is a form of conditioned responding that reflects a predisposition toward developing addictive behaviours (Albertella et al., 2017; Flagel et al., 2009). In this task, participants search for a target stimulus (player on their team) among distractors (players on opposite team, one with brightly coloured hair) on each trial. The faster they find and respond to the target, the more points they earn. Critically, the colour of the player's hair can be one of two colours on any one trial, and the colour influences the size of the reward

available on the current trial, such that one colour (the high-reward colour) signals that a large reward is available, and the other (low-reward) colour signals that a small reward is available. Notably, while the colour of the distractor signals reward magnitude, it is never the target that participants respond to receive the reward. That is, the player with the coloured hair is never the player that participants must kick the ball to get the reward. Thus, distractors have a Pavlovian, but not instrumental, relation to reward. In 'sign-trackers', i.e. those with reward-related attentional biases thought to be at risk of PUI (Albertella et al., 2020) responses to the target are significantly slower for trials with a high-reward distractor compared to low-reward distractor (i.e., the VMAC effect, as indexed by the VMAC score). This suggests that the signal of high reward is more likely to capture participants' attention, slowing their response to the target – even though this enhanced capture is counterproductive. In 'goal-trackers', i.e. those theoretically less likely to develop addiction, responses to the target are faster for high-reward trials than low-reward trials.

Reversal learning. We extend the above VMAC task to include a reversal phase (referred to as the VMAC-reversal, or VMAC-R task), where the relation between stimulus and reward in the training phase is reversed in the subsequent (reversal) phase. This extension is designed to gauge rigidity and persistence of reward-related attentional biases (Albertella et al., 2020).

Inhibitory executive control. The ***Stop-Signal-Task*** (SST) is one of the most commonly used response inhibition tasks (Verbruggen et al., 2019). We found response inhibition to be reliably affected compared to controls (effect size g = 0.42 (s.e. = 0.17-0.66)) in a meta-analysis of PUI studies, irrespective of the form of PUI (Ioannidis et al., 2019). Therefore, we expect SST performance to reflect generic PUI risk. In the **BrainPAC** (*Project - The BrainPark Assessment of Cognition (BrainPAC) Project | BrainPark*, n.d.) **enhanced SST**, players engage in a battlefield game to replenish arrow supplies of team-mates on the battlefield. Players press left or right to move the character up the grid to restock arrows as quickly as they can when signalled by one of two archers (i.e., the go signal). In a minority of trials (i.e., 30%), the enemy dragon breathes fire on the battlefield (i.e., the stop signal), necessitating the player to withhold their response. We incorporate a reward system to incentivise faster go responses using a points system (and reduce the chance of players 'waiting' for the stop signal as a strategy) as previously recommended by consensus. A progress bar and sound effects are included to further enhance engagement. There are 10 practice trials and 150 test trials, with SSD starting at 200ms and stair-cased by 50ms. The key parameter (stop signal response time; SSRT) is calculated using integration methods (Verbruggen et al., 2019).

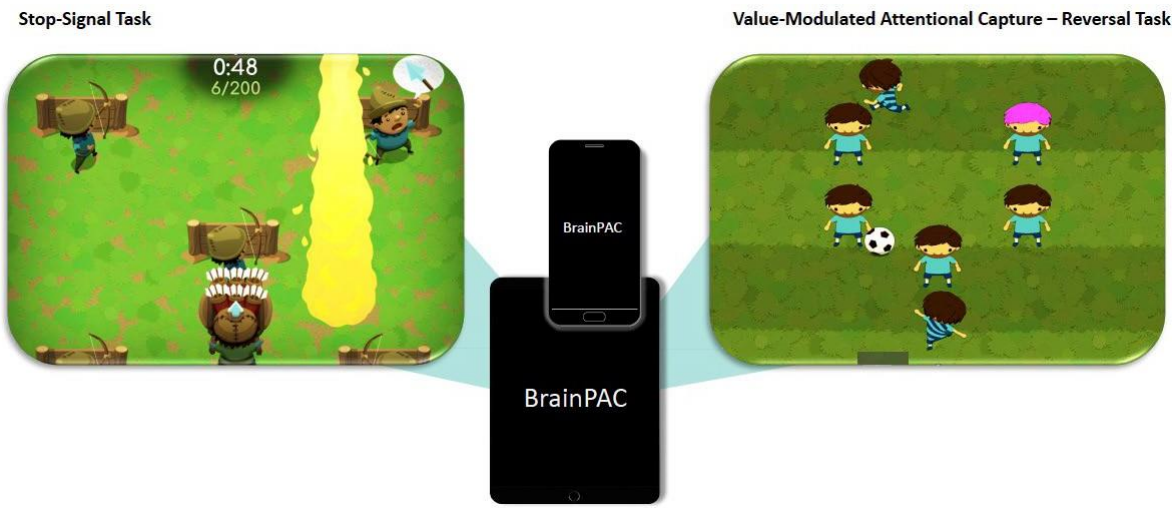

Figure 5: The BrainPAC-enhanced SST and VMAC

Two additional questions will be asked every eight days to serve as indicators for affect regulation and inhibitory control throughout the six months period. One question about the participants **mood** „*How was your mood today?*" (*1 = very stable, 10 = like a yo-yo)* will reflect affect regulation, with the regulation aspect being integrated into the anchors of the scale, not the item directly. The other question „*How patient have you been today?*" (*1 = not at all, 10 = very much)* will reflect **patience**, which is a related to inhibitory control, but which does not ask active control over specific impulses or behaviors.

Moderating/mediating variables – Measured + 3 months after baseline.

Person's characteristics

The **short 10-item version of the *Big-Five-Inventory*** (BFI-10) (Rammstedt & John, 2007) will be used to assess the five personality dimensions openness, conscientiousness, extraversion, agreeableness, and neuroticism on five subscales with two items each.

The ***Urgency – Premeditation - Perseverance - Sensation Seeking - Positive Urgency*** (UPPS-P) (Geurten et al., 2021; Lynam et al., 2006) impulsive behavior scale will be used in its short version to measure five facets of impulsivity on respective subscales, namely negative urgency, lack of premeditation, lack of perseverance, sensation seeking, and positive urgency.

The ***Cambridge–Chicago Compulsivity Trait Scale*** (CHI-T) (Chamberlain & Grant, 2018) will be used to assess aspects of compulsivity covering the need for completion or perfection, reward seeking, desire for high standards, and avoidance of situations that are hard to control.

Physical health

Students' height (in cm) and weight (in kg) will be recorded and used to calculate the *body mass index* (BMI) that will be compared against a national BMI-for-age reference standard since the BMI varies with age and sex (Must & Anderson, 2006).

Similarly, we will record students' ***favorite sport interests*** or exercise activities in order to account for physical activity as a protective factor for physical health.

Internet use expectancies, experiences, FoMO

The ***Internet Use Expectancies Scale*** (IUES) (Brand et al., 2014) will be used to assess consequential expectancies of internet usage.

To assess ***Misinformation***, study participants will be asked to rate on a visual analog scale how much of the information on the internet they believe to be true (0% to 100%).

Participants will be asked about ***Restriction*** of their online activity in the past month, what the reasons for restricting online activity were and how they did it (Table 4).

Table 4. Restriction of online activity.

How hard have you tried to reduce your online activity in the last four weeks?
0 = not hard at all
1 = rather not hard
2 = rather hard
3 = hard
If > 1
What was the reason? [multiple choice]
I thought I was online too much.
My parents thought I was online too much.
My friends thought I was online too much.
Other [open text field]
How have you limited your online activities? [multiple choice]
By a time limiter (e.g. on the smartphone)
Through content filters
Through parental control
Other [open text field]

The ***Experience of Gratification and Compensation Scale*** (EGCS) (Wegmann et al., 2022) will be used to assess the experience that individuals have while using the internet.

The ***Fear of Missing Out Scale*** (Przybylski et al., 2013) will be used in an adapted version (Wegmann et al., 2017) that can assess an online-specific FoMO. Only the online-specific FoMO subscale will used for hypotheses and analyses in this study.

School performance, family background, vaccine hesitancy

To assess ***school performance*** of the adolescents, we will ask them in the form of an open text field to type in their mean marks of the last school year.

To assess the ***family background***, we will ask for the two important family resources among adolescents, namely affect (i.e., "How do you rate the quality of relationships in your family?") and communication (i.e., "How do you rate the communication in your family?"). Both questions can be answered on 5-point Likert scales ranging from 0 = not good at all to 4 = very good.

To assess socioeconomic status, three items of the ***Family affluence scale III*** (FAS) (Torsheim et al., 2016) are used. The three items with the highest factor loadings (the family owning a car, number of bathrooms and presence of a dishwasher) were chosen for this study (Torsheim et al., 2016).

A custom designed ***Vaccine Hesitancy Scale*** (VHS) will be used to assess the degree to which individuals would like to receive a vaccination if it was available. Items of the Oxford Covid-19 Vaccine Hesitancy Scale (Freeman et al., 2022), the Vaccine Attitudes Examination scale (Martin & Petrie, 2017) and Vaccine Hesitancy Scale (Luyten et al., 2019) were integrated and modified according to the needs of this study.

Ambulatory Assessment

BootStRaP exploits ambulatory assessment and structured diary approaches for capturing different mental state domains of relevance to self-management of internet use i.e., cognition, affect, perception, behaviour, alongside 'real time' contextual information. Participants complete a 5-minute end of day assessment over two 7- consecutive day periods (after t1, T2) including questions about urge, mood, experience of pleasure, compulsive use, and interference with daily activities (items see Table 5).

Table 5. Questions asked during ambulatory assessment.

Thank you for participating in our end-of-day survey! The following questions refer to your mood and your online activities. Whenever you read "Internet", we mean your online activities regardless of the device you might use.
How was your mood today? (1=very bad, 10=very good)
How stressed did you feel today? (1=not at all, 10=very stressed)
How strong was the temptation to use the Internet today? (1=not at all, 10=very strong)
Did you use the Internet today?
If yes:
Which activity did you do mostly on the Internet today? (Open textfield)
How strong was the experience of pleasure while doing this activity on the Internet? (1=not at all, 10=very strong)
How strong was experience of relief while doing this activity on the Internet? (1=not at all, 10=very strong)
How strong did this activity on the Internet interfere with other things? (1=not at all, 10=very strong)
If no:
Tell us another activity that you did today! (Open textfield)
How strong was the experience of pleasure while doing this activity? (1=not at all, 10=very strong)
How strong was experience of relief while doing this activity? (1=not at all, 10=very strong)
How strong did this activity interfere with other things? (1=not at all, 10=very strong)

Mobile sensing

Mobile sensing (Montag & Rumpf, 2021) mines behavioural data passively, without user involvement by sensor devices to overcome disjunctions between self-reports and objective data and prevent experienced time distortions due to the immersivity of many online platforms, which might be a critical indicator of PUI (Carmi et al., 2022). The BootstrApp will therefore record digital footprints of the study participants across the whole 6 month period from t1-t2, providing insights into variables being linked to PUI. Beyond actual app usage, this methodology will provide an overview of overall screen time, log in frequency, duration of each smartphone session and so forth. Smartphone usage will be time stamped and the time variables will be exploited in the Machine Learning analysis. From the recorded digital footprints not only insights into technology use can be ascertained, but also psychological states/traits can be "sensed" via the passive smartphone log data, as different forms of smartphone use have been associated with many important psychological variables (Carmi et al., 2022). Table 6 provides an overview of mobile sensing data that will be collected. Importantly, all mobile sensing data we will collect is known to be routinely collected daily by digital provider companies. We will not access, nor will we be able to access, the content of the online activities the participants engage in i.e., what participants are doing or saying on their apps, in their messages or in their calls (see section 6.2).

Table 6 – Mobile sensing variables

Data category	Data type	Data format
Mobile sensing data	Device sessions (Timestamps, Duration)	screen_on_timestamp, unlock_timestamp, screen_of_timestamp, locked_duration, unlocked_duration, total_duration
	Contact list (Number of contacts)	count, timestamp
	Calls (Timestamps per Call, Duration, incoming, outgoing, missed)	contact_id, anonymized phone_number type, duration, timestamp
	SMS (Timestamps per SMS, Text length, incoming/outgoing)	contact_id, anonymized phone_number type, duration, timestamp
	Installed apps (Number of apps)	count, timestamp
	App Sessions (Timestamps per session, duration)	package_id, start_timestamp, end_timestamp, duration
	App Statistics (Count and Usage time per app)	package_id, range_start_timestamp, range_end_timestamp, total_usage_duration times

	GPS / Locations (Timestamps, Anonymized position)	anonymized projected lat, lng, alt, speed, accuracy, provider, gps_timestamp
	Accelerometer (Timestamps and axis data)	x, y, z, timestamp
	Rotation Rate (Timestamps and axis data)	x, y, z, timestamp
	Pedometer (Count of steps per day)*	startDate, endDate, numberOfSteps, distance, floorsAscended, floorsDescended, currentPace, currentCadence
	Visits (Like GPS but aggregated)*	arrivalDate, departureDate, locationCategory, distanceFromHome
Mobile sensing - Device information	Screen size	Width, Height
	Operating system (OS)	Android/iOS
	OS version	Version number
	country	Country code
	language	Language code
	device	manufacturer, brand, model, product, version_codename, device
	BootstrApp version	version_release, app_version_code, app_version_name, version_sdk

Note. * Final data format is not known yet; the assumed data format is provided.

6.1.2. Timing of Assessments

Table 1 shows the timing of the assessment tools. PUI variables, clinical variables and cognitive variables are assessed at baseline and 6 Months after baseline (T1, T2). Moderating and Mediating variables are assessed at T1a, 3 months after baseline. The S-CIUS as an indicator for PUI is assessed each month. In addition, two items on mood and patience will be queried every eight days. Ambulatory assessments are conducted for 7 days after T1 and T2. Mobile sensing variables are continuously recorded over the six months.

6.2. Data Management

Data governance and management will be undertaken according to relevant ICH, GDP and EU GDPR guidelines, as outlined in by the UH Quality Management System (QMS). The BootStRaP project includes a data management plan and where required an institution-specific DPIA, which apply to this study and

describe the data management in detail. In addition, a data dictionary for the study database is available. The data management plan will be implemented across all study sites, coordinated by the PO. All study sites will be trained on the study related processes and procedures, and ongoing monitoring of study processes and procedures will be undertaken on a regular basis by an independent monitor reporting to the PO and steering committee.

The mobile app BootstrApp is an assessment and intervention application developed from scratch by the Department of Molecular Psychology at Ulm University. The app will record subjective (e.g., self-report) and objective (e.g., mobile sensing) data. The questionnaire data of the BootstrApp will be stored each on a Google Firebase (Google Cloud Platform; Alphabet Inc., 1600 Amphitheatre Pkwy, Mountain View, CA 94043, USA) server located in Belgium. The mobile sensing data of the BootstrApp will be stored on a server of Hetzner Online GmbH (Hetzner Online GmbH, Industriestr. 25, 91710 Gunzenhausen, Germany) located in Germany. The BrainPAC data, which is recorded via the Dragon Game App, will be stored on a Google Firebase (Google Cloud Platform; Alphabet Inc., 1600 Amphitheatre Pkwy, Mountain View, CA 94043, USA) server located in Belgium. As part of the Machine Learning, anonymized participant data from the BootstrApp and the BrainPAC tasks will be stored on a Microsoft Azure server in the Netherlands. The databases are accessible only to the designated study personnel to fulfil their role within the project, regulatory authorities where needed, and are password protected. Who will have access to the data is described in detail in the data management plan. Server norms and certifications and other data protection measures are listed in the data management plan. Measures are taken to prevent the generation of duplicate records in the database and the database will be checked for duplicate records. The “BootStRaP Analytics” dashboard allows the research centres to monitor and download the data. Access to the dashboard is password protected and access to different functions is organized according to the role in the project.

Random participant identifiers (accessible through the BootstrApp) are automatically created and assigned by the app. They will be used to link participant information, if a participant changes their phone during the study. Within the app no name or contact data is collected. All questionnaire and mobile sensing data except for the gender identity data and the parental consent codes are either anonymous by default or will first be anonymised before transmitted from phones to servers. The parental consent codes are linked to the parent’s names on the written parental consent forms and are stored separately from the data at the respective study site. When paper-based consent or assent is used, name and signature are present on paper, but stored separately from the young person's data (on servers described above) in locked filing cabinets at the respective recruitment centers, according to local regulations.

The consortium is aware of and informed about the pitfalls around digital assessments and mobile sensing procedures. The Team at ULM and at UH have experience with establishing high privacy standards and in the field of digital phenotyping and mobile assessment by also having conducted abundant research in this area. For the transmission from phones to servers, strong hash algorithms such as SHA-2 algorithms will be employed (see data management plan, server backend for more information about the data transmission). Data stored on mobile devices will be protected by built-in sandboxing mechanism. This means that by design no other apps can access data from the BootStRaP. The team from Ulm University will follow ‘privacy by design’ principles to protect the privacy of the study participants. To illustrate this: When GPS data is tracked, the location will be projected to a random global location enabling the persons activity to be studied without relying on actual position information. Moreover, encryption principles will make sure that individual telephone numbers are not encoded but retain the

ability to map a person's social network size. Here, it would be possible to study the active style of a person without relying on actual position information. Moreover, encryption principles will make sure that telephone numbers are secure on the phone of the study participants (but it would still be possible to see if persons have a larger or smaller active social network as presented on their phones). Following sandboxing principles, communication in messenger/social media apps will not be tracked. Instead, it will be investigated what apps are installed and how often/frequent these apps are used. The depth of the digital phenotyping principles will be here also restricted to what is allowed from Android/Apple. Although the apps can be downloaded via the Google Play Store and the Apple App Store, access to the BootstrApp is restricted by an access code (which will be provided in participating school classes). The use of the app will only be possible after the adolescents and parents gave informed consent.

Reporting rules will be introduced to prevent young people being re-identified in publications or archived data based on their answers (e.g. few children in a school identifying with a 3rd gender). For example, the anonymization of the questionnaire variable gender identity will rely on the number of cases in the different groups. This will be monitored throughout the project and the variable gender identity will be handled as not fully anonymous until there are sufficient cases in the different groups. As long as the gender identity variable is not deemed fully anonymous, only BootStRaP partners that sign the Data Sharing Agreement will get access to this variable. In addition, only BootStRaP partners that sign the Data Sharing Agreement can get access to the parental consent code. Only the fully anonymized data set will be made available to other researchers.

Student and teacher ambassadors, as described in section 9. Public and Participant Involvement, are involved as citizen scientists and not as study participants. Nevertheless, ambassador contact information, dietary and medical information and parent contact data is needed for study related co-creation activities (e.g. organization of a "Bootcamp"). Ambassador contact information will be stored centrally at the University of Hertfordshire, using a RedCap Database. Dietary and medical information and parent contact data needed to organize co-creation activities will be included in this database. The database manager has access to all information in the database. One or two team members from each recruiting centre will be given limited access to the database to enter the Ambassadors' information. All personal health data of ambassadors will be deleted without undue delay when they are no longer required to achieve the purpose for which the data was collected. After 10 years all other personal identifiers that would allow an individual to be identified will be removed from the data.

6.3. Data Analysis

6.3.1. Preparatory steps

Behavioural data of all measures will be combined to specific sum scores or mean scores, as required. Missing data will be evaluated to determine potential estimation bias. If the data is MAR multiple imputation will be used to model the influence of missingness. Where missingness demonstrates other properties, other methods of sensitivity analysis will be considered.

6.3.2. Primary analyses

1) Determine the multifactorial determinants of healthy vs. unhealthy internet usage among European adolescents aged 12-16 years and develop algorithms for quantifying individual risk of PUI.

To predict psychological phenotypes from multisource big data we use a ML approach rigorously underpinned by psychological theory (Montag & Rumpf, 2021). We will develop algorithms for predicting individuals at risk and identify actionable variables for application to subjects as intervention in future studies. We will use both classical (logistic regression, random forest) and modern methods (deep neural networks, domain adaptation, deep representations, adversarial training) to associate the assessments to the S-CIUS (Besser et al., 2017) at the individual level.

The collected data is heterogeneous by nature, in three main aspects:

- **The type of variables** (continuous, ordinal, and categorical, both structured and unstructured, some of which are highly sparse (e.g. log data) while other have little to no missing values (e.g. sensor data));
- **Resolution/Frequency** (e.g. mobile metrics are sampled continuously 24/7, clinical assessments are conducted only at specific times, demographic data is essentially static);
- **Data collection protocol** (mobile data is passive, clinical data is mostly collected with the awareness of the subjects, and self-assessment data, such as the EQ-5D-Y questionnaire, can be considered as a form of intervention).

This poses major challenges for the modelling and the algorithmic design. Our approach to risk prediction therefore comprises of two steps:

- **Learning useful representations:** We will represent information contained in these heterogeneous data sources in a format suitable to develop risk prediction models.
- **Predictive modelling:** Risk prediction based on learned representations and other available information.

Learning useful representation: The goal is to learn data transformations that will exploit and preserve important information for the downstream predictive modelling tasks. Toward this aim we plan to utilize recent advances in *deep learning*, where variational inference (Kingma & Welling, 2015), Generative Adversarial Networks (GANs)(Goodfellow et al., 2014), and embedding methods (e.g. patient2vec (Zhang et al., 2018) inspired by word2vec) will play a key role. Representation learning in this setting is mainly unsupervised, namely label-free, which is highly relevant for the mobile data. However, task aware (supervised) representation learning (e.g. variational information bottleneck (Alemi et al., 2017), where knowledge of the task is in the form of labels and assessments, will also be used. With the right architectural and modelling design, these methods can handle many of the heterogeneous data challenges, such as integration of heterogeneous data sources (e.g. AttnSense (Ma et al., 2019)), sparsity, and sequence data (e.g. Variation Autoencoders with Gaussian Process prior for time series imputation, GP-VAE (Fortuin et al., 2020)).

Downstream predictive modelling: Using the learned representations and the task-aware information, such as labels and clinical assessments, we will use a blend of classical methods (logistic regression,

support vector machines (SVMs), Random Forest, and boosted trees (XGBoost)), deep learning methods (both static, like CNN and ResNets, and dynamic, such as LSTM and GRUs), and mixed (e.g. Deep Markov Models, DMM (Krishnan et al., 2017)). Classical methods are less data consuming and therefore suitable for a supervised setting with limited labelled data available. However, although modern deep learning models require larger amounts of labelled data, they provide extra predictive strength and state-of-the-art results. We plan to handle this challenge by using semi-supervised learning (van Engelen & Hoos, 2020) (use a mix of labeled and unlabeled data) and self-supervised learning (Jaiswal et al., 2020) generated labeled from unlabeled data and train in a supervised manner), transfer learning (Weiss et al., 2016)(use a pre-trained model for one task and adapt it to handle another task), and multi-source domain adaptation (Hoffman et al., 2018) (models learned to perform the same task on multiple distinct datasets, adapted to perform the task on a target domain). The latter is also one possible method to handle sites bias, where each recruitment site is a source domain, and the target domain is an (unknown) mixture of the source domains.

Finally, although our primary approach is supervised discriminative, as a secondary effort we plan to apply unsupervised learning to detect and model patterns of common behaviours, and then use anomaly detection as a means for detection and scoring of abnormal behaviour at different risk levels. These methods were developed and successfully used in efforts aimed to detect "interesting" behavioural patterns.

Once learning is completed, and we have an estimate of the final downstream predictive modelling performance (based on the test set), we will apply the final hypothesis testing.

Validation of models

Generalization and validation will be assessed using common cross-validation methods at the individual level. In both steps (representation learning and predictive modelling), data for learning will be split to training, validation, and test sets, where all tasks will be done retrospectively, as part of the learning and evaluation procedures. To ensure that predictive models generalize to data from new sites, and to control for site-based confounding factors, the classifiers will be trained and tested using leave-one-site-out cross-validation. The contribution of single variables to the overall prediction will be analysed using SHAP, which is expected to reveal actionable variables for the interventions in future studies (i.e. risk and protective factors). This approach has been validated previously and has guided the development of eHealth applications.

2) Determine the health economic impact of PUI for European adolescents.

We report Health Economic Impact as Cost and Burden of PUI in Europe. Due to methodological issues with current assessment tools of Quality of Life, especially when used in children (different tools are appropriate for different age-ranges, scales focus primarily on physical rather than mental health), we will combine the information from multiple scales (EQ-5D-Y and PQ-LES-Q) to calculate utility values. All scales will use Time Trade-Off (TTO) weights and discrete choice experiment (DCE) valuation techniques for calculating utility scales. Based on these utility values, Quality Adjusted Life Years (QALYs) due to PUI are calculated and reported as a measure of Societal Cost. We will explore possible burden by a sensitivity analysis of possible subgroups.

These data will further be used to estimate the cost-effectiveness of health and social policy changes and in addition to estimate the cost-effectiveness of preventive PUI interventions that will be introduced in subsequent studies.

6.3.3. Secondary analyses

Secondary analysis, beyond comparing group differences (e.g., those at-risk versus no risk – based upon symptoms of PUI and burden, gender comparisons, and comparisons regarding subtypes of at-risk adolescents), will use multiple- hierarchical (moderated) regression analyses to test interactions between predictor and moderator variables in predicting PUI symptoms and clinical variables (including burden) at t2 structural equation modeling (including mediators) on both manifest and latent level will be used to analyse relationships and interactions among symptoms of PUI and other clinical variables as well as symptoms of PUI and the moderating, or mediating variables (t1+3 assessment). The structural equation models will follow the BootStRaP logic model (see Figure 2).

7. Ethical Considerations

The study will be undertaken according to the principles of ICH Good Clinical Practice (GCP), and all relevant ethics and governance processes, including the HRA approvals Guidance will be provided by the University of Hertfordshire, providing a set of documentation relating to governance that complies with Good Clinical Practice and EU Governance Regulations, and with the European General Data Protection Regulation (GDPR). The Hertfordshire team have access to legal and regulatory advice with regulatory alignment with EU regulations, and working with partner organisations will ensure that the most up-to-date and appropriate guidance is available across the consortium. An external Ethics Advisory Board is attached to the project.

Working with local teams, the coordinator will provide a common set of study related documentation (protocol, information sheets in plain language) that can be localised to meet the needs of local ethics committees. Information about the study (normally in the information sheet) will be provided via the BootstrApp and supported by local supplementary information where required. These study related materials will be included in the submissions to local ethics committees for approval. Copies of the process (both general and site specific) will be recorded and stored on the Trial Master File.

According to the local QMS, no study site will be allowed to start recruiting study participants until given a green light by the coordinator. To ensure that no data can be collected, the study database will not be made available to a study site until the specified study documentation has been recorded, and site initiation has been completed. The final process will be sign-off by the CI.

Substantial amendments will be implemented only after approval by the responsible ethics committees.

Reporting will follow the regulations specified by the competent authorities at each recruitment center. Declaration of end of study forms will be completed by the recruitment center leads and sent to each local Ethics Committee in line with their timelines and regulations e.g. within 90 days of the end of study where appropriate.

Biannual progress reports will be submitted to Horizon Europe. In addition, a midterm recruitment report will provide information about the number of participants enrolled in the study.

Following advice from the BootStRaP ethics advisory board, the originally intended procedures for consenting and anonymity of the data were adapted in accordance. The consent giver will now be identifiable based on the registered code and the consenting procedure will in essence be the same for all research centers.

7.1. Risk-Benefit Assessment

The study is expected to give unprecedented scientific knowledge on the psychological mechanisms underlying risk for developing PUI, early detection of adolescents 'at risk' of PUI before it is apparent, and potential interventions. Policy recommendations will be developed based on the BootStRaP project, which could positively impact the prevention of problematic internet use across Europe. Results are expected to be generalizable as study participants are recruited in nine different European countries and from the whole adolescent population including all genders, different socioeconomic backgrounds and rural and urban areas.

The risk for participants is expected to be small as the study is survey-based and mostly takes the form of validated questionnaires. The purpose of the study is explained to the young people before participating and they are informed about the type of questions that will be asked. Participation is voluntary and participants can withdraw from the study at any time without giving a reason. In case that participants experience distress, the study app contains a dedicated help submenu where participants are signposted to local services available to children to support with mental health conditions which children and parents (where appropriate) can access if needed. Much emphasis was put on data protection and confidentiality and on making the study as anonymous as possible, as outlined in sections Data Management (6.2) and Data Protection and Participant Confidentiality (11).

The study does not immediately benefit study participants, as there is no treatment intervention. However, it is expected to provide unprecedented scientific knowledge on the psychological mechanisms underlying risk for developing PUI, early detection of adolescents 'at risk' of PUI before it is apparent, and potential interventions. Thus, the results of this project will benefit future individuals with these conditions. Study participants themselves will receive a certificate and monetary voucher as a token of gratitude for their time and effort.

8. Quality Assurance and Control

Quality Assurance (QA) is defined as all the planned and systematic actions established to ensure the trial is performed and data generated, documented and/or recorded and reported in compliance with the principles of GCP and applicable regulatory requirements. Quality Control (QC) is defined as the operational techniques and activities performed within the QA system to verify that the requirements for quality of the trial related activities are fulfilled.

The UH QMS will be adapted to provide study specific documents relating to study set up and site initiation, the ethical management and safety of study participants, quality management, and data monitoring and integrity. Data management will be undertaken by ULM but will be guided as required by the UH QMS.

8.1. Risk Assessment

QA and QC considerations for the study should be based on the formal Risk Assessment performed, that acknowledges the risks associated with the conduct of the study and proposals of how to mitigate them through appropriate QA and QC processes. Risks are defined in terms of their impact on: the rights and safety of participants; project concept including trial design, reliability of results and institutional risk; project management; and other considerations.

The Project Office will overview the overall risk management of the project. In case a partner identifies a risk for the project he/she must fill the Risk Assessment Form. The risk assessment form can be found in the trial master file folder of the BootStRaP Teams channel. All Risk Assessment forms must be logged as a file note and on the file note log and sent to the Project Office for review.

Risk will be constantly evaluated by the Project Office and evaluated depending on the severity of consequences and chance of happening through an overall Risk Matrix. All reported risks will be entered into the risk management register and mitigation for these risks identified. Progress and barriers to progress will be monitored and solutions sought from the SC, and the Advisory Boards as required to enable any issues to be resolved in a timely fashion.

8.1.1. Project related risk

Development of the technology:

Completing development of the BootstrApp in time for mid-2024 is a key objective. Development and planning of the app can start during 2023, giving 9 months or more to ensure that the App is correctly developed and tested prior to commissioning.

Recording regulatory and ethical approvals, and site initiation:

The Coordinating centre will work across all study sites to ensure timely and appropriate recording of regulatory and ethics approvals. Copies of the process (both general and site specific) will be recorded and stored on the Master File. According to the local QMS, no study site will be allowed to start recruiting study participants until given a green light by the Coordinator. To ensure that no data can be collected, the study database will not be made available to a study site until the specified study documentation has been recorded, and site initiation has been completed. The final process will be sign-off by the CI. This will ensure that the sites are supported to put in place all study related processes and procedures (including relevant staff training) and that all governance processes and procedures have been completed before recruitment starts.

Completion of recruitment:

Given that engagement with schools is ensured prior to the study starting, and that a plan of engagement with classes has been agreed, the process of recruitment should be completed rapidly once started. To ensure that issues and problems are dealt with quickly a number of local study related staff will be available, staff in ULM (data management centre) and UH (the Coordinator) will ensure that there is sufficient staff availed to address issues rapidly as they arise.

Drop out:

Given the design of the study, most of the final assessments will be online, completed by young people who are already engaged with the online app, or completed as organised within the school class. As outlined, much emphasis will be placed on ensuring ongoing engagement with the young people involved, and a payment compensation (approximately 10 Euro) will be offered for those who complete a minimum dataset. Some elements of study testing are specifically designed to be engaging for young people to complete (e.g., BrainPAC) (*Project - The BrainPark Assessment of Cognition (BrainPAC) Project | BrainPark*, n.d.). While every effort is made to ensure continued engagement of the young people recruited into the study, it is expected that some young people will cease to engage with the app over the study period, and we estimate that this will be in the order of 30%.

8.2. Monitoring

The UH QMS will be adapted to provide study specific documents relating to data monitoring and integrity.

The data will be monitored on a weekly basis by the Coordinator or a delegated individual, and data integrity monitored on a routine basis by an independent monitor. Part of the monitoring process will include identifying systematic data errors either at study sites, or due to systematic structural issues with the data collection process. Where required, a data recovery process will be recorded and specified, and training of all relevant individuals will be undertaken to ensure that ongoing errors are avoided. Serious data breaches will be reported within 48 hours to the Sponsor and to the PI at the concerned study site. The breach will be followed up within 7 days to ensure that appropriate action to taken by the study team and by the relevant organisations involved.

Monitoring of progress and potential mitigation: Study adherence will be centrally monitored via the mobile app and automated reminders will be sent (based on ethical protocols). Monitoring of data collection is done via the "BootStRaP Analytics" Dashboard (an internal website accessible for recruitment centers). Our recruitment centres are located in 9 different countries, each recruiting around 400 participants from local schools with differing operating policies. The researchers will make themselves available to participants, staff and parents for the duration of the study supporting retention and troubleshooting problems.

The PO will provide a monthly report, which will be available to all study partners, committees and the EU Commission as required specifying progresses against all deliverables and milestones

8.3. Study Oversight

The governance structure of the BootStRaP Project is displayed in Figure 6. The study will be continuously supervised by two external committees, the Scientific Advisory Board (SAB) and the Ethics Advisory Board (EAB) to ensure all necessary consultation is available for the duration of the BootStRaP project. The Sponsor is the University of Hertfordshire, an academic institution, based in the United Kingdom. The University of Hertfordshire leads on management and coordination of the whole project including governance, data management, analysis. The Interdisciplinary Center (IDC) leads on digital data management and analysis. As outlined below, the Project Office is based at the University of Hertfordshire who will provide oversight and coordination for the project (the coordinator). The coordinator will report directly on a monthly basis to the Steering Committee who will be represented by all the work-

package leads (or deputy). The Coordinator will also report to the General Assembly and to all the Advisory Boards ensuring seamless coordination and communication between all parties.

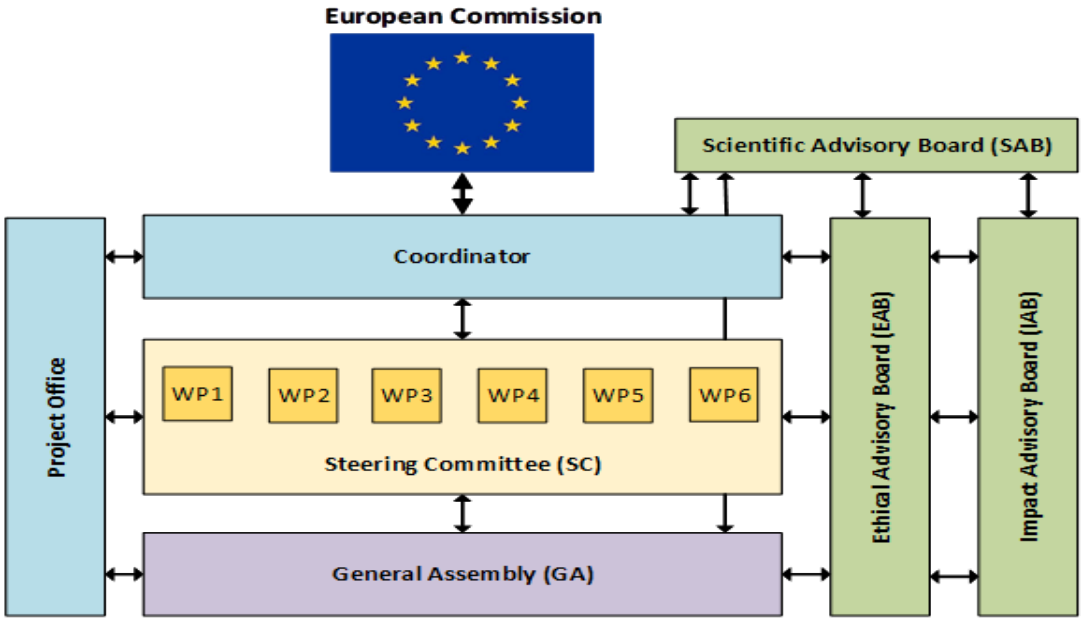

Figure 6: BootStRaP governance structure

A Project Office (PO) will be established at UoH, including the coordinator, a project manager and support staff. The PO is responsible for central, day-to-day operational management and smooth and timely execution of the project, acting as an accessible helpdesk and consultation and communication point on all matters related to study conduct. In addition, the PO is responsible for assisting the General Assembly (GA), Steering Committee (SC) and the boards of external advisers (Scientific Advisory Board (SAB), Ethics Advisory Board (EAB), Impact Advisory Board (IAB)) on all operational management issues. Data management will be led by (UULM), IDC, the Coordinator and the PO.

The General Assembly (GA), as the strategic and ultimate decision-making body of the project including any aspect affecting the Consortium Agreement and/or Grant Agreement, comprises one representative per beneficiary. The GA is responsible for quality and progress monitoring, financial monitoring, overall risk management, conflict resolution and decisions on any corrective measures in case of (un)anticipated contingencies, including resolving any disputes.

The Steering Committee (SC), consisting of all Work Package (WP) leaders and chaired by the coordinator, is the central management team and supervisory body for execution of the project. The SC is responsible for overall monitoring of the scientific and financial progress, based on the agreed deliverables and milestones, monitors and facilitates alignment between WPs and organizes all management meetings (assisted by the PO).

The Project Office (PO) implements standard quality procedures, including meeting procedures, a guide on reporting procedures, standard procedures for data collection and procedures on conflict mediation and corrective actions. The PO will use the Clinical Trials Support Network Quality Management System adapting Standard Operating Procedures where necessary.

The Consortium's credentials are enhanced by 3 exceptional Advisory Boards covering all aspects of the project with broad trans-cultural and multidisciplinary expertise; including a Scientific Advisory Board, an Impact Advisory Board, and an Ethics Advisory Board.

8.3.1. Steering Committee

The Steering Committee (SC), consisting of all WP leaders and chaired by the Coordinator, is the central management team and supervisory body for execution of the project. The SC is responsible for overall monitoring of the scientific and financial progress, based on the agreed deliverables and milestones, monitors and facilitates alignment between WPs and organizes all management meetings (assisted by the PO).

8.3.2. Data Monitoring and Ethics Committee

The PO will provide a six monthly report which will be available to all study partners, committees and the EU Commission as required specifying progresses against all deliverables and milestones.

8.3.3. Trial Management Group

The Sponsor is the University of Hertfordshire, an academic institution, based in the United Kingdom. BootStRaP engages a whole work package on the project management where the scientific and operational governance will be enacted. WP6 is responsible for management and coordination of all study activities across the different sites. The Project Office (PO), based at UoH (UK), will implement standard quality procedures, standard procedures for data collection and procedures on conflict mediation and corrective actions.

9. Public and Participant Involvement

9.1. BootStRaP Ambassadors

We will designate a teacher and 2-3 students in each school to act as a BootStRaP Ambassador for the duration of the project to maximise school community's engagement in the research project. Involvement of Ambassadors has already started. Their role is advisory and as research collaborators in the research process. They are not research participants. Activities planned together with ambassadors will include:

- Collaborate with researchers to recruit other students as research participants, maximize retention, and engagement of schools
- Provide feedback to increase the accessibility of the smartphone app used for assessments
- Co-designing how to involve schools and students
- Influence the overall project coordination, by sitting in the management board
- Help reviewing information- and advertisement material
- Help in planning and conducting local dissemination events
- Represent the school and peers in the international research project

These involvement activities will be performed in virtual workshops, regular online-meetings, face-to-face meetings with local researchers, and a BootStRaP Bootcamp (15th /16th March 2024) with ambassadors from included schools. Therefore, to become ambassadors, students need good English skills and need to be able to travel to the UK, for attending the Bootcamp. Ambassadors will receive a

monetary compensation comparable to the study participants' compensation as a "thank you" for their effort.

Youth, Student and Teacher Ambassadors will be involved in the process of co-designing the BootstrApp digital tool. This involvement is to ensure that the tools are appropriate to young people's needs and demands, to increase engagement in using the App, to make sure the design is appealing and functional and to ensure usability. Co-creation activities will be used to design the engagement strategy for the project and also to co-create the BootstrApp. During online meetings, students, teacher ambassadors and researchers will collaborate with members of the research team to identify and prioritize needs regarding the engagement of students in the project. The results will then be used as a starting point for the co-creation activities at the Bootcamp, where the teams will brainstorm ideas to boost engagement and create specific solutions to design an engagement strategy.

At the University of Ulm, young people have been consulted about their opinions on the smartphone app, e.g. which feedback they would find interesting. Other youth advisory groups will be involved in providing advice and support to the project at different stages. In particular, young people (over 18 years) from **Euro Youth Mental Health (EYMH)**, which is a non-profit organisation that works with young people with direct or indirect experience of mental health difficulties across Europe, and the **EU-PUI PPI (patient-public involvement) Reference Group** will support different stages of the research project. EU-PUI is an established international group of young people with training on involvement in PUI research, which was created in the COST Action European Network of Problematic Internet Usage, known as Internet & Me. These groups are involved in the planning and conduction of the BootStRaP project and facilitate public and especially youth involvement. Involvement activities will include commenting on study materials, co-designing the project website and advising on the dissemination activities.

10. Protocol Compliance

The CI will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements including but not limited to the Research Governance Framework and Research Office policies and procedures and any subsequent amendments.

A log of any non-compliances will be stored to ascertain if there are any trends developing which to be escalated. The sponsor will assess the non-compliances and action a timeframe in which they need to be dealt with. Each action will be given a different timeframe, dependant on the severity. If the actions are not dealt with accordingly, an appropriate action will be agreed, including an on-site audit.

Part of the monitoring process will include identifying systematic data errors either at study sites, or due to systematic structural issues with the data collection process. Where required a data recovery process will be recorded and specified, and training of all relevant individuals will be undertaken to ensure that ongoing errors are avoided. Serious data breaches will be reported within 48 hours to the Sponsor and to the PI at the concerned study site. The breach will be followed up within 7 days to ensure that appropriate action is taken by the study team and by the relevant organisations involved.

11. Data Protection and Participant Confidentiality

Where necessary, personal data shall be handled in accordance with applicable data protection laws and shall cooperate in order to enable one another to fulfil legal obligations arising under those laws. Fundamental ethical principles outlined under Article 8 (protection of personal data) of the Charter of Fundamental Rights of the European Union, the European Union (EU) Regulation 2016/679 (General Data Protection Regulation (GDPR)), the United Kingdom (UK) Data Protection Act 2018 (DPA 2018) and as outlined in the UH Quality Management System will be adhered to. The CI will ensure that the trial is conducted in compliance with the principles of the Declaration of Helsinki (1996), and in accordance with all applicable regulatory requirements.

Data management will be led by Ulm University (UULM), IDC, the Coordinator, and the PO. The team from UULM will follow specific principles such as anonymizing data before transmitting them from phones to servers, sandboxing mechanism, and 'privacy by design' to protect the privacy of the study participants, as described in the Data Management section (6.2). The content of the online activities the participants engage in i.e., what participants are doing or saying on their apps, in their messages or in their calls, are not accessed. Within the app no name or contact information is collected. Any named consent and assent forms will be stored separately to any other data collected for the study as these other data will be collected online directly on to the BoostrApp and the Dragon Game app. Only designated study personnel will have access to the data, to fulfil their roles within the project. The Chief Investigator (Naomi Fineberg) is the 'Custodian' of the data. All data will be jointly controlled by the BootStRaP partners signing the Data Sharing and Joint Controller Agreement. Institution-specific DPIAs for the BootStRaP project are prepared and approved locally by partner organisations, as required.

11.1. Case Report Form (CRF)

The CRF is electronic located on the BootstrApp and will be self-completed by the participants as required.

11.2. Archiving and deletion of participant data

All participants can withdraw from the study participation at any time. Due to anonymization of data for Machine Learning and the data backup strategy, already transmitted data cannot be deleted. Further processing will either take place pseudonymously (only for BootStRaP partners that have signed the Data Sharing Agreement) or anonymously (everyone else). After deleting the BootstrApp and the Dragon Game app, no personal data that was collected by the BootstrApp, remains on the smartphone of the participants. Participants will be informed in both the participant information and consent process that the deletion of data up to the point of withdrawal will not be possible.

After the completion of the study and reporting of results, all identifying data will be removed from the electronic data collected. Anonymous data will be kept for 10 years for use in future research in this area. Anonymous data will be uploaded to a data repository as a requirement of the study funders.

12. Publication and Dissemination

A detailed dissemination, communication and exploitation (DEC) plan for the BootStRaP project (Horizon project including this study) has been created and is continuously updated. Dissemination is the act of spreading research results, findings, scientific knowledge, and discoveries to the scientific community.

Exploitation involves practical application of scientific knowledge and research outcomes for societal benefits. Communication encompasses translating aforementioned research findings into language that the public understands and communicating it to various public stakeholders.

DEC activities follow the DEC plan and are monitored by the scientific and impact external advisory boards and steering committee of the BootStRaP project. Dissemination outcomes in the BootStRaP project comprises intellectual products such as open-access publications, digital assessment tool, self-management tool, policy toolkit, etc. All of these outcomes will have a potential to be exploitable. A designated Innovation Manager will be responsible for stimulating and monitoring exploitation throughout the project. A communication lead team has been established and will be in contact with local groups via a designated members (national representatives) to communicate on dissemination activities. All DEC activities will be performed according to Horizon Europe regulations, including acknowledging funding by Horizon Europe, Innovate UK program (UKRI) and Swiss State Secretariat for Education Research and Innovation (SERI). Results will be communicated primarily via the following channels:

- Open access publications in peer reviewed journals
- Presentations at scientific conferences and to stakeholders
- Social media channels (Facebook, LinkedIn, YouTube, etc.)
- Traditional media (e.g. Newspaper, radio, TV or podcast appearances)

Project news, links referencing media articles and publications of the study will be available on the BootStRaP project website Net and Me – BOOTSTRAP (internetandme.eu). We will also run a national and international publicity campaign (supported by university press offices) in which delegates from candidate schools in each recruitment region will be invited to participate, to generate interest and enthusiasm in our European project among local schools. After the main study results have been published, the anonymous data set will be made publicly available on open access repositories.

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