MENTAL DISORDERS AMONG SPANISH UNIVERSITY STUDENTS: A LONGITUDINAL STUDY

Laura Ballester Coma

DOCTORAL THESIS

Mental disorders among Spanish university students: a longitudinal study

Laura Ballester Coma

2021

Universitat de Girona

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Doctoral Programme in Psychology, Health and Quality of Life

Supervised by: Dr. Jordi Alonso Caballero

Tutor: Dr. MªEugènia Gras Pérez

Presented to obtain the degree of PhD at the University of Girona

Universitat
de Girona

Dr Jordi Alonso, of Institut Hospital del Mar d'Investigacions Mèdiques-IMIM,

I DECLARE:

That the thesis titled *Mental disorders among Spanish university students: a longitudinal study*, presented by Laura Ballester Coma to obtain a doctoral degree, has been completed under my supervision.

For all intents and purposes, I hereby sign this document.

Signature

Barcelona, 29 September, 2020

Universitat de Girona

Itxaso Alayo, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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2. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Philippe Mortier, and Jordi Alonso
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[Barcelona], [15 September 2020]

Universitat de Girona

Dr Gemma Vilagut, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Barcelona, 15th September 2020

Dr [José Almenara], as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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[Cádiz], [15/09/2020]

Universitat de Girona

Dr Ana Isabel Cebrià, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Barcelona, 22th September 2020

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Dr Enrique Echeburúa , as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Signature

San Sebastián, 15th September, 2020

Universitat de Girona

Dr Andrea Gabilondo, as co-author of the following articles:

1. Authors: Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Donostia-San Sebastian
16 de septiembre 2020

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Dr Margalida Gili, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Palma de Mallorca, 16/9/ 2020

Universitat de Girona

Dra. Carolina Lagares, as co-author of the following articles:

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Cádiz, 16/09/2020

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de Girona

Dr Jose A. Piqueras, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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2. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Philippe Mortier, and Jordi Alonso
Title: Validation of an online version of the Alcohol Use Disorders Identification Test (AUDIT) for alcohol screening in Spanish university students
To be submitted to the *International Journal of Environmental Research and Public Health*

3. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Philippe Mortier, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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4. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, Philippe Mortier, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Andrea Miranda-Mendizabal, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Elche, 09/16/20

Dr Miquel Roca, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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2. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Philippe Mortier, and Jordi Alonso
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4. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, Philippe Mortier, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Andrea Miranda-Mendizabal, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Palma 15 September 2020

Universitat de Girona

Dr Vitoria Soto Sanz, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Signature

Elche, 15/09/2020

Universitat de Girona

Dr Maria Jesús Blasco Cubedo, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili,Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C.Kessler, and Jordi Alonso
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2. **Authors:**Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili,Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Philippe Mortier, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Barcelona, September 18th, 2020

Universitat
de Girona

Dr Pere Castellvi, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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3. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Philippe Mortier, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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4. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, Philippe Mortier, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Andrea Miranda-Mendizabal, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Pere Castellvi Obiols

Barcelona, September 15, 2020

Dr Carlos García Forero as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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2. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Philippe Mortier, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Barcelona, Sept 15th 2020

Universitat de Girona

Dr Andrea Miranda Mendizabal, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, Philippe Mortier, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Andrea Miranda-Mendizabal, Ronny Bruffaerts, Randy P. Auerbach, Matthew K. Nock, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Barcelona, 29th September 2020

Universitat de Girona

Dr Philippe Mortier, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

Signature

Barcelona, 15/09/2021

Dr RONNY BRUFFAERTS, as co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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And for all intents and purposes, I hereby sign this document.

LEUVEN, 17 SEPTEMBER 2020

September 15, 2020

To Whom It May Concern,

This document acknowledges that I am a co-author of the following articles:

1. **Authors:** Laura Ballester, Itxaso Alayo, Gemma Vilagut, José Almenara, Ana Isabel Cebrià, Enrique Echeburúa, Andrea Gabilondo, Margalida Gili, Carolina Lagares, José Antonio Piqueras, Miquel Roca, Victoria Soto-Sanz, Maria Jesús Blasco, Pere Castellví, Carlos G. Forero, Ronny Bruffaerts, Philippe Mortier, Randy P. Auerbach, Matthew K. Nock, Nancy Sampson, Ronald C. Kessler, and Jordi Alonso
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Barcelona, 15 September 2020

*A l'Albert i
als meus pares,*

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List of publications

- Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià A I, Echeburúa E, et al. (2019) Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students.Results of the WHO World Mental Health-International College Student initiative. *PLoS ONE* 14(9):e0221529.
  https://doi.org/10.1371/journal.pone.0221529.
   IF: 2.740; Q2 (27 of 71, Multidisciplinary Sciences).

- Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià A I, Echeburúa E, et al. (submitted February 2021) Validation of an online version of the Alcohol Use Disorders Identification Test (AUDIT) for alcohol screening in Spanish university students. *International Journal of Environmental Research and Public Health.*
  IF: 2.849; Q2 (58/193, Public, Environmental & Occupational Health)

- Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià A I, Echeburúa E, et al. (2020) Mental disorders in Spanish university students: Prevalence, age-of-onset, severe role impairment and mental health treatment. *Journal of Affective Disorders*, 273, 604-613.
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  IF: 3.892; Q1 (50/204, Clinical Neurology); Q2 (39/155, Psychiatry)

List of abbreviations

aOR - Adjusted Odds Ratio
ASRS - Adult ADHD Self-Report Scales
AIC- Akaike's information criterion
AUD - Alcohol use disorder
AUDIT - Alcohol Use Disorders Identification Test
AUC - Area Under the Curve
ADHD - Attention-deficit/hyperactivity disorder
CIDI-SC - Composite International Diagnostic Interview Screening Scales
CI - Confidence Interval
DALY – Disability-adjusted life year
DSM-IV –Diagnostic and Statistical Manual of Mental Disorders, fourth edition
DUD - Drug use disorder
ENSE - Encuesta Nacional de Salud de España
ESEMeD - European Study of the Epidemiology of Mental Disorders
EU – European Union
GAD - Generalized anxiety disorder
GDP – Gross Domestic Product
IHME - Institute for Health Metrics and Evaluation
ITC - International Test Commission
IPW - Inverse-probability weighting
MDE - Major Depressive Episode
MI - Multiple Imputation
OR - Odds Ratio
OECD - Organization for economic co-operation and development
PD - Panic disorder
PREDICT - Prediction of depression in European general practice attendees
SDS - Sheehan Disability Scale
SE - Standard Error
SD - Standard Deviation
UCA - University of Cádiz
UIB - Balearic Islands University
UMH - Miguel Hernández University
UPF - Pompeu Fabra University
UPV-EHU - Basque Country University
WHO – World Health Organization
WMH-ICS - World Mental Health International College Student initiative
YLD – Years lived with disability
YLL – Years of life lost due to premature mortality

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ABSTRACT

Mental disorders are common among university students, while longitudinal evidence on mental disorders among Spanish university students is scarce. The general aim of this doctoral thesis was to estimate the frequency (prevalence, incidence and persistence) of mental disorders among Spanish university students, as well as to provide evidence about their association with role impairment and the use of mental health treatment. Also, to identify risk and protective factors associated with the onset and persistence of two common mental disorders (depression and/or generalised anxiety disorder).

This thesis is based on the UNIVERSAL project, a multicentre observational cohort study of students between 18 and 24 years of age starting their first course in five Spanish universities. Data was collected using confidential and secure online surveys.

The accuracy of the online mental health measures used in the project was assessed through clinical reappraisal interviews of a sample of participants (n=287). Overall, the online UNIVERSAL measures of mental disorders had an adequate agreement with the MINI-International Neuropsychiatric Interview (MINI), in particular for major depressive episode, generalised anxiety disorder and alcohol dependence (area under the curve-AUCs>0.7). Results provided evidence that online survey might be useful for screening mental disorders in university students.

Data from baseline and 12-month follow-up online surveys of the UNIVERSAL project were used to estimate the frequency of mental disorders. A total of 2,118 first-year university students completed the baseline survey and of those, 1,253 students completed at least 40% of the 12-month follow-up survey. At baseline, the 12-month prevalence of any mental disorder was 35.7%. The most

prevalent disorders at 12-month were major depressive episode (MDE) (18.9%) and generalised anxiety disorder (GAD) (16%). Twelve-month mental disorders were associated with role impairment (29.2%). Only 12.6% of university students with 12-month mental disorders received any mental health treatment in the last year.

At the 12-month follow-up, the first onset of major depressive episode and/or generalised anxiety disorder (MDE-GAD) was 13.3%; and persistence among those with MDE-GAD at baseline was 46.7%. The strongest predictors for first-onset MDE-GAD were childhood/adolescence emotional abuse or neglect, prior suicidal ideation and lifetime symptoms of MDE and GAD; and for persistence MDE-GAD, the strongest predictors were prior suicidal ideation and lifetime GAD symptoms.

Results showed that mental disorders are common among Spanish university students, highlighting the need for monitoring at university entrance, allowing the early identification of at-risk students of onset and persistence of mental disorder and, subsequently, the deployment of timely prevention strategies.

RESUM

Els trastorns mentals són comuns entre els estudiants universitaris, mentre que l'evidència longitudinal sobre els trastorns mentals entre els estudiants universitaris espanyols és escassa. L'objectiu general d'aquesta tesi doctoral va consistir a estimar la freqüència (prevalença, incidència i persistència) dels trastorns mentals entre els estudiants universitaris espanyols, així com aportar evidència sobre la seva associació amb la discapacitat i l'ús de tractament de salut mental. Així mateix, va consistir a identificar factors de risc i de protecció associats amb l'inici i persistència de dos trastorns mentals comuns (depressió i/o trastorn d'ansietat generalitzada).

Aquesta tesi es basa en el projecte UNIVERSAL, un estudi de cohort observacional multicèntric aplicat a estudiants d'entre 18 i 24 anys que inicien el seu primer curs en cinc universitats espanyoles. Les dades es van recopilar mitjançant enquestes en línia, confidencials i segures.

La precisió dels instruments de mesura de salut mental en línia utilitzats en el projecte es va avaluar mitjançant entrevistes de reavaluació clínica en una submostra de participants (n = 287). En general, els instruments de mesura UNIVERSAL en línia de trastorns mentals van tenir una concordança adequada amb la MINI-Entrevista Neuropsiquiàtrica Internacional (MINI), en particular per a l'episodi depressiu major, el trastorn d'ansietat generalitzada i la dependència de l'alcohol (àrea sota la corba-AUCs >0,7). Els resultats van proporcionar evidència que l'enquesta en línia podria ser útil per al cribratge de trastorns mentals en estudiants universitaris.

Dades de les enquestes en línia del projecte UNIVERSAL, basal i de seguiment als 12 mesos, es van utilitzar per a estimar la freqüència de trastorns mentals. Un total de 2.118 estudiants universitaris de primer any van completar

l'enquesta basal i d'ells, 1.253 estudiants van completar almenys el 40% de l'enquesta de seguiment de 12 mesos. A l'inici, la prevalença als 12 mesos de qualsevol trastorn mental va ser del 35,7%. Els trastorns més prevalents als 12 mesos van ser l'episodi depressiu major (EDM) (18,9%) i el trastorn d'ansietat generalitzada (TAG) (16,0%). Els trastorns mentals de 12 mesos es van associar amb discapacitat (29,2%). Només el 12,6% dels estudiants universitaris amb trastorn mental de 12 mesos va rebre algun tractament de salut mental en l'últim any.

Als 12 mesos de seguiment, la incidència de l'episodi depressiu major i/o trastorn d'ansietat generalitzada (EDM-TAG) va ser del 13,3%; i la persistència entre aquells amb EDM-TAG en el basal va ser del 46,7%. Els principals factors associats amb l'aparició de EDM-TAG per primera vegada van ser l'abús o la negligència emocional en la infància/adolescència, la ideació suïcida prèvia i els símptomes de EDM i TAG en algun moment de la vida; i per a la persistència de EDM-TAG, els principals predictors van ser la ideació suïcida prèvia i els símptomes de TAG en algun moment de la vida.

Els resultats mostren que els trastorns mentals són comuns entre els estudiants universitaris espanyols, destacant la necessitat d'un monitoratge en l'ingrés a la universitat que permeti la identificació precoç dels estudiants en risc d'inici i persistència de trastorn mental i, posteriorment, el desplegament d'estratègies de prevenció oportunes.

RESUMEN

Los trastornos mentales son comunes entre los estudiantes universitarios, mientras que la evidencia longitudinal sobre los trastornos mentales entre los estudiantes universitarios españoles es escasa. El objetivo general de esta tesis doctoral consistió en estimar la frecuencia (prevalencia, incidencia y persistencia) de los trastornos mentales entre los estudiantes universitarios españoles, así como aportar evidencia sobre su asociación con la discapacidad y el uso de tratamiento de salud mental. Asimismo, consistió en identificar factores de riesgo y de protección asociados con el inicio y persistencia de dos trastornos mentales comunes (depresión y/o trastorno de ansiedad generalizada).

Esta tesis se basa en el proyecto UNIVERSAL, un estudio de cohorte observacional multicéntrico aplicado a estudiantes de entre 18 y 24 años que inician su primer curso en cinco universidades españolas. Los datos se recopilaron mediante encuestas en línea, confidenciales y seguras.

La precisión de las mediciones de salud mental en línea utilizadas en el proyecto se evaluó mediante entrevistas de reevaluación clínica en una sub-muestra de participantes (n = 287). En general, las mediciones UNIVERSAL en línea sobre trastornos mentales tuvieron un concordancia adecuada con la MINI-Entrevista Neuropsiquiátrica Internacional (MINI), en particular para el episodio depresivo mayor, el trastorno de ansiedad generalizada y la dependencia del alcohol (área bajo la curva-AUCs >0,7). Los resultados proporcionaron evidencia de que la encuesta en línea podría ser útil para el cribado de trastornos mentales en estudiantes universitarios.

Datos de las encuestas en línea del proyecto UNIVERSAL, basal y de seguimiento a los 12 meses, se utilizaron para estimar la frecuencia de trastornos mentales. Un total de 2.118 estudiantes universitarios de primer año

completaron la encuesta basal y, de ellos, 1.253 estudiantes completaron al menos el 40% de la encuesta de seguimiento de 12 meses. Al inicio, la prevalencia a los 12 meses de cualquier trastorno mental fue del 35,7%. Los trastornos más prevalentes a los 12 meses fueron el episodio depresivo mayor (EDM) (18,9%) y el trastorno de ansiedad generalizada (TAG) (16,0%). Los trastornos mentales de 12 meses se asociaron con discapacidad (29,2%). Solo el 12,6% de los estudiantes universitarios con trastorno mental de 12 meses recibió algún tratamiento de salud mental en el último año.

A los 12 meses de seguimiento, la incidencia del episodio depresivo mayor y/o trastorno de ansiedad generalizada (EDM-TAG) fue del 13,3%; y la persistencia entre aquellos con EDM-TAG en el basal fue del 46,7%. Los principales factores asociados con la aparición de EDM-TAG por primera vez fueron el abuso o la negligencia emocional en la niñez/adolescencia, la ideación suicida previa y los síntomas de EDM y TAG en algún momento de la vida; y para la persistencia de EDM-TAG, los principales predictores fueron la ideación suicida previa y los síntomas de TAG en algún momento de la vida.

Los resultados muestran que los trastornos mentales son comunes entre los estudiantes universitarios españoles, destacando la necesidad de una monitorización en el ingreso a la universidad que permita la identificación precoz de los estudiantes en riesgo de inicio y persistencia de trastorno mental y, posteriormente, el despliegue de estrategias de prevención oportunas.

PREFACE

This doctoral thesis consists of a compilation of scientific publications that are co-authorised —as the first author— by the PhD candidate and supervised by PhD. Jordi Alonso, according to the procedures of the Doctorate program in Psychology, Health and Quality of Life of the University of Girona (Girona, Spain).

This doctoral thesis has been elaborated in the context of the research project UNIVERSAL[1], which is coordinated by PhD Jordi Alonso, from the IMIM-Hospital del Mar Medical Research Institute. UNIVERSAL is part of the World Mental Health International College Student (WMH-ICS) initiative from the World Health Organization (WHO), which entails administering online surveys among university students worldwide to generate epidemiological data on mental disorders and suicidal thoughts and behaviours, adverse consequences of these disorders, and patterns of help-seeking. Also, longitudinal data provide an integral view of changes in mental disorders and the identification of risk and protective factors.

The PhD student received funding by the Ministry of Universities of the Spanish Government through a grant (FPU15/05728). The purpose of the funding involved collaborating with the research team, especially helping with the data collection and divulgation of the results of the project. Also, the funding involved university professor training, combining the development of the thesis with teaching tasks in the University of Girona. The UNIVERSAL project has received funding from the Institute of Health Carlos III, ISCII-FEDER (PI13/00343), ISCIII (Río Hortega, CM14/00125); ISCIII (Sara Borrell,

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The thesis comprises four publications with the PhD candidate as first author, two already published, one sent to the journal and one to be submitted to the journal. The four publications are the main part of the thesis. All publications used data from the UNIVERSAL project.

The first article, "Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviours in Spanish university students. Results of the WHO World Mental Health-International College Student initiative", published in *PLoS ONE*, describes the study of validation of the online survey administered in the UNIVERSAL sample to assess mental disorders and suicidal thoughts and behaviours.

The second article, "Validation of an online version of the Alcohol Use Disorders Identification Test (AUDIT) for alcohol screening in Spanish university students" was submitted to the *International Journal of Environmental Research and Public Health*, and describes the validation of the online version of the AUDIT administered in the UNIVERSAL sample to measure alcohol consumption and alcohol use disorder.

The third article, "Mental disorders in Spanish university students: Prevalence, age-of-onset, severe role impairment and mental health treatment", was published in the *Journal of Affective Disorders*, and consists of cross-sectional results from the baseline survey of the UNIVERSAL project. This study provides epidemiological data on mental disorders among Spanish university students, both the estimates of prevalence, persistence and age-of-onset, as well as the

association of mental disorders with impairment and use of mental health services.

Finally, the fourth article: "Predictive models for first-onset and persistence of depression and anxiety among university students", was submitted to the *Journal of Affective Disorders*, and offers results from the 12-month follow-up survey of the UNIVERSAL project. This article shows the first baseline multivariable model that predicts the risk of onset and persistence of depression and/or generalised anxiety disorder in university students, facilitating the detection of high risk cases.

The thesis report is organised into seven sections. The first section is the introduction, which provides an overview of literature on empirical background of the mental health research, focusing the interest on mental health in university students. The aim of this section is to assess the evidence for the need of this doctoral thesis and to establish the background for the work presented in the following sections.

The justification of the study, the objectives and the hypotheses proposed in this project are presented in the second and third sections.

In the fourth section, a description of the UNIVERSAL project, the empirical basis of this thesis, is presented. The four studies that were carried out are described, including sampling, data collection, instruments, analysis and ethical considerations. Also, the details of the sub-study of validation of the online survey, carried out within the UNIVERSAL project, are shown.

The fifth section includes the four articles presenting the main methods and findings of the doctoral thesis. This is followed by section six, summarising and discussing the thesis results, and including the limitations of the thesis. It also

provides a discussion of the implications and future lines of research. Final section, seventh, describes the general conclusions of the thesis.

INTRODUCTION

1

1. INTRODUCTION

1.1. Rates and global burden of mental disorders

1.1.1. In the world

Mental health and well-being are fundamental elements of people's quality of life. Mental disorders and, in the worst case, suicide, constitute one of the most significant public health problems in the world. In 2017, according to the Institute for Health Metrics and Evaluation, about 1 in 7 people suffered one or more mental disorder in the world, being an estimate of 970 million (Global Burden of Disease Collaborative Network, 2017). Moreover, it is estimated that 1 in 4 people in the world will experience a mental disorder in their life (World Health Organization, 2008). The most frequent mental disorders are anxiety disorders, with an estimated lifetime prevalence of 4.8%-31%, followed by mood disorders (lifetime prevalence of 3.3%-21.4%) (Kessler et al., 2007).

A systematic review and meta-analysis, published in 2014, estimated that 29.2% of people had a mental disorder at lifetime and 17.6% of people had a mental disorder in the previous year. A gender effect was found in the prevalence of mental disorders, where women had higher rates of mood and anxiety disorders and men had higher rates of substance use disorders (Steel et al., 2014).

In the European Union, in 2016 more than 1 in 6 people in the Member States experienced a mental health problem (about 84 million citizens). The most common mental disorders were anxiety disorders (5.4%), followed by depressive disorders (4.5%) and substance use disorders (2.4%) (OECD/EU, 2018). In 2015, mental disorders in Europe accounted for 4% of GDP (OECD/EU, 2018).

The global burden attributable to mental disorders increased by almost 40% between 1990 and 2010 (Whiteford, Ferrari, Degenhardt, Feigin, & Vos, 2015). According to the Global Burden of Disease (GBD) report 2017, mental disorders accounted for 4.9% of the global burden of disease (disability-adjusted life years-DALYs) and they were among the top ten causes of disability (years lived with disability-YLD) (Global Burden of Disease Collaborative Network, 2017; James et al., 2018; Kyu et al., 2018; Rehm & Shield, 2019; World Health Organization, 2017). According to the World Health Organization (WHO), depression was the largest individual contributor to the global disability in 2015 (7.5% of all YLD) and is projected to rank first in the global burden (DALYs) in 2030 (World Health Organization, 2008, 2017).

However, the contribution of mental disorders to the years of life lost due to premature mortality (YLL) is relatively small, which may be due to suicide and self-harm are excluded from the effect of mental disorders (Vigo, Thornicroft, & Atun, 2016). Nevertheless, a relevant number of indirect deaths from suicide and self-harm are attributed to mental disorders (Arsenault-Lapierre, Kim, & Turecki, 2004). According to the literature, the risk of suicide is around twenty times higher for an individual with depression than an individual without it (Ritchie & Roser, 2020). According to the WHO, almost a million people die by suicide every year, and it is the third leading cause of death among young people (World Health Organization, 2014).

1.1.2. In Spain

According to the last report "Encuesta Nacional de Salud, ENSE 2017" (Ministerio de Sanidad, 2019), more than 1 in 10 people in Spain, reported having been diagnosed with "some mental health problem" (10.8%). Mental health problems were reported more frequently for women than men (14.1% vs. 7.2%). Depression (6.7%) and anxiety (6.7%) were the most common mental disorders. A recent study, published with data from the ENSE (Henares

Montiel, Ruiz-Pérez, & Sordo, 2019), compared the global psychiatric morbidity in Spain in 2006, 2011 and 2017, finding frequencies of around 20% in all years and being higher in women. The prevalence in the Autonomous Communities was similar to the Spanish average. Also, the report of the European Health Survey showed that 10.7% of the general population reported a "mental health problem" (Ministerio de Sanidad, 2014).

In 2015, mental disorders produced 10.5% of the global DALYs in the Spanish population, being greater in women than in men. Depression was the main cause of DALY (9.7% in men and 11.3% in women) (de Pedro Cuesta, Noguer Zambrano, García Lopez, & Rodríguez Blázquez, 2018). According to the report of the Organization for Economic Cooperation and Development (OECD), mental health problems in Spain accounted for 4.2% of GDP, around 40,000 million euros (OECD/EU, 2018).

According to the epidemiological study ESEMeD (The European Study of the Epidemiology of Mental Disorders) (Alonso et al., 2002; Haro, Palacín, et al., 2006), which estimated the prevalence of mental disorders in the general Spanish population, the results showed that 8.4% of the population had a 12-month mental disorder and 19.5% of the population had lifetime mental disorder. The 12-month prevalence estimates of mental disorders in the general Spanish population from the ESEMeD project are shown in **Table 1**.

Table 1

Results from the ESEMeD-Spain study on the 12-month prevalence of mental

disorders

	Total		Males		Females	
	%	95% CI	%	95% CI	%	95% CI
Mood disorders						
Major depression episode	3.96	(3.34-4.59)	2.15	(1.45-2.86)	5.62	(4.66-6.59)
Dysthymia	1.49	(1.10-1.88)	0.52	(0.22-0.81)	2.38	(1.69-3.07)
Any mood disorder	4.37	(3.71-5.04)	2.33	(1.61-3.04)	6.25	(5.20-7.30)
Anxiety disorders						
Generalised anxiety disorder	0.50	(0.30-0.70)	0.44	(0.11-0.78)	1.18	(0.81-1.56)
Social phobia	0.60	(0.33-0.87)	0.57	(0.13-1.00)	0.64	(0.32-0.95)
Specific phobia	3.60	(2.82-4.38)	1.19	(0.68-1.70)	4.20	(3.23-5.16)
Post-traumatic stress disorder	0.50	(0.30-0.70)	0.25	(0.02-0.48)	0.94	(0.50-1.39)
Agoraphobia	0.30	(0.10-0.50)	0.15	(0.02-0.29)	0.60	(0.26-0.95)
Panic disorders	0.60	(1.32-2.09)	0.38	(0.14-0.63)	0.98	(0.60-1.36)
Any anxiety disorder	6.20	(0.40-0.80)	2.53	(1.74-3.31)	7.61	(6.41-8.80)
Alcohol use disorders						
Alcohol abuse	0.10	(0.00-0.23)	0.18	(0.00-0.45)	0.02	(0.51-1.39)
Alcohol dependence	0.69	(0.40-0.98)	1.38	(0.78-1.99)	0.05	(0.00-0.13)
Any alcohol use disorder	0.69	(0.40-0.98)	1.38	(0.78-1.99)	0.05	(0.00-0.12)
Any mental disorder	8.48	(7.53-9.42)	5.25	(4.17-6.33)	11.44	(10.02-12.9)

Source: (Haro, Palacín, et al., 2006)

Also, the PEGASUS-Murcia project found a lifetime prevalence of 15.6% for mood disorders, 15.0% for anxiety disorders and 8.3% for substance use disorders (Navarro-Mateu et al., 2015). According to the recently published study GRANAD∑P, the current prevalence for any mental disorder was 11.3% (Cervilla et al., 2018).

1.2. Mental disorders among adolescents and young adults

Emerging adulthood is an important developmental period from 18 to 25 years of age (Arnett, 2000; Sussman & Arnett, 2014). During this period, individuals experience changes in their social roles, achieve certain autonomy and for some of them, it is the period in which they study higher education. Also, individuals develop new social networks and improve their coping strategies to face adult life (Sussman & Arnett, 2014). Previous research has found that emerging adults are less healthy than adolescents and adults (Stroud, Walker, Davis, & Irwin, 2015).

Also, several studies has showed that 75% of many mental disorders start before the age of 24 (de Girolamo, Dagani, Purcell, Cocchi, & McGorry, 2012; Kessler et al., 2007). A recent publication reported that just about 40% of people experience their first onset of depression before 20 years of age (Malhi & Mann, 2018). Also, results from the National Survey on Drug Use and Health 2017 found the highest prevalence of mental disorders in youth (25.8%) compared to other age groups (22.2%) (Substance Abuse and Mental Health Services Administration, 2014).

Patel et al. (2007) reported that 1 of 5 young people can suffer from at least one mental disorder in a year (Patel, Flisher, Hetrick, & Mcgorry, 2007). A meta-analysis, on the prevalence of mental disorders among children and adolescents, reported a worldwide pooled prevalence of any mental disorder of 13.4%, being the prevalence of anxiety disorders of 6.5% and of depressive disorders of 2.6% (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015).

According to the GBD in 2013, mental disorders were the leading cause of DALYs in the group of 10-24 years of age, and depressive disorders accounted

for the first place of YLDs in females (Mokdad et al., 2016). In Spain, the global burden of mental disorders (14-49 years of age) in 2015 accounted for 23% of the total burden, where depression constituted 6.3% of the total DALYs in men and 9.6% in women (de Pedro Cuesta et al., 2018), finding similar results that those previously found in 2008 (Catalá-López, Gènova-Maleras, Álvarez-Martín, Fernández de Larrea-Baz, & Morant-Ginestar, 2013).

Particularly in Spain, in 2019 almost 49% of young people reported that "they had or thought they had some mental health problem" during the previous year, being higher than in 2017 (30%) (Ballesteros, Sanmartín, Tudela, & Rubio, 2020). Findings indicate a higher percentage among women (33%), than among men (23%). According to the EDADES survey, alcohol use accounted for 7.2% risk-consumption and 0.2% possible dependence (Observatorio Español de las Drogas y las Adicciones, 2019).

1.2.1. Mental disorders among university students

In 2018, within the countries that belong to the Organization for Economic Cooperation and Development (OECD), 44% of young people held tertiary education, which represents an important part of young people (Ministerio de Ciencia e Innovación, 2019).

Among young people, university students are a vulnerable population due to the transition to university may be stressful and increase the risk for the onset of mental disorders. In addition to the stress related to academic achievement, these students may have to face more responsibilities and changes in their personal relationships (Pedrelli, Nyer, Yeung, Zulauf, & Wilens, 2015). In this situation, many university students may experience the first onset of mental disorders while possibly not receiving treatment (Auerbach et al., 2016; Bruffaerts et al., 2019; Zivin, Eisenberg, Gollust, & Golberstein, 2009).

According to a cross-sectional study based on surveys from 21 countries, it was found that 20.3% of university students had 12-month mental disorders, where 83.1% of these cases had pre-matriculation onsets (Auerbach et al., 2016). As in other age groups, among university students women had higher rates of mood and anxiety disorders, and men had higher rates of substance use disorders (Eisenberg, Hunt, & Speer, 2013).

Anxiety disorders are the most prevalent mental disorders among university students, with a prevalence of approximately 11.9% (C. Blanco et al., 2008). According to an study performed in the United States, 2.9% of students reported generalised anxiety disorder and 1.8% panic disorder (Eisenberg, Gollust, Golberstein, & Hefner, 2007). A meta-analysis on the prevalence of anxiety among university medical students found a global prevalence of 33.8% (Quek et al., 2019).

Another common mental disorder among university students is depression, with a prevalence rate of 7% (C. Blanco et al., 2008). A longitudinal study in the US (2007-2009) found that 17.3% of students suffered depression (Eisenberg et al., 2013). A cross-national study with data from 8 countries found depression as the most prevalent of the disorders (18.5% 12-month prevalence) followed by generalised anxiety disorder (16.7%) (Auerbach et al., 2018). Meanwhile, a systematic review reported prevalence rates of depression ranging from 10% to 85% (mean prevalence of 30.6%) (Ibrahim, Kelly, Adams, & Glazebrook, 2013).

Bipolar disorder has been found less common among university students, affecting approximately 3.2 % of them (C. Blanco et al., 2008). The cross-national study carried out by Auerbach et al. (2018) found a 12-month prevalence of 3.1% (Auerbach et al., 2018). These rates may be due to the fact

that bipolar disorder has the typical age-of-onset around the twenties (de Girolamo et al., 2012).

In relation to the alcohol consumption, it has been shown that it has a peak onset during youth, a time that could correspond to the university period (Kelly, Weier, & Hall, 2019). A study conducted in the US by Slutske et al. (2005) found that 18% of university students reported alcohol use disorder in the previous year, and had higher rates of alcohol abuse than the group of non-students (Slutske, 2005). Binge drinking has been defined as "consuming four standard drinks for women and five for men in a 2-hour period" (Dawson, 2011; Parada et al., 2011). In Europe, studies found a prevalence ranging from 12% to 35% (Caamaño-Isorna, Corral, Parada, & Cadaveira, 2008; D'Alessio, Baiocco, & Laghi, 2006; Webb, Ashton, Kelly, & Kamali, 1996). On the other hand, lower prevalence rates of drug use disorders among university students has been reported (C. Blanco et al., 2008), finding marijuana as the most consumed drug (Arria et al., 2017; Cho, Llaneza, Adkins, Cooke, & Dick, 2015). In comparison, the highest rates of substance use disorders have been found among non-students (White, Labouvie, & Papadaratsakis, 2005).

Attention-deficit/hyperactivity disorder (ADHD) onsets during childhood, but it can persist into adulthood in many cases. According to the study carried out by DuPaul et al. (2009), around 8% of university students suffered from ADHD (DuPaul, Weyandt, O'Dell, & Varejao, 2009), which has also been found significantly associated with role impairment (Fayyad et al., 2017).

These high frequencies are relevant to take into consideration for the impact on students' life. Mental disorders have been found associated with low rates on academic performance (Bruffaerts et al., 2018; Vaez & Laflamme, 2008), university attrition (Auerbach et al., 2016), suicidal thoughts and behaviours (Mortier et al., 2020; Mortier et al., 2018) and, in the worst case, with suicide

death (Gunnell, Caul, Appleby, John, & Hawton, 2020; Hawton, Saunders, & O'Connor, 2012).

1.2.2. Mental disorders in Spanish university students

In Spain, 32% of young people (18-24 years old) was enrolled at university in 2018 (Ministerio de Universidades, 2020) and according to the data published by Instituto Nacional de Estadística from the last course 2018-2019, a total of 337,055 students arrived at university for the first-time (Ministerio de Educación y Formación Profesional, 2019). In the latest report of the Organization for Economic Co-operation and Development-OECD, 47% of the Spanish population aged between 25 and 34 had tertiary education in 2019 (OECD, 2020).

The Spanish Educational System offers compulsory and free education from 6 to 16 years old, including primary education (up to 12 years old) and secondary education (up to 16 years old). Upper secondary education (i.e., 2 academic years, from 16 to 18 years old) comprises: baccalaureate or intermediate vocational training. Later, higher education includes university studies and advanced vocational training. University studies in Spain were adapted to the European Higher Education Area according to the Bologna Declaration (1999) and are divided into three cycles: bachelor, master and doctorate. Specifically, bachelor's degrees have a minimum of 240 ECTS credits distributed over four academic years. In the 2018-19 academic year 2,920 bachelor's degrees were offered in Spain, which were classified into five academic fields: Arts and Humanities, Engineering and Architecture, Health Sciences, Science and Social and Legal Sciences (Ministerio de Universidades, 2020). Access to university can be obtained through: the Baccalaureate Certificate and the University Entrance Examination, an Advanced Vocational Training Certificate, entrance exams at 25 and 45 years of age, or by certifying professional experience in the

field at 40 years of age. In the case of foreign students, it is necessary to have accredited studies or the equivalent of the baccalaureate.

In the academic year 2018-2019, there were 83 universities in Spain, 50 of which were public and 33 private. According to the report of the Spanish University System 2020 (Ministerio de Universidades, 2020), the average price per credit ranged between 14.0-21.2 euros depending on the experimental level of the subject, and also, depending on the autonomous community. In Spain, there are public and private financial aid and grants that allows access to university (Ministerio de Ciencia e Innovación, 2020).

Epidemiological data available on mental disorders among Spanish university students is scarce and mostly on specific mental disorders (e.g., depression, anxiety, eating disorder), on regional samples (e.g., Galicia, Murcia) or with a small sample size (Bados, A., Greco, A., & Toribio, 2012; Balanza, Morales, & Guerrero, 2009; Martínez-González et al., 2014; Olmedilla, Ortega, & Candel, 2010; Vázquez & Blanco, 2008; Vázquez, Torres, Otero, & Díaz, 2011). A study performed at the University of Santiago de Compostela, by Vázquez et al. (2011) in a sample of 1,054 female university students, showed that depression (5.3%) and generalised anxiety disorder (2.7%) were the most frequent after nicotine dependence (Vázquez, Torres, Otero, & Díaz, 2011). Another study, carried out by Balanza et al. (2009) in a sample of 700 students from the University of Murcia showed that 55% of students reported depression and 47%, anxiety (Balanza, Morales, Guerrero, et al., 2009).

More studies have been carried out in Spain to study alcohol and substance consumption and related disorders among university students ranging from research among small samples (Garrido-González, Bugarín-González, & Javier, 2016; Timon, Olcina, Maynar, & Maynar, 2012), cross-sectional studies (Chacón et al., 2018; Cortés, Giménez, Motos, Sancerni, & Cadaveira, 2017; García-

Carretero, Moreno-Hierro, & Robles, 2019; Gil-García, Gue Martini, & Porcel-Gálvez, 2013; Hernández, Font-Mayolas, & Gras, 2015; Jiménez-Muro, Beamonte, Marqueta, Gallardo, & Nerín, 2009) and studies with data from cohorts (Arias-de la Torre et al., 2019; Caamaño-Isorna et al., 2008, 2011; Jiménez-Mejías, Medina-García, Martínez-Ruiz, Pulido-Manzanero, & Fernández-Villa, 2015; Moure-Rodríguez et al., 2014). Findings about alcohol consumption showed that binge drinking is highly prevalent among university students (74.2%), being similar for men and women (Motos-Sellés, Cortés-Tomás, & Giménez-Costa, 2019), while the prevalence of risk consumption has been found roughly 21-37% (Caamaño-Isorna et al., 2008; García-Carretero et al., 2019), and the two-year incidence of risk consumption among university students was 24.9% (Mota et al., 2010). Garrido-González et al. (2016) reported that 17.8% of students consumed cannabis, 2.2% tranquilisers/hypnotics, and 2.2% cocaine (Garrido-González et al., 2016). Another study on drug use, found that a total of 46% of the students reported consumption of two or more substances (Hernández et al., 2015).

However, there is no study in Spain that provides information among a broad range of mental disorders through a representative sample of Spanish university students, and that take into account data from the country's different Autonomous Communities.

1.3. Role impairment and use of services associated with mental disorders

1.3.1. Role impairment associated with mental disorders

As previously shown, mental disorders cause considerable burden of disease. While mental disorders comprised about 5% of all burden of disease, they were

responsible for 14.4% of all YLDs (Global Burden of Disease Collaborative Network, 2017; Kyu et al., 2018). A research that used data from Global Burden of Diseases 2010 to estimate the burden of disease attributable to mental disorders found that mental disorders accounted 175 million years lived with disability (YLD), resulting on the leading cause of YLDs worldwide (Whiteford et al., 2013).

A cross-national study of the World Mental Health found that the mental disorders' disability ratings were generally higher than for physical disorders, and bipolar disorder and depression had the highest rates. It also found that across all the four impairment domains (social, close relationships, work and home) evaluated through the Sheehan Disability Scale (SDS), the highest rates of disability of mental disorders were in the social and close relationships domains (Ormel et al., 2008). Similarly, results from the National Survey Replication in the US showed that mental disorders were associated with both domains (i.e., social and close relationships), while chronic medical disorders were mostly associated with work and home functioning (Druss et al., 2009).

A study among the general population in Europe, found that mental disorders were associated with all domains assessed through the World Health Organization Disability Assessment Schedule (WHODAS). In this study, anxiety disorders were the most related to disability (Buist-Bouwman et al., 2006). Also, epidemiological studies have been broadly reported higher rates of impairment in comorbidity conditions both between mental disorders and between mental and physical conditions (Druss et al., 2009; Kessler, Ormel, Demler, & Stang, 2003; Ormel et al., 2008).

Among young people, a systematic analysis conducted by Gore et al. (2011) with data from the GBD, found that the main cause of YLDs for the age group of 10–24 year olds was neuropsychiatric disorders with a contribution to the

global disability of 45% (Gore et al., 2011). Among adolescent samples, Whittchen et al (1998) reported that mental disorders were associated with social role functioning, finding mood disorders, generalised anxiety disorder and panic disorder as the most impairing disorders (Wittchen, Nelson, & Lachner, 1998). In the same direction, other studies found that most young adults with mental disorders reported functional interference in work and daily activities, finding the highest levels of disability associated with mood disorders (Newman et al., 1996; Scott et al., 2014).

1.3.2. Use of mental health services

Results from the World Mental Health (WMH) Survey initiative in 17 countries, found that 11.0%-62.1% of severe mental disorders received health care treatment in the previous 12 months (Wang, Aguilar-Gaxiola, et al., 2007). In Europe, findings from the ESEMeD project among the general population found that 25% of participants with mental disorders reported they consulted mental health services during the last 12 months (Alonso et al., 2004). Those studies also consistently found comorbidity associated with higher rates of use of mental health treatment.

Results from the Canadian Community Health Survey among participants aged 19 to 24 with depression showed that, 42% of them had not used any mental health services and, among young adults with suicidal thoughts and behaviours, 48% of them had not accessed services (Cheung & Dewa, 2007). Consistently, studies carried out in the US found that less than 30%-50% of adolescents and young adults used mental health services (Benjet et al., 2016; Kessler, Avenevoli, & Merikangas, 2001).

In Spain, according to Codony M. et al. (2007), only 35% of the general population suffering any mental disorder received treatment. Also, results

suggested a tendency of using services at an older age (Codony et al., 2007). Also reported by *Barómetro juvenil de vida y salud*, more than half of young people who "have or thought to have mental health problems" did not request health care assistance (Barómetro juvenil de vida y salud, 2017).

1.3.3. Role impairment and use of mental health services among university students

Recently, a study conducted by the World Health Organization's World Mental Health–International College Student (WMH-ICS) Initiative in eight countries across the world found that 42.9% of students with any mental disorder reported severe role impairment, being depression, generalised anxiety disorder and panic disorder highly associated with severe impairment (Alonso et al., 2018). This study also reported higher rates of role impairment among those with comorbid disorders (Alonso et al., 2018). Another study carried out in France, also reported that 51.7% of university students with any mental disorder reported severe role impairment (Verger, Guagliardo, Gilbert, Rouillon, & Kovess-Masfety, 2010).

Results from the WMH Survey initiative showed that only 16.4% of students with 12-month mental disorders received any 12-month mental health treatment (Auerbach et al., 2016). More recently, results of the WMH-ICS showed that 12-month treatment rates were 36.3% and, among severe cases, 45.1% (Bruffaerts et al., 2019). In the Healthy Minds sample, which included over 13,000 respondents, only 36% of students with mental disorders received any treatment in the prior year (Eisenberg, Hunt, & Speer, 2012). Other studies found similar treatment rates across all psychiatric disorders (C. Blanco et al., 2008; Eisenberg, Golberstein, & Gollust, 2007).

The higher rates of role impairment reported among university students and, on the other hand, lower rates of service utilisation, increase the need for an in-depth study of the situation among Spanish university students.

1.4. Risk and protective factors in mental health

The onset and persistence of mental disorders can be attributed to a large number of risk and protective factors that are in interaction (World Health Organization, 2002). Therefore, an important element in research is to identify potential factors to allow implementing prevention programs and treatments (Ritchie & Roser, 2020).

Genetic factors have been found related to mental disorders in studies carried out among twins (Afifi, Asmundson, Taylor, & Jang, 2010; Kendler, 2001; Skre, Onstad, Torgersen, Lygren, & Kringlen, 1993). Furthermore, a number of studies found an increased risk for onset of mental disorders in the offspring of parents with mental disorders (Kendler, 1992; Lieb, Isensee, Höfler, Pfister, & Wittchen, 2002; McLaughlin et al., 2012). Research has also shown structural-developmental alterations and neuroendocrine predictors associated with mental disorders (Ogłodek, Szota, Just, Moś, & Araszkiewicz, 2014; Whittle et al., 2014).

A strong association has been found between personality traits and mental disorders. Specifically, mood and anxiety disorders have been related to neuroticism, whereas the externalising disorders (e.g., substance use disorders) has been related to extraversion (Clark, 2005; Hankin, B. L., & Abela, 2005; Watson & Naragon-Gainey, 2014). In the same direction, a number of psychological factors have been found associated with mental disorders. Some of them are positive coping strategies, that are negatively associated with the

onset of mental disorders (Crockett et al., 2007; McLafferty et al., 2019; Zong et al., 2010) and, expectations about the future, as intermediary factor between attribution style and depression (Brackney & Karabenick, 1995; Riskind, Rholes, Brannon, & Burdick, 1987).

Also, the evidence has supported the association of some clinical factors with the onset and persistence of mental disorders, such as a prior history of mental disorders or previous symptoms of mental disorders (Horwath, 1992; Kessler et al., 2002; Rueter, Scaramella, Wallace, & Conger, 1999).

Childhood adversities and stressful events have been broadly studied in the context of mental disorders, showing an increased risk for mental disorders (Bandoli et al., 2017; Blazer, Hughes, & George, 1987; Finlay-Jones & Brown, 1981; Kendler, Hettema, Butera, Gardner, & Prescott, 2003; Kessler et al., 2010; Mclaughlin, 2016). Also, research revealed that childhood adversities could lead to dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis (Fries, Shirtcliff, & Pollak, 2008; Tennant, 2002). While negative life events predispose to mental disorders, the presence of social support seems to protect against them (Institute of Medicine (US) Committee on Prevention of Mental Disorders, 1994). There is evidence of a protective effect on the onset of mental disorders in adolescents of family and school support (McGraw, Moore, Fuller, & Bates, 2008), and it has been suggested that social support could buffer the effect of stressful events (Galatzer-Levy, Burton, & Bonanno, 2012).

Sociodemographic characteristics have been also widely studied for their association with mental disorders (de Graaf, Ten Have, Tuithof, & Van Dorsselaer, 2013; Farrer, Gulliver, Bennett, Fassnacht, & Griffiths, 2016; Kessler et al., 2012; Nock et al., 2014; Suvisaari et al., 2009). Female gender has been found more associated with mood and anxiety disorders; while male gender, more associated with behaviour and substance use disorders (Chandra &

Satyanarayana, 2010; Moreno-Peral et al., 2014; Vázquez et al., 2011). Family income, race/ethnicity, education, place of raising or religion, between others, have also been found related with the onset and persistence of mental disorders (Benjet et al., 2019; Breslau, Kendler, Su, Gaxiola-Aguilar, & Kessler, 2005; Brunoni et al., 2020; Kessler et al., 2012).

1.4.1. Conceptual models of risk and protective factors in mental health

A theoretical framework widely used in psychiatric research and that can be useful to understand the relationship between multiple risk and protective factors involved in the onset of a mental disorder is the vulnerability-stress model (Monroe & Simons, 1991). The vulnerability-stress model understands that mental disorders are the result of an interaction between an underlying vulnerability (biological and psychological predisposition) and the stress caused by environmental factors. A large amount of literature has incorporated explanations of vulnerability-stress into its conceptual framework (Burns & Machin, 2013; Chang & Rand, 2000; Chang, Yu, Chang, & Hirsch, 2016; Colodro-Conde et al., 2018; Flett, Hewitt, & Blankstein, 1995; Solberg, Valdez, & Villarreal, 1994). This model provides a helpful framework about the factors (biological, psychological, and environmental) that are involved in the development of mental disorders. Other variant are the transdiagnostic models, which are focused on processes underlying multiple mental disorders, which help to explain comorbidity among those (Nolen-Hoeksema & Watkins, 2011). According to these models, there is a general vulnerability predisposition shared by multiple disorders (Barlow, 1991; Barlow, Allen, & Choate, 2016; Clark & Watson, 2006; Kotov, 2011; Krueger & Eaton, 2015; Krueger & Markon, 2006; Watson, Gamez, & Simms, 2005).

In the field of epidemiology, the risk and protective factors involved in the occurrence of mental disorders can be understood from a life course perspective. The life course approach aims to understand and identify the biological, psychological and social factors that influence health and illness throughout the different stages of life (Ben-Shlomo & Kuh, 2002). This theory emphasises the importance of the temporal study of the effects of exposures to particular factors from gestation, childhood, adolescence, young adulthood and later adulthood on health, understanding the interaction of different risk and protective factors across the life course. This approach provides a broad conceptual framework for understanding the determinants of non-communicable diseases, general health and well-being (Baird et al., 2017; Jacob, Baird, Barker, Cooper, & Hanson, 2017) and thus encourages the implementation of preventive interventions from early in life and throughout the life course, which can be offered according to current knowledge to reduce risk factors and enhance protective factors (D'Arcy & Meng, 2014). The World Health Organization (WHO) suggests this conceptual framework to understand and respond to health determinants by promoting preventive health strategies and interventions involving health agents, policies and services (Jacob et al., 2017; Kuruvilla et al., 2018).

In relation to mental health, the World Health Organisation provides an overview of some of the risk factors for the development of mental disorders based on the life course approach (World Health Organization, 2012). This summary distinguishes individual, family, community and cultural at different stages of development: prenatal and early childhood, childhood, adolescence, adulthood and late adulthood, as shown in **Figure 1**. Thus, according to the life course approach, the importance of different exposures across life stages for the development of mental illnesses is highlighted, identifying determinants in the early stages as risk factors in later stages of development.

Figure 1

Mental health risk factors across the life course summarised from the World

Health Organization (WHO)

Setting	Home / family	School	Media / information	Work	Community / home
Culture	Low socioeconomic status	Adverse learning environment	Adverse media influences	Discrimination / social inequalities	Social exclusion
Community	Poor housing / living conditions		Neighbourhood violence / crime		Poor civic amenities
Family	Parental mental illness, Substance use in pregnancy	Difficulties at school	Peer pressure, Family violence or conflict	Job intensity or insecurity, Unemployment	Debt / poverty
Individual	Insecure attachment, Malnutrition, Low self-esteem	Trauma or maltreatment, Poor nutrition, Physical ill-health	Criminal or anti-social behaviour, Psychoactive substance use	Harmful alcohol use, Physical ill-health	Bereavement, Elder abuse
	Prenatal period and early childhood	Childhood	Adolescence	Adulthood	Older adulthood

Source: (World Health Organization, 2012)

1.4.2. Prediction models in mental health

Identifying risk factors involved in the development of mental disorders can help to create and validate methods to predict the onset of these disorders. In medicine, there are some widely-known prediction algorithms, such as the Gail model for predicting breast cancer (Corbelli et al., 2014) or the Framingham risk score for coronary events (Greenland, LaBree, Azen, Doherty, & Detrano, 2004).

Although the work to develop risk prediction models is relatively new in psychiatry, compared to other fields of medicine, some models have been published directly to clinical or adult populations (Bernardini et al., 2017). An international example is Predict, a study that aimed to develop a risk index for the onset of depression (Bellón et al., 2011; King et al., 2006). Based on this project, a predictive model also emerged to develop a risk index for the onset of generalised anxiety disorder and panic disorder (King et al., 2011). Among university students, prediction risk algorithms have been developed for depression, suicide and self-harm, finding similar performance than those for other diseases (Ebert, Buntrock, et al., 2019; Kiekens et al., 2019; Mortier, Kiekens, et al., 2017).

The mounting evidence about the high prevalence of mental disorders and their associated disability suggests the need of having predictive models that allow the identification of individuals with a higher risk of onset and persistence of mental disorders in order to carry out specific interventions.

1.5.   Screening instruments for the assessment of mental disorders

Brief screening tools are essential for improving epidemiological knowledge about mental disorders, and also for allowing early detection and the deployment of subsequent interventions. Screening instruments for assessing mental disorders have the potential to be brief tools and provide accurate measurements (Ali, Ryan, & De Silva, 2016) and thus, facilitate the monitoring and treatment of mental disorders.

Screening instruments have been shown more suitable than structured diagnostic interviews, such as the Structured Clinical Interview for DSM-III-R

(SCID) (Spitzer, Williams, Gibbon, & First, 1990) or the Mini-International Neuropsychiatric Interview (Sheehan et al., 1998) because in these instruments, administration is time-consuming and they can only be administered by well-trained interviewers (Meuldijk et al., 2017).

However, a meta-analysis found that depression prevalence's estimates based on screening tools were 14% higher than those based on diagnostic interviews, highlighting that screening instruments may overestimate prevalence. Calibrating the cut-off points in the screening tools to estimate the real prevalence in the population could be a solution, as proposed by these authors (Levis et al., 2019).

1.5.1   Self-administered instruments

Screening methods to detect mental disorders can be self-reports or interviews (Gega, Kenwright, Mataix-Cols, Cameron, & Marks, 2005). Self-administered instruments are one of the most widely used methods and would help to reduce social desirability bias (i.e., socially acceptable responses to sensitive questions) by allowing participants to respond more honestly than in interviewer-administered assessments. Furthermore, the brevity and ease of administration of self-administered instruments could facilitate the evaluation of mental disorders in epidemiological studies (Chad Cook, 2010; Head et al., 2013; Short et al., 2009).

Some studies have demonstrated that self-administered instruments show good diagnostic accuracy in youth and adult samples, such as the Composite International Diagnostic Interview (CIDI), where self-administered and interviewer-administered versions showed good kappa agreement (Andrews & Peters, 1998), or the self-administered General Health Questionnaire (GHQ), which showed good concordance with the interviewer-administered version of

the Clinical Interview Schedule-Revised (CIS) (Stansfeld & Marmot, 1992). Another study, which evaluated operating characteristics of both self-administered and interviewer-administered questionnaires to screening anxiety and depression, indicated that self-administered version showed high sensitivity and positive predictive values (Gega et al., 2005).

1.5.2 Web-based self-administered instruments

Within mental health screening measures, there are self-administered computerised instruments that can be useful for assessing mental disorders and have proven to be a reliable method for collecting epidemiological data (Lewis, 1994; van Gelder, Bretveld, & Roeleveld, 2010). Some findings show that web-based surveys are generally faster to administer and less expensive than traditional methods (Knapp Whittier, Seeley, & St. Lawrence, 2004; Parks, Pardi, & Bradizza, 2006). Another advantage is that web-based surveys can improve data quality by allowing automatic data validation, programming alerts for participants to complete responses and automating skip-patterns to eliminate unnecessary questions (Coyne et al., 2009; van Gelder et al., 2010). However, there are still few web-based questionnaires validated in samples of university students and which assess a wide range of mental disorders (van Ballegooijen, Riper, Cuijpers, van Oppen, & Smit, 2016).

Table 2

Validated online instruments for the assessment of mental disorders in university

students

Instrument	Disorder	Authors	Country
Hospital Anxiety and Depression Scale (HADS)	Depression; anxiety	(Whitehead, 2011)	New Zealand
Depression Anxiety Stress Scales (DASS)	Depression; anxiety; stress	(Zlomke, 2009)	US
Center for Epidemiologic Studies Depression Scale (CES-D)	Depression	(Fortson, Scotti, Del Ben, & Chen, 2006) (J. Herrero & Meneses, 2006)	US; Spain
Beck Depression Inventory II (BDI-II)	Depression	(Holländare, Gahnström, Nieminen, & Engström, 2009)	Sweden
Montgomery–Asberg Depression Rating Scale Self Report (MADRS-S)	Depression	(Holländare et al., 2009)	Sweden
Zagazig Depression Scale (ZDS)	Depression	(Ibrahim, Kelly, Challenor, & Glazebrook, 2010)	UK
Kandel & Davies mood scale	Depression	(Roane et al., 2013)	US
University student depression inventory (USDI)	Depression	(Romaniuk & Khawaja, 2013)	Australia
Social Phobia Scale (SPS)	Social phobia	(Hirai, Vernon, Clum, & Skidmore, 2011)	US
Obsessive Compulsive Inventory (OCI)	Obsessive-compulsive disorder	(Coles, Cook, & Blake, 2007)	US
Obsessive Beliefs Questionnaire-44 (OBQ-44)	Obsessive-compulsive disorder	(Coles et al., 2007)	US
PTSD Symptom Scale (PSS)	Post-traumatic stress disorder	(Elhai et al., 2012)	US
Traumatic Stress Schedule (TSS)	Post-traumatic stress disorder	(Fortson et al., 2006)	US
PTSD CheckList – Civilian Version (PCL-C)	Post-traumatic stress disorder	(Read, Farrow, Jaanimägi, & Ouimette, 2009)	US

Source: (van Ballegooijen et al., 2016)

THESIS RATIONALE

2. THESIS RATIONALE

Mental disorders and suicide are considered one of the most significant public health problems around the world. Prevention of mental disorders and suicide and the existence of e-health interventions are priorities for the European Union and the World Health Organization. Among adolescent and young people, mental disorders are common and one of the leading causes of disability. Specifically, there is a considerable increase of mental disorders during the transition from adolescence to adulthood. In this period, a large part of young people go to university. Hence, characteristics of the development period and stressors converge in the entrance to the university.

Interest in the mental health among university students has increased in recent years. Previous studies have reported a high prevalence of common mental disorders (i.e., depression and anxiety disorders) as well as the risk for the start and increase of alcohol and drug consumption during the university period. In Spain, similar evidence is limited, and longitudinal data about the mental health of Spanish university students are scarce. There is a need to improve the knowledge about the frequency (prevalence and incidence) of mental disorders among Spanish university students to understand the specific needs of this population group.

Mental disorders among university students are significant not only for the high prevalence, but also because they are associated with substantial impairment on psychosocial functioning and educational achievement. Despite the high prevalence of mental disorders and the associated impairment, previous research indicates that many of those students do not receive treatment. In addition, affected students often do not seek professional treatment. Thus, identifying that a large proportion of mental disorders remain

untreated. These rates have not been assessed in Spain, where there are free-of-charge, but limited, psychological assistance centres.

Producing reliable evidence about mental disorders of Spanish university students is indispensable for the development of specific strategies that improve the mental health of the university community.

Screening mental disorders at university
The high prevalence of mental disorders among university students requires the need to validate screening instruments that allow their identification. Web-based screening instruments could be potential tools to be deployed in a broad university population. Even though screening self-reported instruments have been shown to be valuable for providing accurate measurements, some limitations have been found. On one hand, self-reported instruments tend to be shorter and simplified than clinical interviews, leading to diagnoses that may not be as accurate as those achieved with clinical judgement. On the other hand, although web-based screening instruments make possible the quickly detection of mental disorders, capturing the vast majority of true cases, yet little evidence has been provided about their validity. It is worth mentioning there is evidence of the validity of longer versions of the Composite International Diagnostic Interview (CIDI), the Self-Injurious Thoughts and Behaviours Interview (SITBI) and the Columbia Suicide Severity Rating Scale (C-SSRS), however, there is not for the modified versions of these screening scales applied in the UNIVERSAL study. Also, there is evidence of the validity of Alcohol Use Disorders Identification Test (AUDIT) and its abbreviated versions, but a validation study is required from the online version of the AUDIT.

Beyond screening for mental disorders among Spanish university students, there is the need to develop tools that identify students who are at high risk of developing mental disorders in the future for an early identification and early

intervention. Universities have a range of resources, and in recent years some of them have developed programs to screen and link students to mental health services. It is a challenge for universities to determine how to identify high-risk university students who could benefit from preventive interventions and, how to offer these interventions to large numbers of students.

OBJECTIVES AND HYPOTHESES

3

3. OBJECTIVES AND HYPOTHESES

3.1. Objectives

The general aims of this doctoral thesis are to provide evidence about the frequency of mental disorders among Spanish university students, as well as to identify the association between both mental disorders and role impairment and mental disorders and the use of mental health treatment. In addition, this thesis intents to examine a broad range of potential risk and protective factors for the onset and persistence of common mental disorders.

Specific objectives among first-year Spanish university students:

1. To assess the diagnostic accuracy of the online screening survey for measuring common mental disorders(major depressive episode, mania/hypomania, generalised anxiety disorder, panic disorder and alcohol use disorder) and suicidal thoughts and behaviours

2. To estimate the frequencies (prevalence, incidence and persistence) of common mental disorders

3. To assess the association of common mental disorders with role impairment and mental health treatment

4. To identify risk and protective factors associated with the onset and persistence of depression and/or generalised anxiety disorder

3.2. Hypotheses

1. The instruments administered in the UNIVERSAL study for screening mental disorders and suicidal thoughts and behaviours have good concordance with the Mini-International Neuropsychiatric interview.

2. Mental disorders are common among Spanish university students, with similar frequency than in other countries and higher than the results found in the Spanish general population.

3. Mental disorders among first-year university students are associated with substantial role impairment.

4. Rates of use of mental health treatments among university students are low, similar to the ones of the general population.

5. A broad range of well-documented risk and protective factors (i.e., childhood adversities, recent stressful events, positive relationships, prior symptomatology, other mental disorders, and psychological factors) are related with the onset and persistence of depression and/or generalised anxiety disorder.

METHODOLOGY

4. METHODOLOGY

The results of this thesis are based on the analysis of the data from the UNIVERSAL project and the clinical reappraisal sub-study on the UNIVERSAL project. The specific methodology used in this doctoral thesis is described in detail in the different articles that constitute this thesis. The most relevant aspects of the methodology are summarised below.

4.1. Design

The UNIVERSAL project is a multicentre, observational and prospective study among first-year university students from five Spanish universities. Participants were evaluated at baseline and followed up at 12, 24 and 36 months. The study began in January 2014 and ended in December 2018.

4.2. Sample

Sample was recruited from five Spanish public universities from different regions: Cadiz University (UCA), Balearic Islands University (UIB), Basque Country University (UPV-EHU), Pompeu Fabra University (UPF) and Miguel Hernández University (UMH). The universities were selected for convenience and represented 8% of the total number of students enrolled in Spanish public universities. Inclusion criteria were: (a) students aged 18 to 24; and (b) being enrolled in the first year of university for the first time. Based on these criteria, 16,332 students were eligible to participate. To participate in the study, students had to fill out an application form on the UNIVERSAL study website and had accepted the informed consent.

Sample recruitment was performed in two phases. First, university authorities sent up to four personal email letters to the eligible students to invite them to participate in the study. Additionally, campus advertising campaigns were carried out (e.g., information stands, university website, classroom presentations). Second, a random subsample of non-respondents of the survey was contacted by email including an economic incentive of 25 € to complete the survey (endgame strategy). At UPV-EHU University, only the first phase was carried out.

Baseline survey was carried out during the first academic year (between October 2014 and October 2015). After the first 12 months, participants were invited to participate in the follow-up survey.

4.3. Survey

Participants underwent an online survey via a secure web-based platform designed for the study. The survey assessed extended information about mental disorders and suicidal thoughts and behaviours, and a wide range of possible risk and protective factors (i.e., sociodemographic, general health, mental wellbeing, use of services, stressful life events and psychological factors). Baseline survey included 15 sections, with a total of 336 items. The follow-up survey (12 months), included 14 sections, with a total of 354 items. In both surveys, to shorten the length of the online survey, logical skips were included in the symptomatology section according to the response of the university students. The mean time to complete the survey was 39 minutes (SD = 8 min; Pc25 = 33 min - Pc75 = 45 min).

The online survey included self-reported screening measures for lifetime and 12-month prevalence of seven common disorders: mood disorders (i.e., major

depressive episode and mania/hypomania), anxiety disorders (i.e., generalised anxiety disorder and panic disorder), substance use disorders (i.e., alcohol abuse or dependence and drug abuse or dependence) and adult attention-deficit/hyperactivity disorder.

Items for assessing mood disorders, anxiety disorders and drug abuse or dependence were based on the WHO Composite International Diagnostic Interview (CIDI) and the Composite International Diagnostic Interview Screening Scales (CIDI-SC) (Kessler, Calabrese, et al., 2013; Kessler & Üstün, 2004). Alcohol abuse or dependence was screened using the Alcohol Use Disorders Identification Test (AUDIT) (Saunders, Aasland, Babor, De la fuente, & Grant, 1993) and adult ADHD was assessed using the Adult ADHD Self-Report Scales (ASRS) (Kessler et al., 2005). The online survey also included assessment of suicidal thoughts and behaviours based on the Columbia-Suicidal Severity Rating Scale (C-SSRS) (Posner et al., 2011) and the Self-Injurious Thoughts and Behaviours Interview (SITBI) (Nock, Holmberg, Photos, & Michel, 2007). The diagnostic algorithms from the ARMY STARRS study (Kessler, Santiago, et al., 2013) were adapted for their use in the WMH-ICS survey. **Table 3** shows the summary of the adapted instruments included in the WMH-ICS survey.

Table 3

Summary of the adapted instruments for the screening of mental disorders and suicidal thoughts and behaviours in the UNIVERSAL online survey.

Variable	Instrument	Author
Major depressive episode; Mania/hypomania;	CIDI 3.0	(Kessler & Üstün, 2004)
Generalised anxiety disorder; Panic disorder; Drug use disorder	CIDI-SC	(Kessler, Calabrese, et al., 2013)
Alcohol use disorder	AUDIT	(Saunders et al., 1993)
Suicidal thoughts and behaviours	SITBI	(Nock et al., 2007)
	C-SSRS	(Posner et al., 2011)

AUDIT: Alcohol Use Disorders Identification Test; CIDI: WHO Composite International Diagnostic Interview; CIDI-SC: Composite International Diagnostic Interview Screening Scales; C-SSRS: Columbia-Suicidal Severity Rating Scale; SITBI: Self-Injurious Thoughts and Behaviours Interview.

4.4. Analyses

To achieve the aims of the first and second article of this thesis, diagnostic algorithms of mental disorders and suicidal thoughts and behaviours were validated through the clinical reappraisal study, explained below (section 4.6. Clinical reappraisal study). In addition, sensitivity analyses were performed by modifying the cut-off points of the diagnostic algorithms to evaluate possible improvements in diagnostic accuracy.

To achieve the aims of the third and fourth article, frequencies of mental disorders were estimated. Regression logistic models were carried out to examine the associations between mental disorders and severe role impairment and mental health treatment. Finally, risk prediction models were developed and cross-validated with a wide range of potential risk factors for mental disorders.

Detailed information about the variables assessed and the analysis conducted is presented in the results section (articles 3 and 4).

4.5. Ethical statement

The data collection platform designed for the study followed international recommendation guidelines for web-based assessment (International Test Commission -ITC-, 2005) (International Test Commission, 2019). At the end of the online survey, all respondents received information on how to access local health services. Individuals with positive responses on suicide items received a specific alert with indications to consult a health professional. Ethical approval was provided by the Parc de Salut Mar-Clinical Research Ethics Committee (Reference: 2013/5252/I).

4.6. Clinical reappraisal sub-study

A clinical reappraisal study was carried out with a subsample of university students participating in the UNIVERSAL project. A subsample of students who responded to the online survey were invited to participate in a telephone clinical interview. Eligibility was determined based on whether they: (a) provided a contact phone number; (b) gave full informed consent to participate in the reappraisal study; and (c) completed the diagnostic sections of the online survey. Eligible students were invited by phone and asked for their consent to participate within 4 weeks of completing the online survey.

Interviews were conducted via telephone by seven clinical psychologists who were blind to the online survey responses. The interviewers did not receive any personal information, apart from the phone number.

Adapted versions of the Spanish structured interview Mini-International Neuropsychiatric Interview-MINI 5.0.0 (Bobes, 1998) and 6.0 (Sheehan, Janavs, Harnett Sheehan, Sheehan, & Gray, 2010) were administered for mental disorders diagnostics and suicidal thoughts and behaviours according to the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV] (American Psychiatric Association, 1994) criteria and referred to the previous 12-months. 7-day Timeline Followback-TLFB (Sobell, 2003) was administered for alcohol consumption and referred to the previous 7 days.

In summary, **Figure 2** shows the samples included in the analyses and study design of the articles that compose the current doctoral thesis, according to the temporality in the data collection of the UNIVERSAL study.

Figure 2

Summary of the study design and the samples included in the articles, according to the temporality in the data collection of the UNIVERSAL study

PUBLICATIONS

5
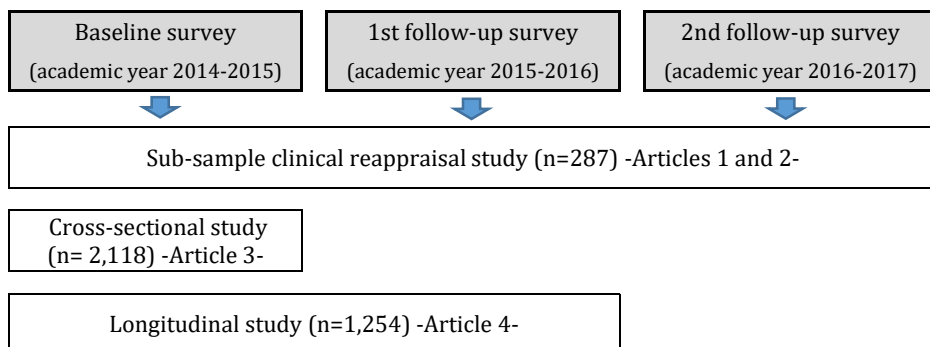
5. PUBLICATIONS

5.1. Article 1. Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students. Results of the WHO World Mental Health- International College Student initiative.

Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià AI, Echeburúa E, et al. (2019) Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students. Results of the WHO World Mental Health- International College Student initiative. *PLoS ONE* 14(9): e0221529.

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Supplementary material for this article can be found in ANNEX 1 (page 296)

PLOS ONE

Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students. Results of the WHO World Mental Health-International College Student initiative

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¶Membership of the UNIVERSAL study group is provided in the Acknowledgments.
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Abstract

Objective

To assess the accuracy of WMH-ICS online screening scales for evaluating four common mental disorders (Major Depressive Episode[MDE], Mania/Hypomania[M/H], Panic Disorder[PD], Generalized Anxiety Disorder[GAD]) and suicidal thoughts and behaviors[STB] used in the UNIVERSAL project.

Methods

Clinical diagnostic reappraisal was carried out on a subsample of the UNIVERSAL project, a longitudinal online survey of first year Spanish students (18–24 years old), part of the WHO World Mental Health-International College Student (WMH-ICS) initiative. Lifetime and 12-month prevalence of MDE, M/H, PD, GAD and STB were assessed with the Composite International Diagnostic Interview-Screening Scales [CIDI-SC], the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

Trained clinical psychologists, blinded to responses in the initial survey, administered via telephone the Mini-International Neuropsychiatric Interview [MINI]. Measures of diagnostic accuracy and McNemar χ^2 test were calculated. Sensitivity analyses were conducted to maximize diagnostic capacity.

Results

A total of 287 students were included in the clinical reappraisal study. For 12-month and life-time mood disorders, sensitivity/specificity were 67%/88.6% and 65%/73.3%, respectively. For 12-month and lifetime anxiety disorders, these were 76.8%/86.5% and 59.6%/71.1%, and for 12-month and lifetime STB, 75.9%/94.8% and 87.2%/86.3%. For 12-month and lifetime mood disorders, anxiety disorders and STB, positive predictive values were in the range of 18.1–55.1% and negative predictive values 90.2–99.0%; likelihood ratios positive were in the range of 2.1–14.6 and likelihood ratios negative 0.1–0.6. All outcomes showed adequate areas under the curve [AUCs] (AUC>0.7), except M/H and PD (AUC = 0.6). Post hoc analyses to select optimal diagnostic thresholds led to improved concordance for all diagnoses (AUCs>0.8).

Conclusion

The WMS-ICS survey showed reasonable concordance with the MINI telephone interviews performed by mental health professionals, when utilizing optimized cut-off scores. The current study provides initial evidence that the WMS-ICS survey might be useful for screening purposes.

Introduction

According to the World Health Organization, based on a systematic review and meta-analysis carried out (n = 829,673 from 63 countries; age-range = 16–65 years old), the population 12-month prevalence of mental disorders is 17.6% [1]. At the same time, estimates based on data from 28 countries throughout the world (n = 85,052; age = 18 years old or more), indicate a 12-month prevalence of 9.8–19.1% (interquartile range, 25th–75th percentiles across countries) in the general adult population[2]. Many mental disorders (phobias and impulse-control disorders) have an early age of onset (before 15 years old) and others (mood, anxiety and alcohol) have a peak period during college years [3,4]. Mental disorders with early manifestation might become chronic if not effectively treated [5–7].

Thus, research in the young population is clearly needed to develop better epidemiological approaches to diminish the burden of mental disorders[8]. University students make up a significant fraction of the population younger than 25 in developed countries [9]. Epidemiological studies suggest that mental disorders and suicidal thoughts and behaviors are common among university students, and that less than 25% of individuals with a mental disorder sought treatment in the year prior to the survey[10–12].

Screening instruments for the assessment of mental disorders are valuable for providing accurate measurements [13,14] as well as the accessibility to brief and simple tools that can facilitate the investigation of mental disorders[15]. Some studies have demonstrated that self-administered instruments show good psychometric properties in younger and middle-aged adults, such as the General Health Questionnaire (GHQ) vs. interviewer-administered version

of the Clinical Interview Schedule-Revised (CIS) (Sensitivity = 72.2, Specificity = 78.0, Positive Predictive Value = 40.0, Negative Predictive Value = 93.4)[16]. Another study that evaluated psychometric properties of a questionnaire for screening people with anxiety/depression self-administered vs. interviewer-administered, self-administered version showed high sensitivities (87.0–92.0) and PPVs (86.0–87.0), but lower specificities (29.0–45.0) and NPVs (38.0–50.0) [17]. Also, self-administered and interviewer-administered versions of the Composite International Diagnostic Interview (CIDI) showed good kappa agreement[18].

Self-administered computerized assessments have great potential for screening mental disorders in different settings [19]. Self-administered computerized assessments of mental disorders have been developed with similar ascertainment of morbidity as when identical questionnaires are administered by an interviewer [19]. Self-administered instruments permit participants to respond more truthfully than in interviewer-administered assessments without social desirability bias [20]. Another significant advantage of self-administered instruments is their brevity and ease of administration, which facilitates assessing mental disorders in epidemiologic studies [21–24].

The UNIVERSAL project, a part of the World Mental Health International College Surveys (WMH-ICS) initiative [25], is a multi-center, cohort study to assess the prevalence and incidence of mental disorders and suicidal thoughts and behaviors, as well as to identify the main risk factors and associated protectors among Spanish university students[26]. The online survey of UNIVERSAL and WMH-ICS include screening scales for the assessment of mental disorders derived from the WHO Composite International Diagnostic Interview (CIDI)[27] and the Composite International Diagnostic Interview Screening Scales (CIDI-SC) [28]. In addition, suicidal thought and behavior items are assessed using items derived from the Self-Injurious Thoughts and Behaviors Interview (SITBI) [29]and the Columbia-Suicidal Severity Rating Scale (C-SSRS)[30]. The concordance of CIDI screening scales (CIDI-SC) with the Structured Clinical Interview from DSM-IV (SCID) was exhaustively evaluated showing good individual-level concordance between the two instruments among active duty Army personnel [13]. But diagnostic accuracy remains untested in samples of college students [25].

The objective of this study is to assess the diagnostic capacity of the WMH-ICS online survey screeners for four common mental disorders (Major Depression Episode [MDE], Mania/Hypomania [M/H], Panic Disorder [PD], and Generalized Anxiety Disorder [GAD]) and for Suicidal Thoughts and Behaviors [STB] among university students.

Methods

The UNIVERSAL study

The UNIVERSAL project is part of the World Mental Health International College Student (WMH-ICS) initiative for the study of mental disorders among first-year college students (https://www.hcp.med.harvard.edu/wmh/college_student_survey.php). More detailed description of the WMH-ICS initiative can be found elsewhere[25,31,32]. UNIVERSAL is a multi-center, observational cohort study of all students starting their 1st course in 5 Spanish universities from 5 Spanish autonomous regions (Andalusia, Balearic Islands, Basque Country, Catalonia and Valencia). A total of 2,343 incoming first year students, during the 2014/15 academic year, were recruited for the study and answered the online baseline survey. Inclusion criteria for eligible students at baseline were: (i) age range from 18 to 24 years old; and (ii) first time enrolment at a university degree. The students participating in the study were re-contacted every year, from 2015/16 to 2017/18 courses, for follow-up online assessments.

Students were invited to complete the study registration form through the UNIVERSAL website (https://www.upf.edu/web/estudiouniversal; https://encuesta.estudio-universal.net)

and after agreeing with the informed consent, they were asked to provide personal contact information so they could be re-contacted to complete the survey. The data collection platform follows the international recommendations and guidelines for computerized assessment (International Test Commission -ITC-, 2005)[33]. Further information on the UNIVERSAL project has been published elsewhere[32].

Clinical reappraisal sample

A clinical reappraisal study of a subsample of university students participating in the UNIVERSAL project was carried out. After responding to the online survey, a sub-sample of eligible students was invited to participate in a telephone clinical interview using the Mini International Neuropsychiatric Interview (MINI)[14]. Eligibility for the clinical reappraisal sub-study was determined by whether individuals: (i) provided a contact telephone number available; (ii) completed informed consent to participate in the reappraisal study; and (iii) completed the diagnostic sections of the online screeners (i.e., for the baseline sub-sample the lifetime and 12-month prevalence was evaluated and for the sub-sample recruited from the 1st and 2nd follow-up the 12-month prevalence was assessed).

Eligible students were selected for the clinical reappraisal sub-study at different time periods of the baseline and follow-up assessments. Consecutive sampling of cases was applied for students reappraised at baseline (starting in May 2015, academic course 2014/2015) and 1st year follow-up assessment (academic course 2015/16, starting in March). For the second year of follow-up (academic course 2016/17, starting selection in November 2016) the method of recruitment of the subjects interviewed was modified to assure sufficient number of individuals with a disorder. To preserve the possibility of restoring the original distribution of the online survey sample, a probabilistic selection was carried out, with over-sampling of students who screened positive in the corresponding online screeners. Specifically, we selected 100% of those who screened positive in any of the following GAD, PD, M/H, suicide plan, and suicide attempt; 20% of individuals with MDE or suicidal ideation (but none of the above); and, 10% of the rest of the sample were selected. S9 Table shows prevalence estimates in each reappraisal sample, selected in each follow-up to carry out the reassessment.

Eligible students were systematically invited by telephone and asked for consent to participate in the re-appraisal interview within 4 weeks of completing the online survey whether it was at baseline, 1st year follow-up assessment or 2nd year of follow-up. They were blind to the results of the online survey responses. At least 5 phone call attempts were made on different days of the week and hours of the day. If a participant could not be contacted, he/she was considered missing for the clinical reappraisal.

Online screening measures

The online survey used in this project gathers self-reported data about mental health and a wide range of possible risk and protective (i.e., sociodemographic, general health, mental well-being, mental disorders, STB, use of services, stressful life events). Overall, the survey was composed of 291 items, but includes logical skips in the symptomatology section according to the students' response to shorten the length of the survey. The mean time for completion of the survey was 39 min (SD = 8 min; Pc25 = 33 min—Pc75 = 45 min).

The online survey included short self-report screening scales for lifetime and 12-month prevalence of four common disorders (MDE, M/H, GAD, and PD). This subset of four disorders of the WMH-ICS surveys is associated with the highest levels of role impairment among college students in the WMH surveys[25]. The items were based on the Composite International Diagnostic Interview Screening Scales (CIDI-SC)[13,27,28], an integrated series of

multi-lingual diagnostic screening scales chosen for their good psychometric properties[13] and concordance with clinical diagnoses[25]. The online survey also included assessment of STB based on the Columbia-Suicidal Severity Rating Scale (C-SSRS)[30] and the Self-Injurious Thoughts and Behaviors Interview (SITBI)[29] instrument that has been translated to Spanish as the "*Escala de Pensamientos y ConductasAutolesivas*" (EPCA) [34], showing good clinical diagnosis concordance in Spanish adult psychiatric patients (mean age = 43.3 years) [34].

Screening scales diagnostic algorithms from the ARMY STARRS survey were adapted for their use in the WMH-ICS self-administered questionnaire [12]. More information about characteristics of the survey was published by Blasco et al. (2016) [32].

Clinical reappraisal interview

The Spanish MINI 5.0.0 [35] and 6.0[36] for mental disorders and suicidal thoughts and behaviors were administered in the re-appraisal interview. The MINI is a structured interview that assesses DSM-IV-TR axis I mental disorders[37], and one of its major advantages is the short administration time [mean (SE) 18.7(11.6) minutes] [38]. For most mental disorders, the MINI shows values higher than 0.70 for sensitivity (SN) and 0.85 for specificity (SP) in relation to the Structured Clinical Interview for DSM-III-R Patients (SCID-P) [38]. In relation to psychiatrist's diagnostic judgement, the Spanish MINI shows values higher than 0.90 for SN and 0.60 for SP for most mental disorders[35].

For consistency with the online survey recall periods, we added a 12-months assessment period together with lifetime assessment in corresponding sections of the MINI structured interview for all disorders evaluated. Since telephone vs. in-person modes seem not to influence findings [39–42], interviews were performed via telephone. Interviewers were blind to the online survey responses, and no personal information (other than telephone) was provided to them.

Re-appraisal interviews were performed by seven clinical psychologists with a range of 1 to 15 years of clinical experience. Two senior clinical psychologists developed the protocol to perform the MINI telephone interview in a standardized way. Also, a registry was created to introduce dates of five phone call attempts with students and the reason of refused/fail contact. The experts supervised *in situ* the first five to ten interviews carried out by the each interviewer to ensure standardized procedures were satisfactorily followed.

Analysis

As noted earlier, diagnostic algorithms used in the present study are taken from the ARMY STARRS survey. We compared lifetime and 12-month prevalence estimates among the overall sample and the reappraised sub-sample according to the online screening index tests using chi-squared test. The McNemar χ^2 test was also calculated for evaluating the prevalence differences between index test diagnosis and reference standard.

Agreement was assessed by comparing each online screening index test diagnosis with the reference standard (MINI). Estimates of disaggregated measures were performed: Sensitivity SN (% of reference standard cases detected by the index test), Specificity SP (% of reference standard non-cases correctly classified as non-cases by the index test), Positive Predictive Value PPV (% of index test cases confirmed by the reference standard), Negative Predictive Value NPV (% of index test non-cases confirmed as non-cases by the reference standard) and likelihood ratio positive LR+ (proportion of reference standard cases testing positive according to the index test divided by the proportion of non-cases testing positive in the index test) and likelihood ratio negative LR- (proportion of reference standard cases testing negative divided by the proportion of non-cases testing negative in the index test). Likelihood ratio is a constant value and can be used to arrive at a posttest probability, which facilitates appraising how a

particular test result predicts the risk of disease [43,44]. Receiver Operating Characteristics (ROC) analyses were performed for diagnostic capacity of the instruments, including area under the curve (AUC), considering the MINI diagnoses as the reference standard. Labels of agreement were assigned to the different ranges of AUC according to Landis and Koch as slight (0.50–0.59), fair (0.6–0.69), moderate (0.7–0.79), substantial (0.8–0.89) and almost perfect ($\geq$0.9) [13,45]. The AUC can be used between a dichotomous predictor and a dichotomous outcome, where AUC equals (SN+SP)/2[40].

Inverse probability weighting was applied to adjust for the sampling method applied in the reappraisal selection carried out during the 3rd year follow up (2016/17). Weights were obtained as the inverse of the probability of selection within each stratum in 3rd year follow up and normalized to the total sample size of the clinical reappraisal study. Post-stratification weights were calculated and applied in order to correct for imbalances of gender, academic field and nationality characteristics between the clinical reappraisal sample and their respective UNIVERSAL sample, as their reference population. Analysis were performed using SAS v9.4 [46] and SPSS v23.0 [47].

Sensitivity analyses to improve diagnostic accuracy

Sensitivity analyses were performed for specific disorders of MDE, M/H, PD and GAD to evaluate potential improvements of diagnostic capacity by modifying cut-off points of diagnostic algorithms. We present results to improve diagnostic accuracy according to two different criteria, given that the most useful cut-off points in screening scales may differ depending on the objectives and purpose of the study[13]. For instance, an epidemiological study could prioritize the accurate estimation of the gold standard prevalence, while in a clinical study the cut-off point could be lowered with the aim of optimizing sensitivity.

First we estimated a cut-off point with high SN ($>$0.80) and acceptable SP ($>$0.70), or failing this, the best Youden's Index score which balances SN and SP result[48]. Subsequently, we estimated a cut-off point to optimize concordance on prevalence estimate between online survey test and MINI interview[49]. For a binary response, this is assessed with McNemar's test, a modification of the ordinary chi-square test that takes the paired nature of the responses into account. A statistically significant result (p$<$0.05) shows that there is evidence of a systematic difference between the proportion of cases from the two tests. If one test is the gold-standard, the absence of a systematic difference implies that there is no bias on prevalence estimate[49]. Inherently, we created a dichotomization of screening scales to differentiate predicted cases from non-cases. As a result, we presented these analyses for 12-month and lifetime diagnoses.

Results

Participants

Between May 2015 and July 2017, 575students were assessed for initial eligibility and invited to participate in the clinical reappraisal. In total, 287 (49.9%) completed the reappraisal study (the other288 could not be contacted or refused the phone interview). Fig 1 shows the flow of included participants through the study.

Table 1 compares the overall UNIVERSAL sample and the clinical reappraisal subsample. The majority of the latter were female (n = 216), with ages 18 and 19 (n = 231), Spanish (n = 258) and came from Social (n = 108) and Health Sciences (n = 85) study fields. After weighting, the distribution of the reappraisal subsample was very similar to the overall UNIVERSAL sample, except for age. In the reappraisal sub-sample at baseline survey, mood disorders and anxiety disorders were more frequent than in the overall sample,
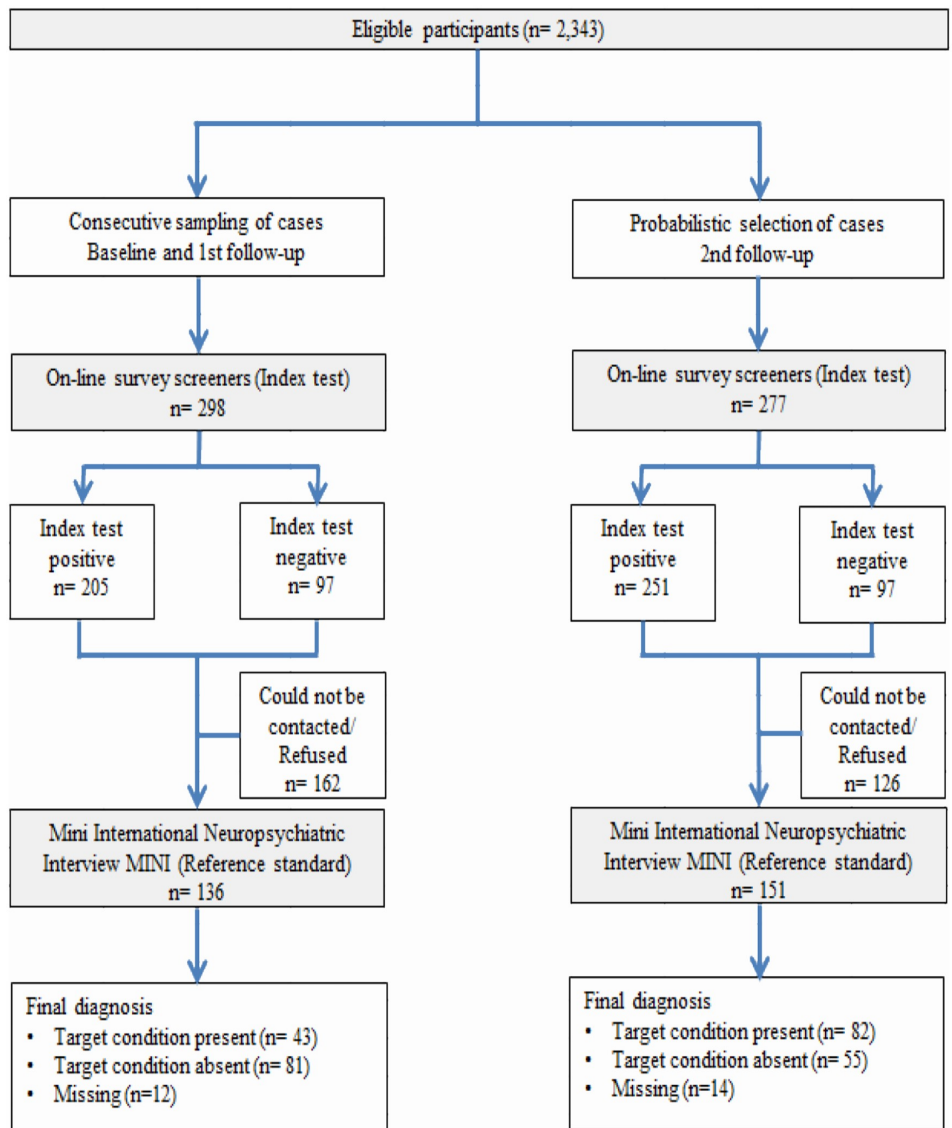
Fig 1. Modified version of STARD 2015 flow diagram of participants through clinical reappraisal study.

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both in the last 12-months and lifetime.12-month STB was 7.2% in the clinical reappraisal sub-sample and 9.2% in the overall sample, while STB lifetime in the reappraisal sub-sample was more frequent (21.8%) than in the overall sample (24.0%). There was significant difference in prevalence in the initial sample and the clinical reappraisal sample on anxiety disorders lifetime (p = 0.004) in spite of the use of post-stratification weights were used (Table 1).

Table 1. Characteristics of the *UNIVERSAL* baseline online survey on the overall sample and clinical reappraisal sub-sample (unweighted observations and weighted percentages).

		Overall sample n = 2,343		Clinical reappraisal sub-sample n = 287		
		n	**%**	**n**	**%**	***p-value***
Sex	Female	1,691	55.4	216	55.3	*0.97*
Age	18	1644	61.0	177	70.0	*0.007**
	19	358	20.2	54	14.5	
	20+	341	18.7	56	15.5	
Nationality	Non-Spanish	128	2.9	29	2.9	*1.00*
Field of studies	Arts & Humanities	267	9.8	37	9.8	*1.00*
	Health Sciences	595	15.7	85	15.7	
	Social Sciences	947	47.6	108	47.6	
	Science	216	8.4	25	8.4	
	Engineering & Architecture	318	18.6	32	18.6	
Any mood[a]	12m	536	19.6	79	20.7	*0.64*
	Lifetime	644	23.8	100	25.9	*0.40*
Any anxiety[b]	12m	463	16.3	85	18.9	*0.23*
	Lifetime	547	20.1	104	26.9	*0.004**
Suicidal thoughts and behaviors[c]	12m	238	9.2	37	7.2	*0.24*
	Lifetime	538	21.8	98	24.0	*0.37*

[a].- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[b].- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[c].- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (Blasco MJ et al, *Suic. Suicide Life Threat Behav*. 2019) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with questions from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

*P-value statistically significant 0.05.

Prevalence estimates of the MINI based on the WMH-ICS online survey screeners

Weighted prevalence estimates according to the online survey screeners and MINI showed statistically significant differences for most of the disorders (p<0.05), except for 12-months and lifetime M/H and PD (Table 2). The online screening scales showed a higher prevalence than the MINI estimates for mood disorders 12-month (15.4% vs. 7.3%) and lifetime (34.3% vs. 18.6%). However, prevalence disagreements varied across individual mood disorders, with statistical significant differences in 12-month and lifetime MDE (5.8% vs 13.7%; 16.5% vs. 32.9%, respectively); and not statistically significant differences on M/H prevalence. Disagreement in prevalence estimates were also found for 12-month and lifetime anxiety disorders (16.3 vs. 3.7%; 32.4% vs. 10.6%, respectively) but disagreements varied across individual disorders:12-month and lifetime GAD prevalence was higher for online survey screeners than for the MINI while the opposite was found for PD, although differences were not statistically significant. Prevalence estimates of WMH-ICS online survey screeners were higher than the MINI for 12-month and lifetime STB (8.5% vs. 5.0%; 25.7% vs.16.2%, respectively)(Table 2).

Operating Characteristics of WMH-ICS online survey screeners

In Table 3, the online screeners showed a SN in detecting mood disorders of 67.0% at 12-month and 65.0% lifetime. In the case of anxiety, corresponding values were 76.8%, and

Table 2. Prevalence estimates of common mental disorders and suicidal thoughts and behaviors in the clinical reappraisal sample, according to the WMH-ICS online survey screeners and the MINI (n = 287) (unweighted observations and weighted percentages).

		Clinical Reappraisal sample						McNemar	
		Online survey screeners^			MINI				
		n	%	CI 95%	n	%	CI 95%	χ^2	p-value
Mental disorders									
Any mood[a]	12-m	67	15.4	11.2–19.5	32	7.3	4.3–10.3	14.6	0.0001*
	Lifetime	136	34.3	28.8–39.8	66	18.6	14.1–23.1	22.7	<.0001*
Major depressive episode	12-m	60	13.7	9.8–17.7	26	5.8	3.1–8.5	15.9	<.0001*
	Lifetime	129	32.9	27.5–38.4	58	16.5	12.2–20.8	24.9	<.0001*
Mania/Hypomania	12-m	14	2.9	1.0–4.8	7	1.8	0.2–3.3	1.03	0.310
	Lifetime	25	4.9	2.4–7.4	13	3.0	1.1–5.0	1.52	0.218
Any anxiety[b]	12-m	70	16.3	12.0–20.6	19	3.7	1.5–5.9	29.8	<.0001*
	Lifetime	129	32.4	27.0–37.8	32	10.6	7.0–14.1	44.3	<.0001*
Panic disorder	12-m	5	1.3	0.0–2.6	17	3.3	1.2–5.4	3.35	0.067
	Lifetime	20	6.0	3.2–8.7	28	9.3	6.0–12.7	2.34	0.126
Generalized anxiety disorder	12-m	67	15.4	11.3–19.6	7	1.4	0.0–2.7	38.3	<.0001*
	Lifetime	123	30.7	25.4–36.1	11	2.5	0.7–4.4	78.2	<.0001*
Suicidal thoughts and behaviors									
Suicidal thoughts and behaviors[c]	12-m	35	8.5	5.3–11.8	25	5.0	2.5–7.5	6.29	0.012*
	Lifetime	104	25.7	20.7–30.8	71	16.2	11.9–20.5	17.9	<.0001*

[a].- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[b].- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[c].- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (Blasco MJ et al, *Suic. Suicide Life Threat Behav*. 2019) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with questions from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

^Prevalence estimates according to the reappraisal temporary moment (see the Methods section)

*P-value statistically significant 0.05. CI95%: Confidence interval according 0.05 error.

59.6%. For specific mental disorders, SN for 12-month and lifetime MDE was 70.8% and 61.8%, respectively; for both 12-month and lifetime GAD, SN was 100.0%. SN for PD was lower than 20%, and for M/H, it was lower than 33.6%. Proportions of correctly detected of12-month and lifetime STB cases were 75.9%, and 87.2%, respectively. Proportions of online screener cases confirmed by the MINI (PPV) ranged from 8.4% to 55.1%.

The proportion of non-cases correctly classified (SP) ranged from 71.1% to 99.3% for all 12-month and lifetime disorders and the proportions of online screeners non-cases confirmed by the MINI (NPV) were 90.2%-100.0%. The highest relative proportions of screened positives versus screened negatives confirmed as cases by the MINI reappraisal (LR+) generated moderate changes in posttest probability for 12-month STB (14.6), 12-month PD (27.1), and 12-month M/H (14.6). On the other hand, LR- values were good for lifetime STB, whilst for all other LR- values, this ranged from 0.3 to 0.9(Table 3).

With the Area Under the ROC curve (AUC) we aimed to obtain a single numerical value for the overall diagnostic accuracy of the screen measures. Individual-level concordance was fair to substantial for all disorders, obtaining AUCs ranging from 0.7 to 0.9, except slightly lower for lifetime M/H and for 12-month and lifetime PD (just below 0.6) (Table 3).

Improving diagnostic capacity through cut-off point changes

In order to improve diagnostic capacity for MDE, M/H, PD and GAD, we carried out a sensitivity analysis according to two different criteria to select optimal cut-off points for each

Table 3. WMH-ICS online survey screeners operating characteristics for estimating reference standard (MINI) prevalence (n = 287) (weighted values).

| | | Cut-point | Positive operating characteristics | | | | | Negative operating characteristics | | | | | AUC |
			SN	SE(SN)	PPV	SE(PPV)	LR+	SP	SE(SP)	NPV	SE(NPV)	LR-	
Mental disorders													
Any mood[a]	12-m	—	67.0	10.3	31.6	7.0	5.9	88.6	2.0	97.1	1.1	0.4	0.78
	Lifetime	—	65.0	6.7	35.6	5.0	2.4	73.3	3.0	90.2	2.2	0.5	0.69
Major depressive episode	12-m	15	70.8	11.0	29.6	7.3	6.8	89.6	1.9	98.0	0.9	0.3	0.80
	Lifetime	15	61.8	7.2	31.3	4.9	2.3	73.3	2.9	90.7	2.1	0.5	0.68
Mania/Hypomania	12-m	4	33.6	21.1	20.6	13.5	14.6	97.7	0.9	98.8	0.7	0.7	0.66
	Lifetime	4	20.9	13.5	12.9	8.9	4.6	95.5	1.2	97.5	1.0	0.8	0.58
Any anxiety[b]	12-m	—	76.8	13.4	18.1	5.7	5.7	86.5	2.1	99.0	0.7	0.3	0.82
	Lifetime	—	59.6	9.1	19.1	4.1	2.1	71.1	2.9	93.9	1.7	0.6	0.65
Panic disorder	12-m	2	19.0	12.4	47.5	25.0	27.1	99.3	0.5	97.3	1.0	0.8	0.59
	Lifetime	2	18.3	7.6	27.8	10.9	3.8	95.2	1.3	92.1	1.7	0.9	0.57
Generalized anxiety disorder	12-m	21	100.0	0.0	9.1	4.4	7.2	86.2	2.1	100.0	0.0	NA	0.93
	Lifetime	21	100.0	0.0	8.4	3.0	3.5	71.4	2.7	100.0	0.0	NA	0.86
Suicidal thoughts and behaviors													
Suicidal thoughts and behaviors[c]	12-m	—	75.9	11.9	43.3	10.1	14.6	94.8	1.4	98.7	0.7	0.3	0.85
	Lifetime	—	87.2	5.0	55.1	5.9	6.4	86.3	2.3	97.2	1.2	0.1	0.87

[a].- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[b].- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[c].- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (Blasco MJ et al, *Suic. Suicide Life Threat Behav*. 2019) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with questions from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

SN: Sensitivity (% of MINI cases detected by the UNIVERSAL instrument); PPV: Positive Predictive Value (% of UNIVERSAL cases confirmed by the MINI);LR+: likelihood ratio positive (proportion of reference standard cases testing positive according to the index test divided by the proportion of non-cases testing positive in the index test); SP: Specificity (% of MINI non-cases classified as non-cases by the UNIVERSAL instrument); NPV: Negative Predictive Value (% of UNIVERSAL non-cases confirmed as non-cases by the MINI); LR-: likelihood ratio negative (proportion of reference standard cases testing negative divided by the proportion of non-cases testing negative in the index test); SE: Standard Error. AUC: area under the receiver operating characteristic curve.

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diagnostic: a) maximization of SN; or b) optimization of concordance on prevalence. Table 4 shows operating characteristics for estimating lifetime disorder. When SN was prioritized, an increase of the online survey lifetime prevalence estimate was found for all disorders other than GAD, which presented a lower prevalence in comparison to the initial algorithms. This difference was due to the fact that GAD originally had SN = 100% and when a better balance between SN and SP was achieved, its prevalence estimate decreased slightly, obtaining a SN = 97.3% lifetime. PPVs were higher than the original algorithms, ranging from 10.5 to 36.6. SP decreased slightly in comparison to original algorithms ranging from 59.7% to 83.2% for all disorders, but NPV increased ranging from 96.7 to 99.9. LR+ values for all disorders were higher than the original algorithms and LR- values ranged from 0.1 to 0.3. For mood disorders and anxiety disorders, the AUC increased slightly in comparison to the initial algorithm (from fair to substantial). For M/H and PD the increase in AUC was somewhat higher (from slight to moderate or substantial) (Table 4).

Table 4 also shows the implications of making changes in the cut-off points to obtain comparable prevalence estimates. Special cases were M/H and PD, for which no statistical significant differences were found in prevalence estimates using initial algorithms. Both algorithms could be enhanced by changing cut-off points, but their operating characteristics did not get better. Compared to the original algorithms, prevalence estimates were decreased, getting

Table 4. WMH-ICS online survey screeners operating characteristics for estimating reference standard (MINI) lifetime prevalence when diagnostic cut-off points are changed to maximize sensitivity or have an optimal prevalence (n = 287) (weighted values).

	Cut-point	Online survey screeners prevalence estimate^		Positive operating characteristics						Negative operating characteristics						McNemar		AUC
		%	SE(%)	SN	SE(SN)	PPV	SE(PPV)	LR+		SP	SE(SP)	NPV	SE(NPV)	LR-		χ^2	p-value	
Mental disorders																		
Any mood[a]																		
High SN	--	51.0	2.9	94.8	3.1	35.1	4.0	2.4		59.7	3.3	98.1	1.2	0.1		82.62	<.0001*	0.77
Optimal for prevalence	--	23.2	2.5	52.8	7.0	42.7	6.2	3.3		84	2.5	88.7	2.2	0.6		2.38	0.123	0.68
Major depressive episode																		
High SN	14	40.1	2.9	88.9	4.7	36.6	4.6	2.9		69.8	3.0	97.0	1.3	0.2		56.0	<.0001*	0.79
Optimal for prevalence	17	21.6	2.4	48.6	7.5	37.3	6.3	3.0		84.0	2.4	89.3	2.1	0.6		3.09	0.079	0.66
Mania/hypomania																		
High SN	2	24.4	2.5	83.7	13.1	10.5	3.7	3.7		77.6	2.5	99.3	0.6	0.2		57.2	<.0001*	0.81
Optimal for prevalence	4	4.9	1.3	20.9	13.5	12.9	8.9	4.6		95.5	1.2	97.5	1.0	0.8		1.52	0.218	0.58
Any anxiety[b]																		
High SN	--	35.7	2.8	91.9	5.1	26.5	4.4	3.1		70.7	2.9	98.7	0.8	0.1		67.02	<.0001*	0.81
Optimal for prevalence	--	9.9	1.8	29.4	8.6	29.9	8.6	3.7		92.1	1.7	91.9	1.7	0.8		0.01	0.942	0.61
Panic disorder																		
High SN	3	21.7	2.4	71.1	9.1	29.6	5.8	4.2		83.2	2.3	96.7	1.2	0.3		25.7	<.0001*	0.77
Optimal for prevalence	5	7.0	1.5	19.8	7.8	25.6	9.8	3.5		94.3	1.4	92.2	1.6	0.9		0.96	0.328	0.57
Generalized anxiety disorder																		
High SN	24	22.7	2.5	97.3	6.1	11.0	3.9	4.7		79.4	2.4	99.9	0.2	0.0		55.6	<.0001*	0.88
Optimal for prevalence	31	4.0	1.2	52.6	18.9	32.8	13.6	18.8		97.2	1.0	98.7	0.7	0.5		1.67	0.196	0.75
Suicidal thoughts and behaviors																		
Suicidal thoughts and behaviors[c]^^	--	25.7	2.6	87.2	5.0	55.1	5.9	6.4		86.3	2.3	97.2	1.2	0.1		17.9	<.0001*	0.85

[a].- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[b].- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[c].- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (Blasco MJ et al, *Suic. Suicide Life Threat Behav*. 2019) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with questions from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

^Prevalence estimates according to the reappraisal temporary moment (see the Methods section).

^^ Suicidal thoughts and behaviors diagnostic algorithm is created according Spanish suicide definition, without cut-off points.

*P-value statistically significant 0.05.

SN: Sensitivity (% of MINI cases detected by the UNIVERSAL instrument); PPV: Positive Predictive Value (% of UNIVERSAL cases confirmed by the MINI);LR+: likelihood ratio positive (proportion of reference standard cases testing positive according to the index test divided by the proportion of non-cases testing positive in the index test); SP: Specificity (% of MINI non-cases classified as non-cases by the UNIVERSAL instrument); NPV: Negative Predictive Value (% of UNIVERSAL non-cases confirmed as non-cases by the MINI); LR-: likelihood ratio negative (proportion of reference standard cases testing negative divided by the proportion of non-cases testing negative in the index test); SE: Standard Error; AUC: area under the receiver operating characteristic curve.

closer to that of the reference measure, at the expense of a lower SN and AUC for overall mood and anxiety diagnoses. PPVs slightly increase regarding to the original algorithm with a range 12.9–42.7 and NPVs were 88.7–98.7.

Table 5 shows operating characteristics for estimating 12-month prevalence when cut-off points were changed. Results in the same direction than Table 4 were found, improving SN in all disorders when SN was maximized. Even though, when the cut-off point was the optimal

Table 5. WMH-ICS online survey screeners operating characteristics for estimating reference standard (MINI) 12-month prevalence when diagnostic cut-off points are changed to maximize sensitivity or have an optimal prevalence (n = 287) (weighted values).

	Cut-point	Online survey screeners prevalence estimate^		Positive operating characteristics					Negative operating characteristics					McNemar		AUC
		%	SE(%)	SN	SE(SN)	PPV	SE(PPV)	LR+	SP	SE(SP)	NPV	SE(NPV)	LR-	χ^2	p-value	
Mental disorders																
Any mood[a]																
High SN	- -	23.9	2.5	76.1	9.3	22.9	5.1	3.8	79.8	2.5	97.7	1.0	0.3	39.58	<.0001*	0.78
Optimal for prevalence	- -	11.9	1.9	50.5	11.2	30.4	7.9	5.5	90.9	1.8	95.9	1.3	0.5	5.44	0.019*	0.71
Major depressive episode																
High SN	14	16.0	2.2	73.0	11.1	26.2	6.5	5.8	87.4	2.0	98.1	0.9	0.3	22.4	<.0001*	0.80
Optimal for prevalence	17	10.0	1.8	49.8	12.5	28.4	8.4	6.5	92.3	1.6	96.8	1.1	0.5	5.30	0.021*	0.71
Mania/hypomania																
High SN	2	11.2	1.9	33.6	21.1	5.3	4.0	3.1	89.2	1.9	98.7	0.7	0.7	21.7	<.0001*	0.61
Optimal for prevalence	4	2.9	1	33.6	21.1	20.6	13.5	14.6	97.7	0.9	98.8	0.7	0.7	1.03	0.310	0.66
Any anxiety[b]																
High SN	- -	13.8	2.0	78.7	12.9	21.7	6.7	7.2	89	1.9	99.1	0.6	0.2	23.82	<.0001*	0.84
Optimal for prevalence	- -	3.6	1.1	39.2	15.4	40.2	15.5	17	97.7	0.9	97.7	0.9	0.6	0.01	0.941	0.68
Panic disorder																
High SN	3	3.7	1.1	44.8	16.6	39.7	15.5	19.5	97.7	0.9	98.1	0.8	0.6	0.12	0.725	0.71
Optimal for prevalence	5	1.8	0.8	17.8	12.1	32.0	19.0	13.7	98.7	0.7	97.2	1.0	0.8	1.55	0.213	0.58
Generalized anxiety disorder																
High SN	24	11.7	1.9	95.0	10.9	11.3	5.5	9.2	89.7	1.8	99.9	0.2	0.1	28.1	<.0001*	0.92
Optimal for prevalence	31	1.9	0.8	41.0	24.6	29.0	18.5	29.3	98.6	0.7	99.2	0.5	0.6	0.42	0.517	0.70
Suicidal thoughts and behaviors																
Suicidal thoughts and behaviors[c]	- -	8.5	1.6	75.9	11.9	43.3	10.1	14.6	94.8	1.4	98.7	0.7	0.3	6.29	0.012*	0.81

[a].- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[b].- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC];

[c].- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (Blasco MJ et al, *Suic. Suicide Life Threat Behav.* 2019) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with questions from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS].

^Prevalence estimates according to the reappraisal temporary moment (see the Methods section).

^^ Suicidal thoughts and behaviors diagnostic algorithm is created according Spanish suicide definition, without cut-off points.

*P-value statistically significant 0.05.

SN: Sensitivity (% of MINI cases detected by the UNIVERSAL instrument); PPV: Positive Predictive Value (% of UNIVERSAL cases confirmed by the MINI);LR+: likelihood ratio positive (proportion of reference standard cases testing positive according to the index test divided by the proportion of non-cases testing positive in the index test); SP: Specificity (% of MINI non-cases classified as non-cases by the UNIVERSAL instrument); NPV: Negative Predictive Value (% of UNIVERSAL non-cases confirmed as non-cases by the MINI); LR-: likelihood ratio negative (proportion of reference standard cases testing negative divided by the proportion of non-cases testing negative in the index test); SE: Standard Error; AUC: area under the receiver operating characteristic curve.

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for prevalence, statistical significant differences were found in mood disorders, MDE and STB prevalence.

The sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) of different cut-off points for MDE, M/H, PD and GAD for estimating reference standard (MINI) lifetime and 12-month prevalence are shown in S1–S8 Tables.

Discussion

This study evaluated the diagnostic concordance of online screener versions of the CIDI-SC, SITBI and C-SSRS with the MINI among Spanish university students. Overall concordance was reasonably adequate, particularly for 12-month and lifetime STB, showing optimal operating characteristics and substantial to almost perfect AUC. For 12-month Major Depressive Episode and Generalized Anxiety Disorder, online screener showed good SN, SP and NPVs with substantial AUC; however, Mania/Hypomania and Panic Disorder results were suboptimal. Overall diagnoses showed low PPVs both in the pre-specified cut-offs and the modified cut-offs. Thus, our findings regarding diagnostic accuracy should be interpreted with some caution.

Comparison with previous studies

In general, results presented here are comparable to those found in previous research of the CIDI-SC—which have shown a good concordance with clinical diagnoses of mood and anxiety disorders [13,28,50,51]—and those of the SITBI and C-SSRS [30,34]. However, we found that individual-level concordance of mental disorders was somewhat lower than in previous psychometric studies of these scales. For the most part, our study found fair to moderate estimates (AUC = 0.60–0.79), whereas most previous evaluations found moderate to substantial concordance (AUC = 0.70–0.89).

The samples in most previous studies were different than university students, including Army personnel [13], primary care patients[28], and general population respondents [30,50]. Also, these studies validated mental disorder screening instruments that are not in conjunction with a suicidal thoughts and behaviors screening instrument, as it is in our study. Our results emphasize the need to carefully consider the characteristics of the population in which there is a desire to use a screening instrument [52,53]. Furthermore, we used screening scales diagnostic algorithms from the ARMY STARRS survey and we adapted them for use in the WMH-ICS self-administered questionnaire[13]. In fact, differences between our sample and that of the previous study could modify the operating characteristics of the online survey screeners. For this reason, we carried out this study to investigate the extent to which the screening scales' diagnostic algorithms were valid and applicable in a sample of different characteristics to the military sample.

Web-based questionnaires have become an important tool in epidemiologic data collection, especially for recruitment and follow-up of large cohorts[54], even though they have often not been validated specifically for the assessment of mental disorders in university populations. Several programs through which people may be assessed for mental disorders through the Internet have evaluated the validity of a web-based instrument for common mental disorders in the general population or in clinical samples [21–23,54]. The WMH-ICS online screening scales showed similar SN, SP and NPVs values to other web-based screening instruments for mental disorders [21–23] (SN:71.0–1.00; SP:73.0–97.0; NPVs:85.0–1.00), when we adjusted the cut-off points according to SN. However, our study showed low PPVs for both the initial algorithms and after obtaining modified cut-offs. Similar low values were also reported in another study (11.0–51.0)[21], whose authors argue that they might be due to a low prevalence of some of the mental disorders assessed. Other studies that validated self-administered instruments showed similarly modest psychometric properties for SN (range from 72.2–92.0) but found higher PPVs (range from 40.0 to 87.0) than our study. Nonetheless, and in contrast with our results, these studies showed also low values for SP and NPVs (SP: 29.0–78.0; NPVs: 38.0–93.0).

College years period is well-known as a peak period to develop first onset on mental disorders[3,4]. Our results provide evidence of validity of online screener measures among this

population, and they might be instrumental to facilitate the implementation of health programs to diminish the impact of mental disorders in this crucial period [3–7]. Further, there is potential to facilitate web-based interventions, which may be valuable to improve student mental health [55–57]. Indeed, the epidemiological surveys in the university context can be the first step to implement state-of-the-art web-based interventions about health promotion and prevention of mental disorders among university students.

Modification of WMH-ICS online survey screeners' cut-off points

Definitions of screened positives and screened negatives could be enhanced by selecting the cut-off point that optimizes the test performance indicators that are deemed useful at each specific research objective. Different applications, like epidemiological as well as clinical, might use screening instruments for different purposes and depending on them, the cut-off point decision can be changed [13]. The accuracy of a diagnostic index test is not constant but varies across different clinical contexts, disease spectrums and even patient subgroups [58]. In a clinical study, screening instruments might be used to select people for treatment more in-depth or invasive diagnosis assessment, and it can be more relevant to achieve high sensitivity to capture real cases by the screening instruments [13,28,40].

We, therefore, investigated whether increasing the cut-off point could reach at a minimum SN of 80% (or the best balance between SN and SP) with the result that most MINI cases would be correctly identified by the online survey. However, we observed low PPVs and research to further improve diagnostic algorithms of these online screeners for clinical purposes is necessary.

Nonetheless, for epidemiological research, it may be important to obtain unbiased estimates of the prevalence of the disorder to assess distribution of mental disorders in the university population through an online survey[13,59]. This approximation would allow to monitor prevalence trends of mental disorders and to evaluate interventions in the university population. Choosing a lower cut-off point would provide a higher concordance on the prevalence estimates based on McNemar test. Other ways to improve diagnostic capacity implies PPV and NPV. However, the predictive values of a study can not be generalized due to the relationship with the prevalence of the disease[60].

Limitations

Several limitations of the study should be taken into consideration when interpreting our results. First, we used the MINI as the "gold standard" diagnostic instrument which might be considered a sub-optimal standard, in particular since it was administered via telephone by more than one psychologist, and it provides a brief content about diagnoses. We nevertheless implemented the MINI for feasibility and because it has shown to have a SN/SP above the minimum acceptable level (.8/.8) with structured interviews [61]. The MINI interview has been used widely in clinical context as well as in the research context. Several studies showed good psychometric properties what could define it as valid "gold standard" [15,61,62]. However, a risk of bias towards positive results has been reported and conducting the MINI after the CIDI could induce a "learning" bias. Nonetheless, the short duration of the MINI may have helped to prevent participants' negative answers to reduce the interview duration [63]. Also, previous research shows that respondents in community surveys tend to report less as they are interviewed more due to respondent fatigue, as a result lower bound estimates of concordance [64]. Given that, the second interview was blinded for interviewers and respondents. In spite of this would have decreased concordance, our concordance results are almost high. Besides, face-to-face interviews are typically enriched with non-verbal information which may increase

diagnostic validity, while we administered the MINI by phone. Nevertheless, research shows that telephone vs in-person modes seem not to influence findings [39,65,66]. In addition, all interviewers were clinical psychologists with experience in the use of the MINI and they had a learning session to maximize the similarity in data collection. Finally, in our study inter-rater reliability was not assessed and therefore we do not know the reproducibility of our study. This reinforces the need to interpret the results cautiously. Further research should estimate inter-rater reliability and test-retest analyses.

Second, although unlikely, it is possible that an undetected disorder in the online survey appeared in the time before the clinical reappraisal. Also, it is possible that the period for an existing disorder at the time of the online evaluation had expired at the time of the reappraisal. We combatted these risks by allowing a maximum of 4 weeks between online and reappraisal evaluations [67], while in other studies recall periods were shorter from the same session to two weeks[13,50,63]. However, disease progression bias are more likely to have significant effects on studies of tests for acute diseases (i.e., infections) that may change more rapidly [68]. Third, current results are based on a relatively small number of cases for some of the mental disorders considered. This is especially true for M/H and PD, with the lowest prevalence and showed poor accuracy. An important task for future studies will be to estimate their accuracy in larger samples, which, at the same time, would allow for subgroup analyses. Fourth, to assure sufficient number of individuals for each disorder studied, we carried out a probabilistic selection of participants in the reappraisal study. We performed weighted analyses that restored the distribution of disorders in the student population, which assures unbiased estimates. Fifth, students could show different levels of trust and confidence to the clinical reappraisal in comparison to a more confidential evaluation as the online survey. Social desirability bias occurs often when a person answers according to the expectation of the other [69]. The degree this might have contributed to a lower prevalence of disorders in the reappraisal assessment and that to the assessment of validity of the screeners remains to be studied.

Finally, we calculated AUC from ROC curves for each dichotomous screening scale. However, dichotomization often discards potentially useful information that would be retained with the interpretation of scores along the continuum of the disease[70]. Therefore future research should address the accuracy of these online survey screeners as a continuous measure that allows valuable information of different severity levels.

Conclusions

Our findings suggest that while the screening scales used in the UNIVERSAL online survey tend to overestimate true diagnostic prevalence, they are nonetheless valuable in making it possible to screen quickly and efficiently for common mental disorders in a way that captures that large majority of true cases. This is especially true for 12-month prevalence disorders, where the instrument showed better diagnostic capacity. Since the post hoc derivation of a diagnostic threshold can introduce a bias into diagnostic test validity, it is necessary replicate these analyses in other countries which use WMH-ICS initiative. Such replication should explore to what extent predictive values from one study should transferred to another setting with a different prevalence of the disease in the population [28].

Supporting information

S1 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Major Depressive Episode 12-month algorithm for estimating reference standard (MINI)

(n = 287).
(PDF)

S2 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Major Depressive Episode lifetime algorithm for estimating reference standard (MINI)(n = 287).
(PDF)

S3 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Mania/ Hypomania 12-month algorithm for estimating reference standard (MINI)(weighted values).
(PDF)

S4 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Mania/ Hypomania lifetime algorithm for estimating reference standard (MINI)(weighted values).
(PDF)

S5 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Panic Disorder 12-month algorithm for estimating reference standard (MINI)(n = 287).
(PDF)

S6 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Panic Disorder lifetime algorithm for estimating reference standard (MINI)(n = 287).
(PDF)

S7 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Generalized Anxiety Disorder 12-month algorithm for estimating reference standard (MINI) (n = 287).
(PDF)

S8 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Generalized Anxiety Disorder lifetime algorithmfor estimating reference standard (MINI) (n = 287).
(PDF)

S9 Table. Prevalence estimates of common mental disorders and suicidal thoughts and behaviors in the clinical reappraisal samples recruited at each follow-up, according to the online survey screeners and the MINI (n = 287) (unweighted values).
(PDF)

S1 STARD Checklist.
(PDF)

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5.2. Article 2. Validation of an online version of the Alcohol Use Disorders Identification Test (AUDIT) for alcohol screening in Spanish university students.

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Validation of an online version of the Alcohol Use Disorders Identification Test (AUDIT) for alcohol screening in Spanish university students

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Abstract: Online alcohol screening may be helpful in preventing alcohol use disorders. We assessed psychometric properties of an online version of the Alcohol Use Disorders Identification Test (AUDIT) among Spanish university students. Longitudinal online survey (the UNIVERSAL project) of first year students (18-24 years old) in five universities including the AUDIT, as part of the WHO World Mental Health-International College Student (WMH-ICS) initiative. A reappraisal interview was carried out with the Timeline Followback (TLFB) for alcohol consumption categories and the Mini-International Neuropsychiatric Interview (MINI) for alcohol use disorder. Reliability, construct validity and diagnostic accuracy were assessed. Results: 287 students (75% women) completed the MINI, of whom 242 also completed the TLFB. AUDIT's Cronbach's alpha was 0.82. The confirmatory factor analysis for one-factor solution of the AUDIT showed a good fit to the data. Significant AUDIT score differences were observed by TLFB categories and by MINI disorders. Areas under de curve (AUC) were very high for dependence (AUC=0.96) and adequate for consumption categories (AUC>0.7). AUDIT cut-points 6/8 (women/men) for moderate-risk drinking and 13 for alcohol dependence showed sensitivity/specificity 76.2%/78.9% and 56%/97.5%, respectively. The online version of the AUDIT is useful for detecting alcohol consumption categories and alcohol dependence in Spanish university students.

Keywords: Alcohol Use Disorders Identification Test; AUDIT; university students; online survey; validity.

1. Introduction

Alcohol consumption is one of the leading risk factors for disability and premature death [1,2]. Particularly, among young people some alcohol consumption patterns are well-recognized as a public health problem [3]. The last report of the European School Survey Project on Alcohol and Other Drugs (ESPAD) showed that 34% of young people reported binge drinking [4]. In Spain, according to the last report from the Survey on alcohol and other drugs in Spain (EDADES) [5], the prevalence of alcohol consumption in the last 30 days was 59.7% in young people.

While alcohol consumption has increased in last decades among young people, there are some risk patterns of alcohol consumption that are more frequent in university students than non-students [6]. Binge drinking has been found one of the most commonly pattern among university students and highly related to other health risk behaviors [7–9]. As well as, a higher prevalence of risk-drinking was found [10–13]. To face this problematic around high levels of alcohol consumption, screening programs have been suggested to identify patterns of alcohol consumption and their severity early, as well as web-based intervention programs that have been shown to be effective in treating excessive alcohol use [14–16].

The Alcohol Use Disorders Identification Test (AUDIT) [17] is a self-administered instrument developed by the WHO, providing classifications of alcohol consumption and dependence. While the Spanish version of the AUDIT has been validated in health care settings [18,19], young people (12-18 years) [20] and university student populations [21–25], to our knowledge, this is the first study that assesses an online version, as part of a longer survey including multiple screening instruments.

The UNIVERSAL project is a multicenter, observational and prospective cohort study that aims to assess the prevalence and incidence of mental disorders among Spanish university students [26], where the screen for alcohol use disorders (AUD) was based on AUDIT [17,27]. This project is part of the World Mental Health International College Student (WMH-ICS) initiative.

The aims of the present study were to assess reliability, construct validity and diagnostic accuracy of the online version of the AUDIT as used in the UNIVERSAL project for measuring alcohol consumption and AUD according to standard reference measures, 7-day Timeline Followback (TLFB)[28] and Mini International Neuropsychiatric Interview (MINI) [29] respectively.

2. Materials and Methods

2.1. Participants

Data were obtained from the UNIVERSAL project. Further information on the UNIVERSAL project has been published elsewhere [26]. In the academic year 2014/15, all first-year students, aged 18-24 from five Spanish universities of five Spanish regions: Andalusia (UCA), Basque Country (UPV-EHU), Balearic Islands (UIB), Catalonia (UPF) and Valencia (UMH) were eligible and they were invited to participate.

These universities represented around 8% of the total number of students in public universities of Spain in the year 2014-15, and their distribution in demographic characteristics (i.e., gender, nationality and academic field) was similar to that of the overall population of students in public universities of Spain (results available upon request). The students participating in the study were re-contacted every year, from 2015/16 to 2017/18 courses, for follow-up online assessments. Ethical approval was provided by the Parc de Salut Mar-Clinical Research Ethics Committee (Reference: 2013/5252/I).

Participating students to the UNIVERSAL project (n=2,343) were eligible to participate in the clinical reappraisal study and were selected for participation at different time periods of the baseline and follow-up assessments (see flow diagram in **Figure 1**). Consecutive sampling of cases was applied at baseline (2014/2015) and 1st year follow-up (2015/16). In order to increase the number of individuals with alcohol use and other mental health problems, a probabilistic sampling was carried out during the 2nd year follow-up (2016/17), by selecting 100% of people who screened positive in the corresponding online mental disorders screeners, except Major Depression Episode or suicidal ideation (but none of the above), of which 20% were randomly selected. Finally, a random 10% of the remaining respondents were selected. The final sample of the clinical reappraisal study was 287 students.
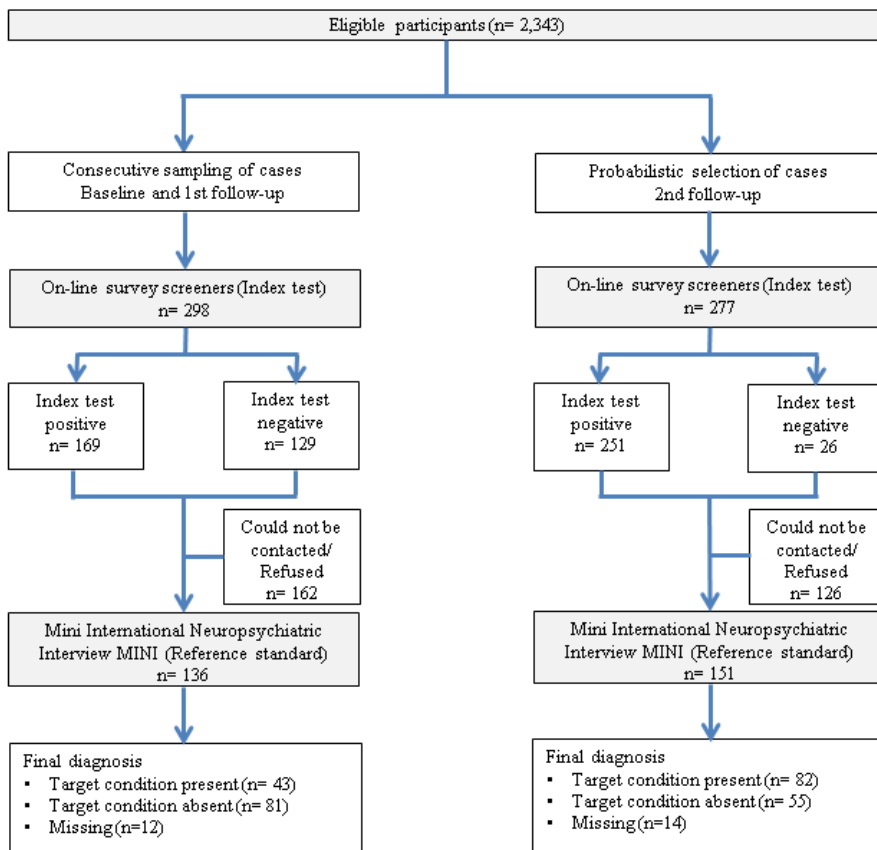
Figure 1. Flow diagram of the Clinical Reappraisal study.

2.2. Online survey

The online survey included an adaptation of the AUDIT questionnaire [17] for estimating current prevalence of alcohol consumption and AUD (abuse or dependence). AUDIT is a self-administered questionnaire composed of 10 items with scoring range of 0-40 points. This questionnaire refers to the quantification of alcohol consumption, the behavior towards drinking, adverse reactions and problems related to alcohol consumption.

Three variables were defined based on the AUDIT total score: a) Binge Drinking (BD), as a dichotomous variable obtained from the third AUDIT question modified in our study to five or more drinks in both genders "How often do you have five or more alcoholic drinks at a single sitting?" [30]. Responses were coded as follows: never/less than once a month=0 and 1-2 days a month/1-2 days a week/3-4 days a week/every day or nearly every day=1 [31,32]; b) Risk drinking, where different cut-off values were established according to gender: 8 in men and 6 in women; as recommended in previous Spanish validation studies [19,21,33]; and c) Probable dependence as dichotomous variable from the AUDIT with cut-off 13 for both genders [21].

2.3. Re-appraisal instruments

Re-appraisal interviews were conducted by clinical psychologists specially trained for structured interviews. Interviews were performed telephone interviews were performed by interviewers, who were blind to the online survey responses. Interviewers had no personal information (only telephone number). Two

standardized measures were selected as gold standard for this validation study: 7-day Timeline Followback (TLFB) and Mini-International Neuropsychiatric Interview (MINI).

The 7-day TLFB is a drinking assessment method that obtains estimates of daily drinking in the past 7 days, using a record of Standard Drink Units (SDU) consumed at different times or occasions throughout the day [28]. The following four categories were considered: a) Non-drinkers (SDUs=0), b) Low-risk drinkers (SDUs ≤ 21 and ≤ 14 for men and women, respectively)[35], c) Moderate-risk drinkers (22-27 for men and 15-16 SDUs for women) and d) High-risk drinkers (≥ 28 and 17 SDUs) [35,36]. Also, BD was defined as the consumption of 5 or more SDUs in a single sitting [36–38].

The adapted version of the Spanish structured interview MINI 5.0.0 [39] was administered for AUD diagnostics according to the Diagnostic and Statistical Manual of Mental Disorders [DSM-IV] [40] criteria and referred to the previous 12-months. Four categories were considered: a) Non-case; b) Alcohol abuse; c) Alcohol dependence; and d) any AUD (abuse/dependence).

2.4. Analysis

We compared characteristics of the clinical reappraisal subsample and prevalence estimates of alcohol consumption categories and AUD according to the reference standards by gender using Chi-squared test and Fisher's exact test. Reliability and confirmatory factor analysis were performed in the overall sample of participants in the UNIVERSAL project (n=2,343). The analysis with MINI as reference standard was performed with the whole sample of reappraised university students (n=287); and the analysis with TLFB as reference standard was restricted to those students from the reappraisal sample who provided all TFLB data (n=242).

Reliability of AUDIT was analyzed using Cronbach's alpha and Guttmann's Lambda-2, as measures of internal consistency. The unidimensionality of the AUDIT was evaluated through confirmatory factor analysis (CFA) with one factor solution, using unweighted least squares estimation. In addition to the chi-square statistic, which is sensitive to sample size [41,42]. We assessed Chi-square statistic and degrees of freedom and its corresponding p-value. Given the sensitivity of this test to large sample sizes, we additionally examined the following goodness of fit indices: comparative fit index (CFI), Tucker-Lewis index (TLI) and root mean square error of approximation (RMSEA). Considering the cut-off criteria of 0.95 in CFI and TLI for good fit and RMSEA <0.06 for good fit [43,44].

Known-groups validity was assessed by computing average scores (standard errors) of AUDIT across TLFB groups: those who do not drink; low-risk drinkers and moderate-risk to high-risk drinkers. Similarly, we computed average scores of AUDIT across MINI diagnosis: no AUD, alcohol abuse and alcohol dependence disorder. Jonckheere-Tepstra test was calculated with the ex-ante hypothesis that there would be a gradient from lower to higher values in AUDIT scores across these groups. Statistical significance was set at the 5% level based on two-sided tests. Cohen's effect sizes were computed for each category as compared to the lowest category ("No drinkers" for TLFB; "Non-case" for MINI) [45] considering an effect size small (0.2), moderate (0.5) and large (0.8) effect size[46]. Criterion validity of the AUDIT scores was assessed with Receiver Operating Characteristics (ROC) and its corresponding Area under the Curve (AUC), considering the TLFB definitions and MINI diagnoses as the reference standards. According to Landis and Koch (1977), different ranges of AUC were assigned labels of agreement: slight (0.50-0.59), fair (0.6-0.69), moderate (0.7-0.79), substantial (0.8-0.89) and almost perfect (≥0.9) [47]. Finally, we studied test characteristics for pre-specified cut-off points of the AUDIT with respect to TLFB and MINI definitions described previously: Sensitivity (SN), Specificity (SP), Positive Predictive Value (PPV), Negative Predictive Value (NPV), likelihood ratio positive (LR+) and likelihood ratio negative (LR-). The AUC for the dichotomous categories of the AUDIT are also presented. In the case of a dichotomous predictor and a dichotomous outcome, the AUC equals (SN+SP)/2[48]. For assessing the differences on the prevalence between online version of the AUDIT and reference standard, McNemar $\chi 2$ test was calculated.

Inverse probability weighting was computed to adjust the sampling method applied in the reappraisal selection carried out during the 2nd year follow-up (2016/17). Weights were obtained as the inverse of the probability of selection within each stratum in 2nd year follow-up and normalized to the total sample size of the clinical reappraisal study. Post stratification weights were applied for the correction of differences of gender, academic field and nationality characteristics between the clinical reappraisal sample and their respective

UNIVERSAL sample, as their reference population Analysis were performed using SAS v9.4 [49] and MPLUS v8.5 [50].

3. Results

Table 1 shows sociodemographic characteristics and prevalence of the reference standard measures in the clinical reappraisal sample. The majority of the sample was women (75.3%), 69.6% were 18 years old and 2.9% had non-Spanish nationality. Most students (47.6%) were enrolled in Social Sciences. According to the MINI, men were significantly more likely than women to meet the criteria of alcohol abuse (14.2% vs. 6.4%, p=0.028) but no gender differences for MINI alcohol dependence were found (1.6% vs. 1.3%). TLFB alcohol consumption categories (i.e., binge drinking, moderate-risk drinking and high-risk drinking) did also not show statistically significant differences between genders.

Table 1. Characteristics of the clinical reappraisal sub-sample and prevalence estimates of alcohol consumption and alcohol use disorder according to the TLFB and the MINI, by gender. (Unweighted observations and weighted percentages)

	Total n = 287	Men n = 71	Women n = 216	
	n (%)	n (%)	n (%)	p-value
Age				
18	177 (69.6)	45 (76.0)	132 (64.4)	.09
19	54 (14.5)	13 (11.6)	41 (16.9)	
20+	56 (15.9)	13 (12.4)	43 (18.8)	
Nationality				
Non-Spanish	29 (2.9)	4 (2.3)	25 (3.2)	.74
Field of studies				
Arts & Humanities	37 (9.8)	2 (7.0)	35 (11.9)	<.01*
Engineering & Architecture	32 (18.6)	21 (32.0)	11 (8.2)	
Health Sciences	85 (15.7)	14 (10.2)	71 (20.1)	
Science	25 (8.4)	11 (8.6)	14 (8.2)	
Social & Legal Sciences	108 (47.6)	23 (42.2)	85 (51.6)	
TLFB Alcohol consumption				
Binge drinking[a]	32 (9.8)	8 (9.6)	24 (10.0)	.93
Low-risk drinkers[b]	112 (51.4)	34 (65.9)	78 (39.6)	<.01*
Moderate-risk drinkers or more[c]	7 (2.0)	1 (1.8)	6 (2.1)	1.0
High-risk drinkers[d]	6 (2.0)	1 (1.8)	5 (2.1)	1.0
MINI Alcohol use disorder				
Abuse	29 (10.0)	11 (14.2)	18 (6.4)	.03*
Dependence	7 (1.5)	2 (1.6)	5 (1.3)	1.0
Abuse/ dependence	35 (11.2)	13 (15.6)	22 (7.6)	.03*

TLFB: Timeline Followback; MINI: Mini-International Neuropsychiatric Interview.

a.- TLFB: ≥5 SDU/Per occasion. b.- TLFB: < 22 SDU males and < 15 SDU females. c.-TLFB: ≥22 SDU/Males and ≥15 SDU/Females. d.- TLFB: ≥28 SDU/Males and ≥17 SDU/Females.

^Prevalence estimates according to the reappraisal temporary moment (see the methods section). P-values obtained from Chi-squared test, and Fisher's exact test when cells are n<5.

*P-value statistically significant 0.05.

The internal consistency of AUDIT evaluated by Cronbach's alpha coefficient was 0.817. Lambda-2 coefficient was 0.829. Corrected item-total correlations ranged from 0.332 to 0.663 (**Table 2**).

Table 2. Internal reliability of AUDIT online questionnaire administered in the UNIVERSAL sample (n=2,343)

AUDIT items	Mean (SD)	Corrected Item-Total Correlation	Cronbach's alpha if item deleted
1	1.69 (0.67)	0.539	0.798
2	0.61 (0.76)	0.509	0.800
3	0.78 (0.88)	0.663	0.781
4	0.29 (0.77)	0.520	0.798
5	0.27 (0.53)	0.558	0.796
6	0.18 (0.53)	0.332	0.816
7	0.46 (0.69)	0.502	0.800
8	0.41 (0.66)	0.623	0.786
9	0.27 (0.79)	0.446	0.808
10	0.06 (0.35)	0.339	0.816

AUDIT: Alcohol Use Disorders Identification Test; SD: Standard Deviation.

Cronbach's Alpha: 0.817. Guttman's Lambda-2: 0.829.

Table 3 shows standardized factor loadings of the one-factor CFA model of the online version of the AUDIT, which ranged from 0.545 to 0.797. Model chi-square statistic was 219.073 (35), p-value<0.001, and the CFA indices had optimal values according to the cut-off criteria, indicating a good fit to the data, with a CFI of 0.973, a TLI of 0.966 and the RSMEA of 0.049 (95%CI 0.043-0.056).

Table 3. Standardized factor loadings from a Confirmatory factor analysis with one-factor of the online version of the AUDIT administered in the UNIVERSAL sample (n= 2,343)

AUDIT Items	Standardized factor loadings	
	Estimate	SE
1	0.696	0.021
2	0.622	0.020
3	0.777	0.015
4	0.759	0.019
5	0.753	0.016
6	0.545	0.026
7	0.688	0.019
8	0.797	0.014
9	0.659	0.023
10	0.569	0.032
RMSEA (95% CI)	0.049 (0.043-0.056)	
CFI	0.973	
TLI	0.966	
χ^2 (DF), p-value	219.073 (35), p<0.001	

AUDIT: Alcohol Use Disorders Identification Test; RMSEA: Root Mean Square Error of Approximation; CFI: Comparative Fit Index; TLI: Tucker Lewis Index; χ^2:Chi-square statistic; CI: Confidence Interval; DF: Degrees of Freedom.

Figure 2.A shows mean AUDIT scores and their 95% confidence intervals, as well as corresponding effect sizes, across the TLFB alcohol consumption categories. A clear upward gradient was observed for the AUDIT scores, rising from the "Non-drinkers" group (mean=2.86, 95%CI=2.31-3.41), through the "Low-risk drinkers" (mean=4.51, 95%CI=3.96-5.06) and finally the "Moderate-risk drinkers or more" group (mean=13.5, 95%CI= 6.46-20.53) (J=10,025.5; p-value<0.001). Similar results were obtained for women. Results for men could not be calculated due to insufficient data in the *"moderate risk drinkers or more"* category (n<5), but differences between non-drinkers and low-risk drinkers were small and not statistically significant. Effect sizes associated to "Moderate-risk drinkers or more" were the highest for the total sample (ES=3.34) and for women (ES=2.72). **Figure 2.B** shows mean AUDIT scores and 95% confidence intervals for alcohol abuse and dependence as assessed by the MINI. Again, a consistent upward gradient was observed for the AUDIT scores rising from "Non-cases" to respondents with "dependence" criteria. Results for men in the *"dependence"* category (n<5) could not be calculated due to insufficient data. Effect sizes associated with "Dependence" were the highest for the total sample (ES= 2.72) and for women (ES=2.98).
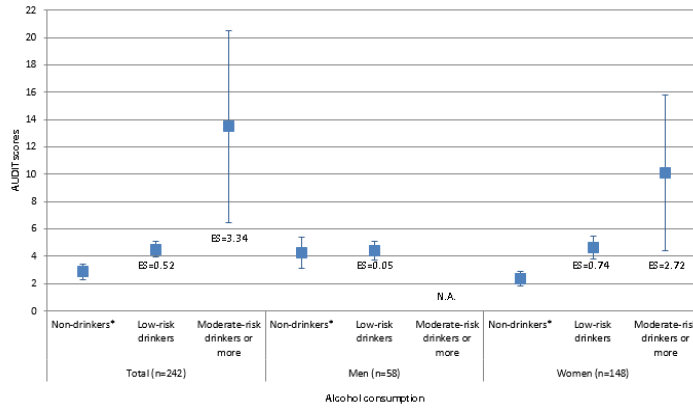
Figure 2.A. AUDIT online mean scores and effect size, by alcohol consumption categories (TLFB). (n=242)

AUDIT: Alcohol Use Disorders Identification Test; TLFB: Timeline Followback; ES: Effect size.

*Reference category

Jonckheere-Terpstra test=10,025.5; p-value<0.001

ANOVA with Tukey post hoc test p-value<0.001
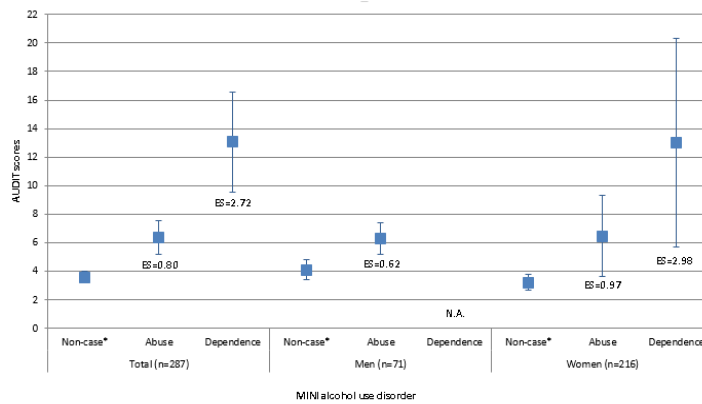
Figure 2.B. AUDIT online mean scores and effect size, by alcohol use disorder (MINI). (n=287)

AUDIT: Alcohol Use Disorders Identification Test; MINI: Mini-International Neuropsychiatric Interview; ES: Effect size.

*Reference category

Jonckheere-Terpstra test=6,337.5; p-value<0.001

ANOVA with Tukey post hoc test p-value<0.001

The ability of the AUDIT scores for detecting alcohol risk-drinking and AUD, using TLFB and the MINI as the respective gold standards, is presented by ROC curves and AUCs in **Figure 3**. AUCs were substantial for the TLFB, with values of 0.84 to detect moderate-risk drinking and 0.85 for high-risk drinking. For the

MINI, AUCs ranged from fair (0.78) for alcohol abuse/dependence to almost perfect (0.96) for alcohol dependence.
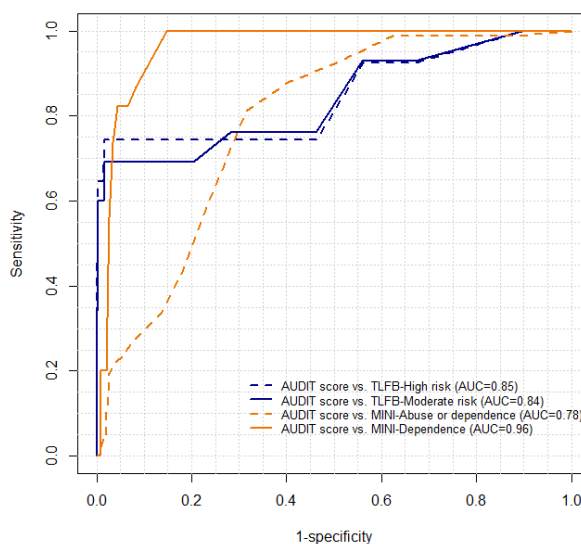
Figure 3. ROC curves and AUC between continuous scores of AUDIT and MINI/TLFB (n=287)

AUDIT: Alcohol Use Disorders Identification Test; TLFB: Timeline Followback; MINI: Mini-International Neuropsychiatric Interview; ROC: Receiver Operating Curve; AUC: Area Under the ROC Curve

Accuracy analyses were first performed for alcohol consumption categories (**Table 4**), comparing different AUDIT cut-off points with the Timeline Followback categories as the gold standard. AUDIT cut-off points had a SN 41.4% and SP 83.6% for detecting binge drinking. Results for pre-specified cut-off points for detecting at least moderate-risk drinkers, were SN=76.2% and SP=78.9% for cut-off point 8 for men and cut-off point 6 for women. Using the cut-off point 13 for both genders provided a SN of 74.4% and SP of 98.3% for high-risk drinkers based on the TLFB. Prevalence estimates are also presented in **Table 4**, which show statistically significant differences between index text and gold standard according to McNemar test for binge drinking and for moderate-risk drinkers. The AUCs were fair to substantial for moderate-risk and high-risk (ranging from 0.7 to 0.9), and fair for binge drinking (0.6).

Table 4. Operating characteristics of AUDIT online questionnaire cut-off points for estimating reference standard (TLFB) prevalence of alcohol consumption in Standard Drink Units (SDU) per week by gender (weighted values)

	Cut-off point	AUDIT % (SE)	TLFB % (SE)	Positive operating characteristics			Negative operating characteristics			McNemar χ2 (p-value)	AUC
				SN (SE)	PPV (SE)	LR+	SP (SE)	NPV (SE)	LR-		
Total (n=242)											
Binge drinking[a]		18.9 (2.5)	9.8 (1.9)	41.4 (9.9)	21.6 (5.9)	2.5	83.6 (2.4)	92.9 (1.8)	0.7	10.1 (0.002*)	0.63
Moderate-risk drinkers or more[b]	6/8	22.2 (2.7)	2 (0.9)	76.2 (19.0)	6.9 (3.4)	3.6	78.9 (2.6)	99.4 (0.6)	0.3	48.91 (<.001*)	0.78
High-risk drinkers[c]	13	3 (1.1)	1.9 (0.9)	74.4 (19.5)	46.2 (17.6)	43.8	98.3 (0.8)	99.5 (0.4)	0.3	1.58 (0.209)	0.86
Men (n=58)^											
Binge drinking[a]		25.4 (5.7)	9.5 (3.9)	50.7 (15.8)	19.0 (7.4)	2.2	77.3 (4.1)	93.7 (2.6)	0.6	11.3 (0.001*)	0.64
Women (n=184)											
Binge drinking[a]		13.6 (2.5)	10.1 (2.2)	34.4 (12.7)	25.5 (10.0)	3	88.7 (2.8)	92.4 (2.4)	0.7	1.05 (0.30*)	0.62
Moderate-risk drinkers or more[f]	6	23.2 (3.1)	2.4 (1.1)	63.9 (27.7)	6.6 (4.3)	2.9	77.8 (3.5)	98.9 (1.0)	0.5	27.06 (<.001*)	0.71
High-risk drinkers[g]	13	3 (1.3)	2.1 (1.1)	59.6 (28.3)	43.0 (24.8)	35.1	98.3 (1.1)	99.1 (0.8)	0.4	0.37 (0.542)	0.79

AUDIT: Alcohol Use Disorders Identification Test; TLFB: Timeline Followback; SN: Sensitivity; PPV: Positive Predictive Value; LR+: likelihood ratio positive; SP: Specificity; NPV: Negative Predictive Value; LR-: likelihood ratio negative; SE: Standard Error; AUC: area under the receiver operating characteristic curve.

a.- Third question in AUDIT online; TLFB: ≥5 SDU/per occasion; b.- TLFB: ≥22 SDU males and ≥15 SDU females; c.- TLFB: ≥28 SDU males and ≥17 SDU females; d.- TLFB:≥22 SDU; e.- TLFB: ≥28 SDU; f.- TLFB: ≥15 SDU; g.- TLFB: ≥17 SDU.

^No sufficient data (n<5) to calculate "moderate-risk drinkers" and "high-risk drinkers".

*P-value statistically significant 0.05.

In **Table 5**, AUDIT cut-off points were compared to the MINI as the gold standard for detecting AUD. The AUDIT cut-off point used for detecting alcohol abuse or dependence was 8, as generally accepted cut-off [27,51]. SN for men was 26.6% and for women 46%, while SP was higher for both genders (81.1%; 90.2%, respectively). The alternative cut-off point of 13 for alcohol dependence, recommended by García-Carretero et al. (2016), showed better accuracy results: SN for overall sample 56% and 54.3% for women, and SP 97.5% and 97.6%, respectively [21]. According to McNemar test (**Table 5**), no statistically significant differences were found in prevalence estimates. The dichotomous AUCs for alcohol dependence were slightly higher than values for alcohol abuse/dependence for overall sample (0.60 vs. 0.77) and women (0.68 vs. 0.76).

Table 5. Operating characteristics of AUDIT online questionnaire cut-off points for estimating reference standard (MINI) prevalence of alcohol dependence and alcohol abuse or dependence by gender (weighted values)

	AUDIT	MINI	Positive operating characteristics			Negative operating characteristics			McNemar	AUC
Cut-off point	% (SE)	% (SE)	SN (SE)	PPV (SE)	LR+	SP (SE)	NPV (SE)	LR-	χ^2 (p-value)	
Total (n=287)										
Alcohol abuse/ dependence	8	15.9 (2.2)	11.2 (1.9)	33.9 (8.4)	23.9 (6.3)	2.5	86.3 (2.2)	91.2 (1.8)	0.8	3.23 (0.072)	0.60
Alcohol dependence	13	3.3 (1.1)	1.5 (0.7)	56 (24.8)	24.9 (14.4)	22.4	97.5 (0.9)	99.3 (0.5)	0.5	3.12 (0.077)	0.77
Men (n=71)^										
Alcohol abuse/ dependence	8	20.1 (4.8)	15.6 (4.3)	26.6 (9.9)	20.7 (8.1)	1.4	81.1 (3.8)	85.7 (3.5)	0.9	0.93 (0.334)	0.54
Women (n=216)										
Alcohol abuse/ dependence	8	12.6 (2.3)	7.7 (1.8)	46 (13.8)	28.1 (10.0)	4.7	90.2 (2.5)	95.3 (1.8)	0.6	2.86 (0.091)	0.68
Alcohol dependence	13	3.2 (1.2)	1.5 (0.8)	54.3 (35.2)	26.4 (19.7)	22.6	97.6 (1.2)	99.3 (0.7)	0.5	1.39 (0.239)	0.76

AUDIT: Alcohol Use Disorders Identification Test; MINI: Mini-International Neuropsychiatric Interview; SN: Sensitivity; PPV: Positive Predictive Value; LR+: likelihood ratio positive; SP: Specificity; NPV: Negative Predictive Value; LR-: likelihood ratio negative; SE: Standard Error; AUC: area under the receiver operating characteristic curve.

^No sufficient data (n<5) to calculate "alcohol dependence".*P-value statistically significant 0.05

4. Discussion

This study shows that the online version of the AUDIT is adequate to detect alcohol dependence among Spanish university students. Also, the online version of the AUDIT was able to discriminate different alcohol consumption categories in addition to alcohol dependence, which has scarcely been studied so far [34].

Reliability is a prerequisite for validity [52]. Internal consistency for the online version of the AUDIT was good on the whole measurement, which reflected the consistency of responses across the items on the instrument. Our results are comparable to those found in previous Spanish studies among university students [21] and the general population [18,19], which found around 0.8. However, corrected item-total correlations were low for some of the items, particularly for the items 6 and 10, which were also shown in previous studies [18,21]. They concluded that it can be due to items from 4th to 10th assess dependence and harmful consumption and these were less frequent in this population.

The unidimensionality evaluation, consistent with the total score of the AUDIT, showed good fit results, as found in previous studies [53,54]. The results obtained for the known-groups comparisons also provide support for the construct validity of the online version of the AUDIT. An upward gradient was observed in both cases, for alcohol consumption and for AUD categories. Increasing scores were obtained across different types of consumption (similar to those reported by García-Carretero et al., 2016).

The results reported also offer evidence of good diagnostic accuracy of the AUDIT for identifying risk-drinking categories with the TLFB and alcohol dependence (assessed by the MINI). The AUC to identify alcohol risk-drinking (0.85) was lower to those obtained in previous Spanish validation studies of the AUDIT among university students (AUC=0.96/0.98 in men/women) [21] or primary care patients (AUCs=0.97 and 0.95)

[25,33], whose studies differ in the mode of administration of the AUDIT. The AUC to detect alcohol dependence was 0.96, similar to the AUC values obtained by García-Carretero et al. (2016)[21]. Finally, the AUC for detecting BD with the AUDIT was fair (0.6) and lower than AUC, which was found by Cortés et al. (2017), who supports the recommendation to change the third item of the AUDIT to four or more drinks in women [30] or using the full instrument to identify BD, such as AUDIT or AUDIT-C [23,55].

In this study, previously suggested cut-off points in AUDIT for alcohol risk consumption among men and women (8 and 6, respectively) resulted in sensitivities and specificities lower to the Spanish validation among university students [21] and primary care [19,33], but similar to the validation carried out in the United States among university students by Kokotailo et al. (2004)[30]. The online AUDIT cut-off score of 13 for detecting alcohol dependence showed worse psychometric properties lower than other previously Spanish validation study [21]. Sensitivity analyses conducted in this study showed better psychometric properties with cut-off point of 12 for detecting alcohol dependence (full results of the additional analyses are available upon request). Also, our study showed low PPVs and NPVs, which might be due to low prevalence of alcohol disorders in our population [56].

The results of this study must be interpreted taking into account the following limitations. First, we used the MINI as the gold standard diagnostic instrument, which is not used as widely as other structured interviews, but we applied it for feasibility and because it has been shown acceptable SN/SP values (0.8/0.8) for structured interviews. Second, although the validity of the online instrument was established in a sample of 287 university students, the low prevalence of alcohol-related problems limited the statistical power of our study. Importantly, our results on the overall sample are consistent with previous findings [21]. But studies with larger samples are needed for the online version of the AUDIT. An additional limitation concerns the recall periods of the instruments. The MINI interview uses a 12-month recall period and the TLFB uses a 1-week period. In contrast, the recall period for the AUDIT implicitly refers to the current time (like in the official version). We decided to respect the original recall periods of all the measures and did not attempt to modify the TLFB recall period, as this could have impacted on its validity. Since the time frames are not equivalent, it is be possible that current time use of alcohol was not representative of the alcohol consumption in the past year. If this is the case, the association among the two measures would be attenuated and we had underestimated the validity of the online AUDIT.

5. Conclusions

We have tested metric performance of the Spanish online version of the AUDIT among Spanish university students. Results indicate good reliability of this version, as well as good construct validity and diagnostic accuracy. If applied in epidemiological research settings, the online version of the AUDIT might be useful to improve the detection of risk alcohol consumption patterns and probable cases of AUD diagnosis. The brevity and easy to administer of the online AUDIT will facilitate including in more complete mental health profile evaluations. It is known that online screening and interventions could reduce drinking in university students [57]. Such programs could be implemented more widely, for instance, among university campuses.

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5.3. Article 3. Mental disorders in Spanish university students: Prevalence, age-of-onset, severe role impairment and mental health treatment.

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Supplementary material for this article can be found in ANNEX 2 (page 308)

Mental disorders in Spanish university students: Prevalence, age-of-onset, severe role impairment and mental health treatment.

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List of abbreviations

Adjusted Odd Ratio (aOR)

Adult ADHD Self-Report Scales (ASRS)

Akaike's information criterion (AIC)

Alcohol use disorder (AUD)

Alcohol Use Disorders Identification Test (AUDIT)

Area Under the curve (AUC)

Attention-deficit/hyperactivity disorder (ADHD)

Balearic Islands University (UIB)

Basque Country University (UPV-EHU)

Cádiz University (UCA)

Composite International Diagnostic Interview (CIDI)

Confidence Interval (CI)

Drug use disorder (DUD)

Generalized anxiety disorder (GAD)

International Test Commission (ITC)

Major depressive episode (MDE)

Miguel Hernández University (UMH)

Multiple Imputation (MI)

Odd Ratio (OR)

Organization for economic co-operation and development (OECD)

Panic disorder (PD)

Pompeu Fabra University (UPF)

Sheehan Disability Scale (SDS)

Standard Error (SE)

Standard Deviation (SD)

World Mental Health International College Student initiative (WMH-ICS)

Highlights

- Mental disorders among first-year Spanish university students are common.
- 35.7% of students screened positive for 12-month mental disorder.
- Depression and generalized anxiety disorder are the most frequent disorders.
- 29.2% of students with mental disorders report severe role impairment.
- 12.6% of students with mental disorder receive mental health treatment.

Abstract

Background

The university period carries risk for onset of common mental disorders. Epidemiological knowledge on mental disorders among Spanish university students is limited.

Aims

To estimate lifetime and 12-month prevalence, persistence and age-of-onset of mental disorders among Spanish first-year university students, as well as associated role impairment and mental health treatment use.

Methods

First-year university students (N=2,118; 55.4% female; mean age=18.8 years) from five Spanish universities completed a web-based survey, screening possible DSM–IV mental disorders (major depressive episode(MDE), mania/hypomania, generalized anxiety disorder(GAD), panic disorder(PD), alcohol abuse/dependence(AUD), drug abuse/dependence(DUD), and adult attention-deficit/hyperactivity disorder(ADHD)). Role impairment and treatment associated with mental disorders were assessed.

Results

Lifetime and 12-month prevalence of any possible mental disorder was 41.3 %(SE=1.08) and 35.7%(SE=1.05), respectively. Persistence (i.e., ratio of 12-month to lifetime prevalence) was 86.4%(SE=1.58). Median age-of-onset was 14 for adult ADHD, 15 for mood disorders and AUD, and 16 for anxiety disorders and DUD. One third (29.2%) of 12-month disorders were associated with role impairment. Twelve-month PD (OR=4.0;95%CI=1.9-8.5) had the highest odds for role impairment. Only 12.6% of students with 12-month disorder received any mental health treatment. Twelve-month treatment was the highest among those students with 12-month GAD (OR=7.4;95%CI=3.7-14.8).

Limitations

The assessment of mental disorders was based on self-reports. Cross-sectional nature of the data prevents causal associations.

Conclusion

One third of Spanish university students report a common mental disorder in the past year, and one third of those report severe role impairment. Only one out of eight students with 12-month mental disorders receives mental health treatment.

Keywords: mental disorders, role impairment, treatment, university students**,** cross-sectional.

Introduction

In the last decades, there has been an increase of young people entering tertiary education across developed countries (OECD, 2018). Entering university is a critical period (Auerbach et al., 2016; Pedrelli et al., 2015) as students face a series of important challenges, such as leaving one's parental home or assuming more responsibilities (Arias-de la Torre et al., 2019). In addition, students enter a new developmental phase, i.e. emerging adulthood, characterized by greater autonomy, changes in social roles, and instability of relationships (Sussman and Arnett, 2014). Emerging adulthood has been described as a peak period for onset of many common mental disorders such as mood, anxiety and substance use disorders (Auerbach et al., 2018b). Prevalence and treatment of mental disorders among university students is therefore an increasing subject of attention (Blanco et al., 2008; Bruffaerts et al., 2018; Eisenberg et al., 2007; McLafferty et al., 2017). A recent cross-national study reported that approximately one third of first-year students screened positive for one or more common mental disorders (Auerbach et al., 2018b). In addition, comorbid mental disorders have been found to be common in this population (Auerbach et al., 2018a).

The occurrence of mental disorders during the university period is associated with considerable impairment of psychosocial functioning and reduced educational achievement (Alonso et al., 2018). Despite the high prevalence of mental disorders among university students, various studies indicate that many of them do not receive treatment, showing rates of mental health treatment use in the range 18-36% (Blanco et al., 2008; Eisenberg et al., 2011; Verger et al., 2010). To our knowledge, there have been no epidemiological studies carried out in Spain to provide a broad epidemiological picture of common mental disorders in university students. While previous studies provided valuable information on mental health among Spanish university students, they were carried out on limited samples (e.g. only female students or in a single university) (Balanza et al., 2009; Vázquez et al., 2011) or they evaluated a limited range of mental health problems (Arias-de la Torre et al., 2019; Caamaño-Isorna et al., 2008; Moure-Rodríguez et al., 2014; Vázquez and Blanco, 2008). In addition, these studies did not report on mental health related role impairment and use of services.

The objectives of the current study were to: i) estimate lifetime and 12-month prevalence, persistence and levels of comorbidity of common mental disorders in first year university students; ii) estimate age-of-onset of mental disorders; and iii) test the association of mental disorders and role impairment and the receipt of mental health treatment.

Methods

Study design

Data come from the *UNIVERSAL* project, a multi-center observational cohort study of all students starting their first course in five Spanish universities. *UNIVERSAL* is part of the World Mental Health International College Student (WMH-ICS) initiative (https://www.hcp.med.harvard.edu/wmh/college_student_survey.php). Information on the rationale and methods of the *UNIVERSAL* project has been published elsewhere (Blasco et al., 2016).

Setting and participants

Web-based surveys were administered between October 2014 and October 2015 in a convenience sample of five public universities from different Autonomous Regions of Spain: Balearic Islands (UIB), Basque Country (UPV-EHU), Andalusia (UCA), Valencian (UMH), and Catalonia (UPF). These universities represented around 8% of the total number of students in public universities of Spain in the year 2014-15, and their distribution in terms of gender, nationality and academic field was similar to that of the overall population of students in public universities of Spain (see **Supplementary table 1**). Inclusion criteria for eligible students at baseline were: (i) age range from 18 to 24 years old; and (ii) first year students enrolled in a university degree for the first time. The only exclusion criterion was non-acceptance of the informed consent for the study. A total of 16,332 students fulfilled inclusion criteria. Eligibility of registered individuals was validated by the corresponding universities.

The sample was recruited in two stages. In the first stage, all eligible students (i.e., census sampling) were invited to participate. In a second stage, a random subsample of non-respondents to the first stage was contacted offering an economic incentive to complete the survey. In UPV-EHU University, only the first stage was carried out. The recruitment method consisted of personal e-mail invitation letters sent by the university authorities to each of the eligible students, and accompanied by advertising campaigns.

Students were invited to complete the study registration form via the *UNIVERSAL* website (http://encuesta.estudio-*UNIVERSAL*-net/), and written informed consent was obtained from all subjects. Students received a personalized link and password to complete

the survey via a secure Web platform designed for the study. The data collection platform followed the international recommendations and guidelines for computerized assessment (International Test Commission -ITC-, 2005) (International Test Comission, 2019). At the end of the web-based survey, all respondents received information on how to access local health services. Individuals with positive responses on suicide items received a specific alert with indications to consult a health professional.

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Ethical approval was provided by the Parc de Salut Mar-Clinical Research Ethics Committee (Reference: 2013/5252/I).

Measures

<u>Sociodemographic and university-related variables</u>

Sociodemographic variables included gender, age, country of birth, parental education, parental marital status, urbanity, religious background and sexual orientation.

A set of university-related variables was also assessed, i.e. academic field and first-term living location during the university period (parents' home vs other type of residence). Academic field was classified according to the official Spanish Government of university degrees, in accordance with the International Standard Classification of Education (UNESCO Institute for Statistics, 2011).

<u>Mental disorders</u>

Mental disorders assessed included: mood disorders (i.e., major depressive episode [MDE] and mania/hypomania [Broad mania]), anxiety disorders (i.e., generalized anxiety disorder [GAD] and panic disorder [PD]), substance use disorders (i.e., alcohol abuse or dependence [Alcohol use disorder-AUD] and drug abuse or dependence [Drug use disorder-DUD]), and attention-deficit/hyperactivity disorder [Adult ADHD]. Note that DUD involves either cannabis, cocaine, any other street drug, or a prescription drug either used without a prescription or used more than prescribed to get high, buzzed, or numbed out.

Items for assessing possible mood disorders, anxiety disorders and DUD were based on the Composite International Diagnostic Interview Composite International Diagnostic Interview Screening Scales (CIDI-SC) (Kessler et al., 2013a; Kessler and Üstün, 2004),

chosen for their good psychometric properties (Kessler et al., 2013b), which also showed overall good concordance with blinded clinical diagnoses in the area under the curve (AUC) range of 0.6-0.9 (Ballester et al., 2019). Possible alcohol abuse or dependence was screened using the Alcohol Use Disorders Identification Test (AUDIT) showing concordance with clinical diagnosis in the range AUC = 0.78-0.91 (Saunders et al., 1993). Adult ADHD was assessed using the Adult ADHD Self-Report Scales (ASRS) with items referring to the previous 6 months, which version was found to have strong concordance with clinical diagnoses (AUC 0.90) (Kessler et al., 2005). Additional items assessed age-of-onset of each disorder as well as the number of lifetime years with symptoms.

Impairment

To assess 12-month role impairment, an adapted version of the Sheehan Disability Scale (SDS) was used (Leon et al., 1997). This scale is composed of four role domains: home management (cleaning, shopping and working around the house), college-related and other work (ability to work as well as most of other people), close personal relationships (ability to initiate and maintain close personal relationships), and social life (without further specification). A visual analogue scale (0-10) was used to rate the degree of impairment for each domains, labeled as no interference (0), mild (1–3), moderate (4–6), severe (7– 9), and very severe (10) interference. Severe self-reported role impairment was defined as having a 7-10 rating. Validation studies on the Spanish version showed good internal reliability with Cronbach's alpha ranging from 0.72 to 0.89 and supported the discriminatory validity between healthy participants and patients (Bobes et al., 1999; Luciano et al., 2010).

Mental health treatment

Items adapted from the CIDI services section assessed mental health treatment receipt. Students were asked whether they ever received psychological counselling or medication for an emotional or substance problem as well as the age of the first time and the last time they received treatment (Kessler and Üstün, 2004). Twelve-month treatment was defined as being currently in treatment or by having a difference of ≤1 between current age and age at the last time receiving treatment.

Analyses

The proportion of missing values on each of the variables ranged from 0.09% to 4.96%. Item-level missing data among respondents were imputed using multiple imputation (MI) by chained equations (van Buuren, 2012) with m=43 imputed datasets, equivalent to the percentage of incomplete subjects (White et al., 2011), and with 10 iterations per imputation. Pooled MI-based parameter estimates, standard errors (SE) and statistical inference were obtained from the weighted analysis of these MI datasets. Inverse-probability weighting was applied to hard-to-reach respondents that were randomly selected and offered a monetary incentive to participate (endgame strategy weights). Post stratification weighting was applied to restore the distribution of the population regarding sex, age, country of birth, and academic field within each university, as well as population distributions across universities (results available upon request). Analyses were performed using SAS v9.4 (SAS Institute Inc., 2014) and RStudio v1.1.383 (RStudio Inc., 2017).

Lifetime and 12-month prevalence of possible mental disorders and comorbidity were estimated. F-tests for independence based on MI examined gender differences in prevalence rates. Persistence was estimated as 12-month prevalence among lifetime cases. Estimates of age-of-onset were reported as median values with associated interquartile ranges.

Bivariate analyses were performed to examine the associations between sociodemographic/university characteristics and 12-month possible mental disorders and to explore the relationships between 12-month possible mental disorders and severe role impairment and mental health treatment. Crude odds ratios (ORs) were estimated and MI-based confidence intervals (CIs) were calculated at the 95% level. Statistical significance level α was set at the 5% level, after adjustment for multiple comparisons using the Benjamini–Hochberg procedure (Benjamini et al., 2001) with a false discovery rate of 5%.

Finally, multiple logistic regression models were performed. Regression coefficients and their MI-based standard errors were exponentiated to generate adjusted ORs and associated 95% CIs. To assess the association of 12-month possible mental disorders and severe role impairment and mental health treatment, a series of five models were developed to evaluate the joint effect of multiple mental disorders. Model 1was composed for separate dummy variables for each of the seven types of mental disorders in the assumption that the joint effect of the multiple disorders is the product of the corresponding disorders' odds ratios.

Model 2 (included of one continuous variable indicating number of disorders) and Model 3 (included a series of dummy variables indicating categorical number of disorders) implicitly assume that the specific disorder is unimportant once number of disorders is known. In addition, Model 3 allowed for interactions in the sense that the coefficients associated with having exactly n disorders can be significantly different form the product associated with having one disorder. Model 4 (included the type of mental disorders and continuous number - different than 1- of mental disorders) and Model 5 (included the type of mental disorders and categorical number –different than 1- of mental disorders) allowed for both differences for the effects of different disorders and their interactions. Models were adjusted by sociodemographic and university variables: age, sex, university, academic field, country, parent's studies, and current living situation. Models that explored the association between 12-month possible mental disorders and mental health treatment were also adjusted for impairment. Statistical significance was evaluated with two-sided F tests based on multiple imputations and a level of significance of 0.05. The area under the curve (AUC) and the Akaike's information criterion (AIC) were calculated to select the best model.

Results

Participants

Of the total of 16,332 students that fulfilled inclusion criteria, 2,862 students registered in the study. Among them, 2,674 were validated participants (the eligibility of the registered students was validated by the corresponding universities). A total of 2,395 students initiated the survey, of which 2,118 completed the survey and were included in this study (see flow diagram in **Figure 1**). The overall weighted response rate was 19%, ranging from 9% (Basque Country University) to 44% (Pompeu Fabra University). We found somewhat unbalanced distributions of the sample with respect to available census information, with higher proportions in the *UNIVERSAL* sample of females (72.5% vs. 55.2%), foreign students (5.3% vs. 3.2%), and health sciences students (25.6% vs. 15.8%). Post-stratification weights restored population distributions on all these variables and have been accounted different response rates at each university weights proportionally to its population of eligible students.

--Figure 1, here--

Table 1 summarizes the weighted characteristics of the *UNIVERSAL* study, overall and by gender. Mean age was 18.8 years (SD = 1.4) and 55.4% were female. More than half (57.3%) had parents without university studies, 13.8% had separated or divorced parents and 66.1% were raised in a city. Over half of students reported no religious affiliation (58.0%) and 89.3% self-identified as heterosexual. Basque Country University represented 43.9% of the students and almost 48% of the students from the participating universities were in the Social and Legal Sciences academic field. More than half of the students were living at parents' home (56.2%).

--Table 1, here--

Prevalence and age-of-onset of mental disorders

Lifetime prevalence of possible mental disorders is presented in **Table 2**. The highest prevalence rates were found for MDE (23.1%) and GAD (19.3%). Females were significantly more likely to experience mood and anxiety disorders than males, while the latter had significantly higher rates of any substance use disorders. Twelve-month prevalence estimates were also highest for MDE (18.9%) and GAD (16.0%). Persistence of possible mental disorders was in the range 80.5–95.2%, except for DUD (41.0%). Overall, 11.0% of students experienced two disorders and 5.6%, three or more disorders, in the 12-months previous to the assessment.

Supplementary table 2 shows the median age-of-onset of each possible mental disorder. Median age-of-onset was 14 for Adult ADHD; 15 for MDE, broad mania and AUD; and 16 for GAD, PD and DUD.

--Table 2, here--

Severe role impairment

A total of 29.2% of the sample with any 12-month mental disorder reported any severe role impairment versus 10.2% for those without mental disorder. As shown in **Table 3**, severe role impairment was common among students who screened positive for 12-month mental disorders, particularly for PD (61.7%) and 12-month broad mania (45.8%), and increased substantially with increasing comorbidity of disorders, up to 52.8% when students reported three or more disorders.

All disorders except DUD were significantly associated with severe role impairment in bivariate models, with odds ratios ranging from 1.6 to 8.4 (Detailed results are shown in the **Supplementary table 3**).

Table 3 also shows the results of the logistic regression models predicting any severe impairment, adjusting for all sociodemographic and university predictors. In Model 1, MDE, GAD, PD and AUD were significantly associated with severe role impairment (median OR=1.8), especially PD (OR = 4.0; 95% CI = 1.9-8.5). Model 2 included only the number of disorders (as a continuous variable), showing an increase in odds for severe role impairment with a factor of 2.0 (95% CI = 1.8-2.2) for each additional mental disorder. Model 3 included number of disorders as a categorical variable with ORs ranging from 2.1 (for exactly one disorder) to 9.0 (for three or more disorders), following approximately a linear pattern in the logit.

Models 4 and 5 show the association of possible mental disorders with severe role impairment taking into account the number of disorders (as a continuous count in Model 4 and as a categorical variable in Model 5). In both models, the ORs for individual disorders are only slightly higher than the first model. This is in line with the ORs for the number of mental disorders in model 5 being smaller than one (0.8), suggesting a slight subadditive effect of the individual disorders on impairment, although this effect was not statistically significant.

Although AUCs were similar, ranging from 0.735 to 0.736, according to Akaike's information, the best-fitting regression model for 12-month impairment was Model 1 (including type of mental disorder).

--Table 3, here--

Mental health treatment

In this study, 12.6% of students with possible mental disorder and 2.3% of those without mental disorder reported receiving treatment in the past year, respectively. As shown in **Table 4**, the receipt of mental health treatment was highest among participants with 12-month anxiety disorders (35.3% for PD and 20.1% for GAD) and increased with increasing comorbidity up to 18.0-19.0% when students reported two or more disorders.

In bivariate models (**Supplementary table 4**), all past year mental disorders were associated with receiving treatment, except SUD. Specifically, PD (OR = 9.6; 95% CI = 4.8-

18.9) and GAD (OR = 7.4; 95% CI = 5.0-10.7) yielded the highest odds for treatment. Also, bivariate models show a gradient between the number of possible mental disorders and receiving treatment.

The multiple model, including both type and number of possible mental disorders, was selected as the best-fitting regression model to estimate factors associated with 12-month treatment (AIC = 798.0; AUC = 0.805) (**Table 4**). The ORs for individual disorders are higher than the first model when number of disorders is included in the model, in line with the OR for number of mental disorders being significantly smaller than 1. This model shows that possible mental disorders are associated with an increase to receive mental health treatment. Also, the model shows a gradient suggesting a subadditive effect in the logit between number of disorders and receiving mental health treatment. The series of multiple logistic regression models are shown in **Supplementary table 5**.

--Table 4, here--

Analyses of the association of 12-month mental disorders and sociodemographic and university variables are presented in **Supplementary table 6** and **Supplementary table 7**. Female gender and having parents with low educational attainment emerged as significant positive correlates of 12-month mood, anxiety and substance disorders. Living at first term in other house than parent's home showed a positive correlation with any substance disorders. Reporting non-heterosexual orientation showed a positive correlation with two or more mental disorders. AUCs of the models ranged from 0.597 to 0.636.

Discussion

Main findings

The current study is the first in Spain that provides an overview of mental disorders, their associations with impairment, and the use of mental health treatment among Spanish university students. The study confirms and extends evidence on the high prevalence and persistence of both lifetime and 12-month mental disorders in this population. Nearly 20% of students reported two or more diagnoses. The median age-of-onset ranged from 15.5 to 17.5. Notably, results indicated that possible mental disorders are associated with severe role

impairment (29.2%), while only under a fifth of university students with a mental disorder received treatment in the last 12 months.

Almost 42% of university students screened positive for at least one lifetime possible mental disorder, with MDE and GAD disorders being the most prevalent. These findings were slightly lower to previous study in Spain which found high levels of depression and anxiety (55.6% and 47.1%, respectively) in university students (Balanza et al., 2009). On the other hand, prevalence estimates were slight higher to the results found in a cross-national study (overall prevalence: 35.3% lifetime, 31.4% 12-months) (Blanco et al., 2008). Gender differences in prevalence of mental disorders were found in our study. In concordance with previously studies (Auerbach et al., 2018b; McLafferty et al., 2017; Vázquez et al., 2011), females had higher prevalence of mood and anxiety disorders and males had higher prevalence of substance use disorders. Persistence was roughly 80% for almost all possible mental disorders, which was higher than persistence found in a previous Spanish study among university students (42.2%) (Vázquez et al., 2011). The age-of-onset found in our study was between 14 and 19 ages, a younger age to those reported for the general population (anxiety disorders:25–53, mood disorders: 25–45, and substance disorders:18–29)(Kessler et al., 2007). Such differences should be interpreted cautiously as they could be influenced by the restricted age range of our sample (18-24 years) (de Girolamo et al., 2012).

Findings show that about 20% of students with one possible mental disorder report severe role impairment, which is lower than the rates of 25-30% described in previous studies (Alonso et al., 2018; Klemenc-Ketis et al., 2011; Verger et al., 2010). The disorder most strongly associated with severe role impairment in our study was PD, although PD showed low prevalence estimates both lifetime and 12-month. This high association of PD with severe role impairment was also found in clinical samples (Barrera and Norton, 2009; Lochner et al., 2003). Another interesting finding is that 31.2% of Adult ADHD cases reported impairment, showing statistically significant association in the bivariate analyses (OR=2.5; CI95%=1.9-3.4). It is likely that these results are due the direct effect being diluted by the presence of other mental disorders (Jacob et al., 2007). These results could be cautiously interpreted that in a student with a mental disorder and its related impairment, a comorbid disorder adds the impairment expected for this latter disorder if it happened in isolation. These results are in contrast with than those reported by Alonso et al. (2018) but in the same direction, pointing to the fact that comorbidity is highly disabling.

Only 12.6% of first year students with a possible mental disorder received any treatment in the last 12-months. These results are similar to findings reported in previous studies (Bruffaerts et al., 2019; Hunt and Eisenberg, 2010; Verger et al., 2010). According to a recent study by Bruffaerts et al. (2018), anxiety disorders are the most frequently treated among university population. The associations of specific disorders are similar to those of the previous study (Bruffaerts et al., 2019) which rates vary across types of mental disorders. Again, PD presents the highest treatment rate, requiring in-depth study in our Spanish sample in further longitudinal analyses. Substance use disorders and Adult ADHD are not significantly associated with receiving treatment. It might be possible that university students were receiving treatment for another emotional problem, as reported in previous studies (Bruffaerts et al., 2019; Hunt and Eisenberg, 2010). Finally, we observed subadditive effects of multiple disorders associated with mental health treatment, suggesting that the comorbidity of possible mental disorders does not imply a greater perceived need for treatment than it could expect for each disorder (Bruffaerts et al., 2019).

This study identified a number of sociodemographic and university-related variables that are associated with 12-month mental disorders, which have been reported in previous studies (Auerbach et al., 2018b; Balanza et al., 2009; Wicki et al., 2010). Having parents with low educational level was a significant correlate of 12-month mental disorders. These results would be in agreement with previous findings of more prevalent among students from low-income families (Eisenberg et al., 2013; Said et al., 2013; Vázquez et al., 2011). In our study, living outside the parents' house was found to be associated with substance disorder, which could be partially explained by lower parental control (Caamaño-Isorna et al., 2008; Wicki et al., 2010). The association between non-heterosexual orientation and mental disorders that we found is in agreement with previous reports (Auerbach et al., 2018b; Kisch et al., 2005; Said et al., 2013), and might be attributed in part to the additional stress that non-heterosexual people experience (Oswalt and Wyatt, 2011; Przedworski et al., 2015).

Limitations

Our findings should be considered in light of several limitations. The first set of limitations could limit the generalizability of results. A convenience sample of universities was used; however, the basic socio-demographic characteristics of the students in the participating universities were very similar to all Spanish universities (results available upon

request). Also, the fact that the sample included only first-year university students could affect the generalizability of the results to the larger community of university students. Low response rates may have caused non-response bias, including incomplete coverage of the target population (Brick, 2013) that affects the generalizability of our results. But this possible bias was minimized by combining population-based adjustments through post stratification with a specific end-game strategy, a combination that resulted in the use of inverse-probability weights in the analyses to restore population representativeness. Another limitation is the fact that monetary incentives were offered in our sample. It has been reported that monetary incentives may encourage the participation of individuals who would not otherwise be motivated to respond, thus improving the representativeness of the sample (Singer and Ye, 2013). Nevertheless, we cannot rule out that such incentive could be a possible source of bias (Moyer and Brown, 2008). The assessment of mental disorders was based on self-reports, not in-depth clinical interviews, which may have diminished the validity of the diagnoses. However, a clinical reappraisal was carried out showing good concordance with blinded clinical diagnoses using the Mini-International Neuropsychiatric Interview (Ballester et al., 2019). The adapted version of the SDS used in our study did not differentiate the physical or mental health conditions that caused the impairment but, according to an earlier study (Ormel et al., 2008), only a small sample reported an impairment of the SDS due to physical conditions. Finally, our data are cross-sectional which prevents interpreting associations presented as causal.

Implications

Despite these limitations, the current study provides relevant information on the high prevalence of mental disorders among Spanish university students and their association with impairment. In addition, this study provides evidence of the low mental health treatment rates. Results suggest the need for conducting a longitudinal monitoring of common mental disorders among university students. This information could allow early identification of those who might benefit from health services. Such monitoring might provide the bases for implementing effective prevention interventions among first-year students (Ebert et al., 2017) to improve mental health during their university years and beyond, as well as, allowing an improvement of mental health services offered.

Author contributions

Jordi Alonso had full access to all of the data in this study and takes responsibility for the integrity of the data, and the accuracy of the data analysis.

Study concept and design: Ballester, L., Alayo, I., Vilagut, G., and Alonso, J.

Acquisition of data: Ballester, L., Vilagut, G., Alayo I., Almenara, J., Blasco, M.J., Barbaglia, G., Castellví, P., Cebrià, A.I., Echeburúa, E., Gabilondo, A., Gili, M., Iruin, A., Lagares, C., Miranda-Mendizábal, A., Parès-Badell., O., Pérez-Vázquez, M.T., Piqueras, J.A., Roca, M., Rodríguez-Marín, J., Sesé, A., Soto-Sanz, V., Vives, M., and Alonso, J.

Statistical analysis and interpretation of data: Ballester, L., Vilagut, G., Alayo, I., Alonso, J.

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Critical revision of the manuscript for important intellectual content: Vilagut, G., Alayo, I., Almenara, J., Blasco, M.J., Cebrià, A.I., Echeburúa, E., Gabilondo, A., Gili, M., Lagares, C., Piqueras, J.A., Roca, M., Bruffaerts, R., Mortier, P., Auerbach, R.P., Nock, M.K., Kessler, R.C., and Alonso, J.

Data availability statement

The data that support the findings of this study are available from the corresponding author, J.A., upon reasonable request.

Conflict of interest

In the past 3 years, Dr. Kessler received support for his epidemiological studies from Sanofi Aventis; was a consultant for Johnson & Johnson Wellness and Prevention, Shire, Takeda; and served on an advisory board for the Johnson & Johnson Services Inc. Lake Nona Life Project. Kessler is a co-owner of DataStat, Inc., a market research firm that carries out healthcare research. Dr. Roca received research funds from Lundbeck and Janssen.

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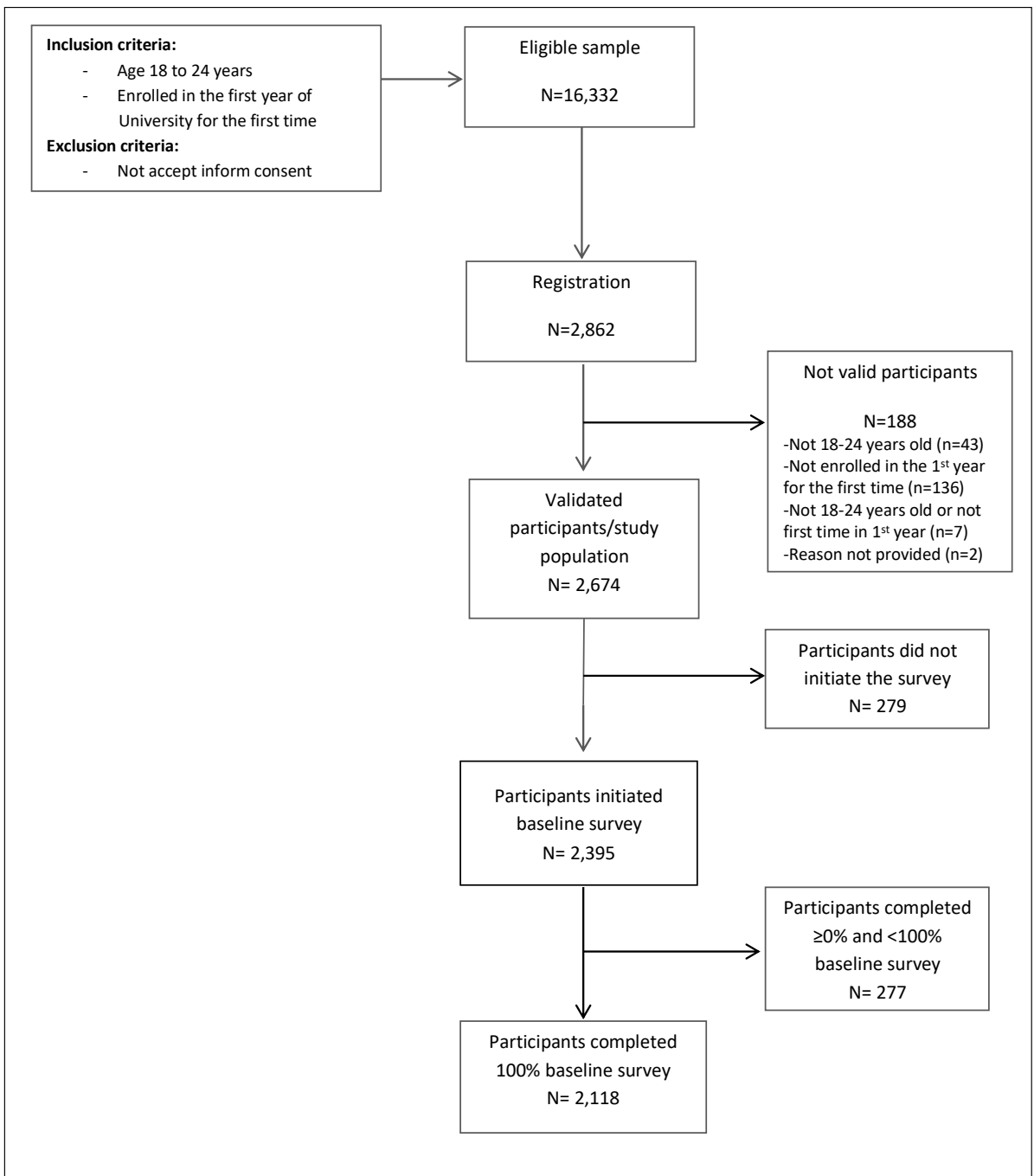
Figure 1. Flow diagram of the study sample. The *UNIVERSAL* (University and Mental Health) project.

Table 1. Description of the students included in the analysis (absolute numbers and weighted proportions)

	Total Sample (n=2,118)		Male (n= 582)		Female (n=1,536)	
	n	%	n	%	n	%
Socio-demographics						
Age						
18	1506	62.1	387	59.6	1119	64.1
>18	612	37.9	195	40.4	417	35.9
Country of birth						
Spain	2005	97.1	551	97.3	1454	97
Other	113	2.9	31	2.7	82	3
Parents University Studies						
At least one	952	42.7	273	44.5	678	41.4
Neither	1166	57.3	309	55.5	858	58.6
Parents separated or divorced						
Yes	369	13.8	82	10.9	287	16.2
No	1749	86.2	500	89.1	1249	83.8
Religion						
Christian	766	40.2	192	38.6	574	41.5
No religion	1306	58.0	377	59.5	929	56.8
Another religion	46	1.8	13	1.8	33	1.7
Place raised						
Large city/Small city	1373	66.1	404	68.7	969	64
Suburbs	99	5.2	26	4.5	73	5.9
Town/village/ rural area	645	28.7	152	26.8	493	30.2
Sexual orientation						
Heterosexual	1882	89.3	497	87.9	1385	90.4
Non-heterosexual	236	10.7	85	12.1	151	9.6
University socio-demographics						
University						
Balearic Islands University (UIB)	300	12.3	62	11.5	238	13
Basque Country University (UPV-EHU)	642	43.9	188	45.9	454	42.2
Cadiz University (UCA)	299	19.7	89	19.2	210	20
Miguel Hernandez University (UMH)	292	10.6	106	11.7	186	9.8
Pompeu Fabra University (UPF)	585	13.5	137	11.7	448	15
Academic Field						
Arts and Humanities	242	9.8	29	7	213	12
Engineering and Architecture	203	8.4	75	8.9	128	8
Health Sciences	543	15.7	116	10	427	20.2
Science	291	18.6	170	31.8	121	7.9
Social and Legal Sciences	839	47.6	192	42.3	647	51.8
Living at first term						
Parents' home	1193	56.2	344	60.5	849	52.8
Other	925	43.8	238	39.5	687	47.2

Table 2. Lifetime and 12-month prevalence, and persistence of mental disorders by gender in the UNIVERSAL study (n= 2,118)

	Lifetime prevalence							12-month prevalence							Persistence[f]						
	Total %	(SE)	Male %	(SE)	Female %	(SE)	F (ndf, ddf)[g]	Total %	(SE)	Male %	(SE)	Female %	(SE)	F (ndf, ddf)[g]	Total %	(SE)	Male %	(SE)	Female %	(SE)	F (ndf, ddf)[g]
Mental disorders																					
Major depressive episode	23.1	(0.92)	17.2	(1.23)	27.9	(1.31)	33.9 (1,1106324349)*	18.9	(0.85)	13.8	(1.12)	23.0	(1.23)	28.9 (1,5578023)*	81.4	(1.77)	80.0	(3.14)	82.2	(2.14)	0.3 (1,871896)
Broad mania	3.4	(0.42)	2.5	(0.51)	4.2	(0.63)	4.6 (1,14520)*	3.1	(0.4)	2.3	(0.49)	3.8	(0.60)	3.9	91.3	(1.80)	92.6	(2.30)	90.7	(2.14)	0.1 (1,428840)
Any mood disorder[a]	24.5	(0.94)	18.2	(1.26)	29.6	(1.34)	36.7 (1,984383)**	20.2	(0.88)	14.8	(1.16)	24.5	(1.26)	30.6 (1,13768)*	82.3	(1.73)	81.3	(3.06)	82.8	(2.34)	0.2 (1,42840)
Generalized anxiety disorder	19.3	(0.86)	11.7	(1.05)	25.3	(1.27)	62.6 (1,2121470)**	16.0	(0.80)	9.3	(0.97)	21.4	(1.20)	55.8 (1,67967)**	83.1	(1.78)	79.5	(3.63)	84.5	(2.02)	1.2 (1,823221)
Panic Disorder	2.5	(0.35)	1.7	(0.43)	3.1	(0.52)	4.2 (1,16944)*	2.0	(0.31)	0.8	(0.31)	2.9	(0.50)	11.3 (1,23551)**	80.5	(2.67)	49.2	(4.81)	94.1	(1.92)	13.3 (1,3162)**
Any anxiety disorder[b]	20.1	(0.88)	12.9	(1.10)	26.0	(1.29)	55.2 (1,428977)**	16.6	(0.82)	9.7	(0.99)	22.2	(1.22)	57.3 (1,46979)**	82.6	(1.81)	75.3	(3.75)	85.5	(1.92)	5.5 (1,)
Alcohol abuse or dependence	7	(0.56)	9.7	(0.97)	4.8	(0.63)	19.6 (1,1501642)**	6.7	(0.54)	9.3	(0.94)	4.6	(0.61)	18.3 (1,966250)**	95.2	(1.05)	95.0	(1.73)	95.5	(1.45)	0.1 (1)
Drug abuse or dependence	5.3	(0.5)	7.1	(0.86)	3.8	(0.57)	11.1 (1,15267)**	2.2	(0.33)	2.9	(0.57)	1.6	(0.39)	4.2 (1,5857)*	41.0	(2.71)	40.9	(4.22)	41.2	(3.83)	0.1 (1,19780)
Any substance use disorder[c]	11.1	(0.69)	15.1	(1.18)	7.8	(0.79)	27.0 (1,52216)**	8.0	(0.6)	11.0	(1.03)	5.5	(0.68)	20.2 (1,44271)**	71.9	(2.17)	72.7	(3.61)	70.7	(2.81)	0.1 (1,26280)
Attention deficit hyperactivity disorder[d]	11.2	(0.68)	9.6	(0.96)	12.5	(0.97)	4.5 (1,38342293)**	11.2	(0.68)	9.6	(0.96)	12.5	(0.97)	4.5 (1,38342293)	NA	NA	NA	NA	NA	NA	NA
Any mental disorder[e]	41.3	(1.08)	35.1	(1.57)	46.3	(1.47)	36.6 (1,122925)**	35.7	(1.05)	29.0	(1.5)	41.1	(1.45)	32.6 (1,87867)**	86.4	(1.58)	82.6	(3.06)	88.7	(1.76)	6.0 (1,6813)*
Number of disorders																					
One disorder	21.3	(0.9)	19.6	(1.31)	22.7	(1.24)	11.0 (3,176409)**	19.1	(0.87)	16.3	(1.23)	21.3	(1.21)	11.5 (3,984276)**	46.2	(2.28)	46.6	(3.97)	46.0	(2.78)	2.7 (3,11019)
Two disorders	11.7	(0.71)	8.3	(0.91)	14.6	(1.04)		11.0	(0.69)	8.0	(0.89)	13.4	(1.01)		26.6	(2.01)	22.7	(3.31)	28.9	(2.53)	
Three or more disorders	8.2	(0.6)	7.2	(0.85)	9.0	(0.84)		5.6	(0.51)	4.7	(0.69)	6.4	(0.73)		13.6	(1.56)	13.3	(2.68)	13.8	(1.93)	

a.-Any mood disorder: Major depressive episode or Broad mania; b.-Any anxiety disorder: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.-Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e.- Any mental disorder: Any mental disorder for the lifetime prevalence and 12-month prevalence, with the exception of ADHD with a prevalence of 6-month prevalence; f.- Persistence defined as 12-month prevalence among lifetime cases; g.-F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom. Raw p-value statistically significant after adjustment for multiple comparisons using Benjamini-Hochberg procedure with false discovery rate 0.05. *p-value <.05; **p-value<.01.

%: weighted proportions; SE: Standard error.

Table 3. 12-month mental disorders as predictors for 12-month of any severe role impairment (Sheehan Disability Scale) in the UNIVERSAL study (n=2,118)

Mental disorders	Any severe role impairment %	SE	Model 1 aOR (95% CI)	Model 1 F (ndf, ddf)[a]	Model 2 aOR (95% CI)	Model 2 F (ndf, ddf)[a]	Model 3 aOR (95% CI)	Model 3 F (ndf, ddf)[a]	Model 4 aOR (95% CI)	Model 4 F (ndf, ddf)[a]	Model 5 aOR (95% CI)	Model 5 F (ndf, ddf)[a]
Major depressive episode	38.0	2.44	2.4 (1.8-3.3)	32.5 (1,397744)**	--	--	--	--	2.5 (1.7-3.7)	21.1 (1,151995)**	2.7 (1.8-4.0)	24.1 (1,69424)**
Broad mania	45.8	6.5	1.8 (1.0-3.4)	3.8 (1,6130)	--	--	--	--	1.9 (0.9-4.1)	2.9 (1,9489)	1.9 (1.0-3.8)	3.4 (1,8352)
Generalized anxiety disorder	38.2	2.65	2.3 (1.6-3.2)	24.7 (1,101327)**	--	--	--	--	2.3 (1.5-3.6)	14.1 (1,52281)**	2.6 (1.6-4.0)	17.1 (1,27859)**
Panic Disorder	61.7	7.9	4.0 (1.9-8.5)	12.6 (1,3077)**	--	--	--	--	4.1 (1.8-9.7)	10.8 (1,4976)**	4.2 (1.9-9.4)	12.5 (1,4872)**
Alcohol abuse or dependence	25.4	3.67	1.8 (1.1-2.8)	5.6 (1,271176)*	--	--	--	--	1.8 (1.3-3.6)	4.9 (1,177513)*	1.9 (1.1-3.1)	6.0 (1,241339)*
Drug abuse or dependence	26.9	6.67	0.8 (0.3-1.8)	0.4 (1,11830)	--	--	--	--	0.8 (0.3-2.0)	0.2 (1,15399)	0.8 (0.3-2.0)	0.2 (1,6626)
Attention deficit hyperactivity disorder	31.2	3.02	1.3 (0.9-1.9)	2.1 (1,260028)	--	--	--	--	1.3 (0.8-2.2)	1.4 (1,169988)	1.4 (0.9-2.3)	2.2 (1,51547)
Number of disorders (continuous)			--	--	2.0 (1.8-2.2)	134.2 (1,152112)**	--	--	1.0 (0.6-1.5)	0.0 (1,52310)	--	--
Number of disorders												
One disorder	19.7	2.01	--	--	--	--	2.1 (1.5-2.9)	43.9 (3,155194)**	--	--	--	--
Two disorders	33.6	3.13	--	--	--	--	3.9 (2.7-5.5)		--	--	0.8 (0.4-1.4)	0.5 (2,30081)
Three or more disorders	52.8	4.63	--	--	--	--	9.0 (5.9-13.7)		--	--	0.8 (0.3-2.1)	
AUC				0.735		0.736		0.736		0.735		0.736
AIC				1729.4		1737.1		1748.0		1731.3		1732.3

a.-F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom.
*p-value <.05; **p-value<.01.
All models are adjusted for the predictors shown in the rows, socio-demographic (gender, age, parental educational level, parental marital status, religion, place raised, and sexual orientation) and university predictors (university, academic field and first-term living location during the university period).
%: weighted proportions; SE: Standard error; aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; AIC: Akaike information criterion

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Table 4. 12-month mental disorders as predictors for 12-month treatment in the UNIVERSAL study (n=2,118)

	Any treatment		Multiple model	
	%	SE	aOR (95%CI)	F (ndf, ddf)[a]
Mental disorders				
Major depressive episode	16	1.83	3.4 (1.8-6.4)	14.6 (1, 32542)**
Broad mania	16.1	4.69	1.7 (0.6-4.9)	1.1 (1, 1316)
Generalized anxiety disorder	20.1	2.2	7.4 (3.7-14.8)	32.7 (1, 4974)**
Panic Disorder	35.3	7.6	4.3 (1.7-10.8)	9.6 (1, 10790)**
Alcohol abuse or dependence	7.6	2.35	1.1 (0.5-2.5)	0.1 (1, 411338)
Drug abuse or dependence	10.7	4.62	2.7 (0.8-9.2)	2.4 (1, 11102)
Attention deficit hyperactivity disorder	10.3	1.97	1.7 (0.8-3.4)	2.0 (1,19327)
Number of disorders (continuous)			--	--
Number of disorders (categorical)				
One disorder	7.6	1.36	--	--
Two disorders	19.0	2.64	0.6 (0.3-1.5)	3.9 (2, 8786)*
Three or more disorders	18.0	3.61	0.2 (0-0.7)	
AUC				0.805
AIC				798.0

a.-F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom.

*p-value <.05; **p-value<.01.

All models are adjusted for the predictors shown in the rows, socio-demographic (gender, age, parental educational level, parental marital status, religion, place raised, and sexual orientation), university predictors (university, academic field and first-term living location during the university period) and impairment.

%: weighted proportions; SE: Standard error; aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; AIC: Akaike information criterion

5.4. Article 4. Predictive models for first-onset and persistence of depression and anxiety among university students

Predictive models for first-onset and persistence of depression and anxiety among university students

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Highlights

- 13.3% students had first-onset of MDE and/or GAD at 12-month follow-up

- Among students with baseline MDE and/or GAD, 46.7% persisted at 12-month follow-up

- Strongest predictors were lifetime symptoms of MDE-GAD and prior suicidal ideation

- Multivariable models provided AUCs 0.76-0.81 to predict first-onset and persistence

- 74.9% onset MDE-GAD cases occur in 30% students at highest predicted baseline risk

List of abbreviations

Adjusted Odd Ratio (aOR)

Adult ADHD Self-Report Scales (ASRS)

Akaike's information criterion (AIC)

Alcohol Use Disorders Identification Test (AUDIT)

Area under the Curve (AUC)

Attention-deficit/hyperactivity disorder (ADHD)

Balearic Islands University (UIB)

Basque Country University (UPV-EHU)

Cádiz University (UCA)

Composite International Diagnostic Interview Screening Scales (CIDI-SC)

Confidence Interval (CI)

Generalized anxiety disorder (GAD)

International Test Commission (ITC)

Inverse-probability weighting (IPW)

Major Depressive Episode (MDE)

Major Depressive Episode and/or Generalized Anxiety Disorder (MDE-GAD)

Miguel Hernández University (UMH)

Multiple Imputation (MI)

Odd Ratio (OR)

Pompeu Fabra University (UPF)

Sheehan Disability Scale (SDS)

Standard Error (SE)

Standard Deviation (SD)

World Mental Health International College Student initiative (WMH-ICS)

Abstract

Background: Depression and anxiety are both prevalent among university students. They frequently co-occur and share risk factors. Yet few studies have focused on identifying students at highest risk of first-onset and persistence of either of these conditions.

Methods: Multicenter cohort study among Spanish first-year university students. At baseline, students were assessed for lifetime and 12-month Major Depressive Episode and/or Generalized Anxiety Disorder (MDE-GAD), other mental disorders, childhood-adolescent adversities, stressful life events, social support, socio-demographics, and psychological factors using web-based surveys; 12-month MDE-GAD was again assessed at 12-month follow-up.

Results: A total of 1,253 students participated in both surveys (59.2% of baseline respondents; mean age=18.7 (SD= 1.3); 56.0% female). First-onset of MDE-GAD at follow-up was 13.3%. Also 46.7% of those with baseline MDE-GAD showed persistence at follow-up. Childhood/Adolescence emotional abuse or neglect (OR= 4.33), prior bipolar spectrum disorder (OR= 4.34), prior suicidal ideation (OR=4.85) and prior lifetime symptoms of MDE (ORs=2.33-3.63) and GAD (ORs=2.15-3.75) were strongest predictors of first-onset MDE-GAD. Prior suicidal ideation (OR=3.17) and prior lifetime GAD symptoms (ORs=2.38-4.02) were strongest predictors of MDE-GAD persistence. Multivariable predictions from baseline showed AUCs of 0.76 for first-onset and 0.81 for persistence. 74.9% of first-onset MDE-GAD cases occurred among 30% students with highest predicted risk at baseline.

Limitations: Self-report data were used; external validation of the multivariable prediction models is needed.

Conclusion: MDE-GAD among university students is frequent, suggesting the need to implement web-based screening at university entrance that identify those students with highest risk.

Keywords: depression, anxiety, epidemiology, universities, prediction, high risk.

DISCUSSION

6. DISCUSSION

6.1. Summary and discussion of results by objectives

In order to provide evidence about the frequency of mental disorders, as well as the role impairment and use of mental health treatments in Spanish university students, we studied mental health among university students that participated in a longitudinal study named UNIVERSAL project. Also, a clinical reappraisal was carried out to evaluate the accuracy of this online survey as a useful tool for screening mental disorders. The findings obtained from four specific articles contribute to respond to the objectives of this thesis.

First, we explored the diagnostic accuracy of an online screening survey for measuring common mental disorders (major depressive episode, mania/hypomania, panic disorder, generalised anxiety disorder and alcohol use disorder), and suicidal thoughts and behaviours, using data from the clinical reappraisal sub-study (**articles 1 and 2**). Then, we described the frequencies of mental disorders in the university context with longitudinal data obtained through the UNIVERSAL online survey (**articles 3 and 4**). We also studied the association of mental disorders with role impairment and the use of mental health treatment (**article 3**) as well as the association of risk and protective factors with the onset and persistence of depression and/or generalised anxiety disorder (**article 4**).

Findings reported in these articles contribute to acknowledge the topics presented on the specific objectives of this thesis. These results are summarised and discussed below.

1. **Is the online screening survey accurate to measure common mental disorders?**

Summary of findings

The first specific objective was addressed with data from the clinical reappraisal study in order to assess the accuracy of the online screening measures.

According to the online survey screeners and the Mini International Neuropsychiatric Interview (MINI), the weighted prevalence estimates showed statistically significant differences for most disorders; finding a higher prevalence on the online screening scales. For 12-month mood and anxiety disorders, sensitivity (SN)/specificity (SP) were 67%/88.6% and 76.8%/86.5%, respectively. For specific mental disorders, SN/SP for 12-month major depressive episode were 70.8%/89.6% and for generalised anxiety disorder, 100%/86.2%. The lowest SN was found for 12-month mania/hypomania (33.6%) and panic disorder (19%). Positive predictive values (PPV) ranged from 8.4% to 55.1%, while negative predictive values (NPV) ranged from 90.2% to 100%. Accuracy analyses for alcohol use disorder showed SN/SP for alcohol abuse/dependence of 33.9%/86.3% and for alcohol dependence, 56.0%/97.5%. Regarding alcohol risk-drinking categories, SN/SP for moderate-risk consumption were 76.2%/78.9%.

The individual-level concordance of the online survey was fair to substantial (Area Under the Curve-AUCs ranging from 0.70 to 0.90); with the exception of lifetime mania/hypomania and lifetime and 12-month panic disorder, which results were suboptimal (AUC<0.6). The AUCs for risk-drinking categories ranged from 0.70 to 0.90 and the AUC for alcohol dependence was 0.77. Lower AUCs were found for alcohol abuse/dependence and binge drinking. In order to improve the diagnostic capacity for major depressive episode, mania/hypomania, generalised anxiety disorder and panic disorder, a

sensitivity analysis was carried out. When SN was prioritized, an increase of prevalence was found together with an improvement of concordance for all disorders (AUCs>0.80). When prevalence was prioritised, a slight increase of PPV and lower values of SN and AUC were obtained.

Discussion

As expected in our initial hypotheses, the instruments administered in the UNIVERSAL study showed, overall, adequate concordance with the MINI for screening mental disorders and suicidal thoughts and behaviours. Although the screening scales tend to overestimate the prevalence, we found acceptable SN and SP values, and substantial AUC for 12-month major depressive episode, generalised anxiety disorder and alcohol dependence. Also, it was possible to find a substantial concordance for suicidal thoughts and behaviours.

These results were comparable, in general, to those found in **previous studies of the CIDI** showing good concordance with clinical diagnoses of mood and anxiety disorders (Haro et al., 2006; Kessler, Calabrese, et al., 2013; Kessler, Santiago, et al., 2013). However, a quite lower individual-level concordance was found for the most part, in comparison with previous CIDI studies conducted among army personnel, primary care patients and the general population, which found moderate to substantial concordance (AUC=0.70-0.89) (Haro et al., 2006; Kessler, Calabrese, et al., 2013; Kessler, Santiago, et al., 2013). Also, the disaggregated operating characteristics of the CIDI (SN, SP and NPV) were similar to other validated web-based screening instruments (Donker, Straten, Marks, & Cuijpers, 2009; Farvolden, McBride, Bagby, & Ravitz, 2003; Lin et al., 2007), except lower PPVs in our study. However, it has been argued that predictive values (PPV and NPV) of a study cannot be generalised due to their relationship with the prevalence of the disease (Vetter, Schober, & Mascha, 2018).

The operating characteristics for **alcohol risk-drinking and alcohol dependence** were similar to the results of validation studies carried out in the United States (DeMartini & Carey, 2012; Kokotailo et al., 2004), but slightly lower than in a previous Spanish validation study among university students (García Carretero et al., 2016). Also, the AUC for identifying alcohol consumption categories was similar to those obtained in previous Spanish validation studies (García-Carretero et al., 2016; Rubio, Bermejo, Caballero, & Santo-Domingo, 1998), but the AUC for detecting binge drinking indicated a lower accuracy (Cortés et al., 2016, 2017). In our study, binge drinking was defined as a dichotomous variable obtained with the third question of the AUDIT: "*How often do you have six or more alcoholic drinks at a single sitting?*" (Saunders et al., 1993) that was modified to five or more drinks for both genders. This lower AUC could support the recommendation to change the criteria to identify binge drinking using the full AUDIT score (Cortés et al., 2016, 2017), decreasing the third item of the AUDIT to four or more drinks for women (Kokotailo et al., 2004) or using the AUDIT-C (Cortés et al., 2017).

An important topic of discussion regarding to the selection of the optimal cut-off point is that the cut-off decision may change depending on the specific purpose of the study. Different purposes could be the clinical practice (e.g., for diagnostic confirmation) or epidemiological research (e.g., for prevalence estimation). (Kessler, Santiago, et al., 2013). In the field of clinical practice, instruments are mainly used to select cases for treatment more in-depth, and it can be more relevant achieving high sensitivities (Kessler et al., 2009). In epidemiological research, on the other hand, it could be more important to obtain unbiased estimates of the prevalence of disease to allow the monitoring of prevalence trends. In this thesis, sensitivity analyses found different results on the operating characteristics, as shown above, depending on whether sensitivity or unbiased prevalence prevail. However, since the post hoc derivation of a diagnostic cut-off point can introduce a bias in the validity of the

diagnostic test, it would be necessary to reproduce these analyses in other samples and countries.

In conjunction, the results of this thesis highlight the importance of validating web-based instruments to ensure that they have optimal psychometric properties to measure outcomes in research. Web-based questionnaires have become an important tool in the collection of epidemiological data, especially for the recruitment and follow-up of large cohorts. While some studies have evaluated the diagnostic accuracy of online instruments for mental disorders, these have targeted general populations or clinical samples (Donker et al., 2009; van Gelder et al., 2010). Web-based instruments could facilitate the implementation of health programs on university campuses to diminish the impact of mental disorders in this population, which is the first step to obtain information about mental health and then, to facilitate the implementation of preventive interventions among university students.

2. What is the frequency (prevalence, incidence, persistence) of mental disorders in Spanish university students?

Summary of findings
In the cross-sectional (baseline) evaluation, we found that nearly 42% of university students (n=2,118) screened positive for any lifetime mental disorder (i.e., major depressive episode, mania/hypomania, generalised anxiety disorder, panic disorder, alcohol use disorder, drug use disorder and adult attention-deficit/hyperactivity disorder). The 12-month prevalence of any mental disorder was 35.7%, while the major depressive episode (18.9%) and generalised anxiety disorder (16.0%) were the most prevalent disorders at 12-month. Overall, 11.0% of students experienced two disorders and 5.6%, three or more disorders, in the 12-months previous to the assessment.

At the 12-month follow-up, a total of 24.9% of students (n=1,253) had major depression (MDE) and/or generalised anxiety disorder (GAD). Among students who had no history of MDE-GAD (n=794), 13.3% had first-onset MDE-GAD during their first academic year. Meanwhile, among students who had a history of MDE-GAD (n=459), 46.7% also had MDE-GAD during the first year of university (persistence).

Discussion

Findings on **prevalence** of mental disorders in Spanish **university students** were consistent with previous epidemiological studies supporting that common mental disorders among this group of population are frequent (Auerbach et al., 2016; Eisenberg, Gollust, et al., 2007; Pedrelli et al., 2015; Said, Kypri, & Bowman, 2013; Verger et al., 2010). However, direct comparisons with national and international studies are not possible due to differences in the measures used (e.g., CIDI, Patient Health Questionnaire-PHQ, Structured Clinical Interview for DSM-IV Axis I-SCID), in their time frames (12-month vs. current), in the mode of administration of the survey (interviewer vs. self-administered) and in the study design (e.g., single-centre, multicentre or cross-national).

In Spain, a previous cross-sectional study among female university students reported a lifetime prevalence of any mental disorder (including 20 mental disorders) of 50.8% and a current prevalence of 37.3% (Vázquez et al., 2011). Also, Vázquez et al. (2011) found depression and generalised anxiety disorder as the most common disorders, after nicotine dependence, similar to our results. For specific disorders, there are no comparable rates in Spain because cross-sectional studies were based on different measures (Goldberg's Anxiety and Depression Scale; Structured Clinical Interview for DSM-IV Axis I) and different characteristics of the sample (e.g., single-centre, female sample), finding a wide range of reported prevalence estimates (5.3%-55.6% for MDE

and 2.7%-47.1% for GAD) (Balanza, Morales, & Guerrero, 2009; Vázquez & Blanco, 2008; Vázquez et al., 2011).

Internationally, the cross-national study from the WMH-ICS, with data from 8 countries, found similar prevalence estimates to our results with a lifetime prevalence of any mental disorder (adult ADHD not included) of 35.3% and a 12-month prevalence of 31.4% (Auerbach et al., 2018). However, our prevalence estimates were slightly higher to the results found in a study conducted in the US (lifetime prevalence: 35.3%; 12-months: 31.4%) (C. Blanco et al., 2008). Regarding the prevalence of specific disorders, previous studies also found MDE and GAD as the two most common disorders (Auerbach et al., 2016, 2018). It seems necessary to implement screening and intervention prevention programs, which have been shown to be effective for preventing the onset of full mental disorders and reducing symptoms (Andersson & Cuijpers, 2009; Buntrock et al., 2016; Davies, Morriss, & Glazebrook, 2014; Josephine, Josefine, Philipp, David, & Harald, 2017).

Our **longitudinal analyses** show a high frequency of first-onset of MDE-GAD and persistence of MDE-GAD. Our results are not directly comparable with previous research due to the aggregation of MDE and GAD in our study. Previous longitudinal studies among university students and young adults have reported lower disaggregate incidence rates for MDE of 6.9% and for GAD of 4.3% (Auerbach et al., 2016; Beesdo, Pine, Lieb, & Wittchen, 2010; Ebert, Buntrock, et al., 2019). Also, in a sample of adolescents, the 8-year incidence of MDE was 12.9% and of GAD, 1.6% (Benjet et al., 2016). In relation to persistence rates, a previous study among university students found an MDE persistence of 26.9% and for GAD of 30.4%, but a study among adolescents found higher persistence rates (70.2% and 51.2%, for MDE and GAD respectively)(Kessler et al., 2012; Zivin et al., 2009). In general, these apparently high incidence rates could suggest that university period might

have a peak for the onset of mental disorders (Auerbach et al., 2018; Eisenberg, Gollust, et al., 2007) albeit evidence on incidence rates is scarce and more research is needed to compare our results in other countries.

Higher prevalence estimates among university students compared to the general population have been found in other countries (Adlaf, Gliksman, Demers, & Newton-Taylor, 2001; Ibrahim et al., 2013; Stallman, 2010). A systematic review on depression by Ibrahim et al. (2013) found higher mean prevalence rates of depression among university students than in the community-based studies (Ibrahim et al., 2013). In the **general Spanish population**, results from ESEMeD and PEGASUS-Murcia studies showed 12-month prevalence of any mental disorder (including a large number of mental disorders) of 8.4% and 16.3%, respectively. In our study, 12-month prevalence estimates were considerably higher than those in general population studies, which found the following rates: 3.9%-5% for MDE, 0.5%-3%for GAD, 0.6%-0.7% for panic disorder, as well as 0.7%-0.9% for alcohol use disorder and 1.0% for substance use disorder (Haro et al., 2006; Navarro-Mateu et al., 2015). However, the mode of administration of the questionnaire (by interviewers vs. self-reported web-based) could limit their comparability. Further investigation of the differences between prevalence estimates over time is required to discern the results produced by changes in the trends or methodological issues. As suggested in previous studies (Mojtabai, Olfson, & Han, 2016; Twenge, Cooper, Joiner, Duffy, & Binau, 2019; Twenge, Joiner, Rogers, & Martin, 2018), these differences could reflect a change in the trends meaning that more young people are suffering mental disorders in the last decade, which implies the need for development of specific interventions for younger cohorts. In addition, all these results reported here were estimated in developed countries, so it is necessary to compare these rates with low- and middle-income countries.

In the comparison among university students and other groups of **young people,** the study published by Blanco et al. (2008) reported similar rates of mental disorders among university students and non-students youngsters (C. Blanco et al., 2008). Another cross-national study also found similar rates between individuals aged 18-22 who were university students, university attriters or non-students (Auerbach et al., 2016). Although in Spain we could not find a similar comparative study, the last report of the *Barómetro juvenil de vida y salud*, showed that 30% of young people declared that they have had or thought they had some kind of mental health problem during the last year (Barómetro juvenil de vida y salud, 2017), which could seem similar to the results we found among university students.

Comorbidity was present in 46.5% of the students who had 12-month mental disorders (12-month prevalence of 35.7%). On the overall sample, 11.0% of students experienced two disorders; while 5.6% of them, three or more disorders. Comorbidity rates around 40% were reported among university students who had mental disorders (Alonso et al., 2018; Auerbach et al., 2019; Vázquez et al., 2011; Verger et al., 2010). Among the Spanish general population, the ESEMED project, found mood disorders being the most comorbid (51.3%), followed by anxiety disorders (33.4%) and alcohol use disorders (23.4%)(Autonell et al., 2007). Similarly, international studies have found higher rates of lifetime comorbidity ranging from 45% to 56% (Alonso et al., 2004a; de Graaf, Bijl, Smit, Vollebergh, & Spijker, 2002).

Gender differences in the prevalence of mental disorders were reported in our study. In concordance with previous studies (Auerbach et al., 2018; McLafferty et al., 2017; Vázquez et al., 2011), females had a higher prevalence of mood and anxiety disorders, whereas males reported higher prevalence of substance use disorders.

Overall, the high rates of common mental disorders found in our study highlight the relevance of mental health as a public health concern among young people. It is well known that emerging adulthood is a crucial period of development (Sussman & Arnett, 2014) during which 75% of common mental disorders will have already appeared (de Girolamo et al., 2012; Kessler et al., 2007). The current study shows that the **age-of-onset** of mental disorders was between 14 and 19 years of age (taking into account a restricted age range of our sample, 18-24 years), in line with the literature that onset of mental disorders during youth is common. However, older age-of-onset has been found in the general population (de Girolamo et al., 2012).

3. Distributions of severe role impairment and mental health treatment among Spanish university students

Summary of findings

In the cross-sectional study, we found that around 30% of students with any 12-month mental disorder reported severe role impairment while among those without mental disorder, that figure was 10.2%. The highest rates of severe role impairment were found among students with panic disorder and mania/hypomania (61.7% and 45.8%, respectively). Severe impairment increased with the number of comorbid disorders (up to 52.8%). Multivariable logistic regression showed that MDE, GAD, panic disorder and alcohol use disorder were significantly associated with severe role impairment (median OR=1.8).

Regarding mental health treatment, only 12.6% of students with any 12-month mental disorder and 2.3% of those without mental disorder reported receiving treatment in the past 12 months. The highest rates of treatment were found among students with panic disorder and generalised anxiety disorder (35.3% and 20.1%, respectively). Treatment rates increased with increasing comorbidity. Multivariable logistic regression showed that MDE, GAD and panic

disorder as well as comorbidity were significantly associated with mental health treatment.

Discussion

Our results showed high rates of any **severe role impairment** among university students (20%), similar than the rate described in a cross-national study (Alonso et al., 2018), and the highest among those with any mental disorder (30%) which was slightly lower than previous international findings with rates in the range of 43%-52% (Alonso et al., 2018; Klemenc-Ketis et al., 2011; Verger et al., 2010). In particular, we found the highest rate among students with panic disorder, despite the fact that this disorder had a low prevalence in our study. Similar results among higher disability on panic disorder were reported in clinical samples (Barrera & Norton, 2009; Lochner et al., 2003), arguing these rates related to the inherent characteristic symptoms or comorbidity. However, in the multivariable logistic regression, students with MDE, GAD and alcohol disorder also showed a higher risk of disability. Another noteworthy finding was that rates of severe role impairment increased according to comorbidity of disorders. This was also found in a cross-national study (Alonso et al., 2018). Concretely, Alonso et al. (2018) reported a subadditive effect of individual disorders when taking into account the number of mental disorders (i.e., a comorbid disorder adds less impairment than expected for this disorder if it happened in isolation), which was not found statistically significant in our analyses.

We found significantly higher rates of severe role impairment among those with mental disorders than those without mental disorders. Also, we found positive associations between the number of mental disorders and severe role impairment. However, we cannot interpret that the overall disability rates were attributable solely to mental disorders. This is because, in our study, the measure of disability was generic, and makes no distinction between mental

and physical health. Previous studies on condition-specific disability among the general population showed that the highest rates were attributed to mental disorders rather than physical disorders (Ormel et al., 2008). Another critical issue to consider is that, while we report the results of any severe role impairment, it would be important to address the specific affected domains to reduce the impact of mental disorders. Recently, Alonso et al. (2018) reported that the highest levels of role impairment were for the domains of close relationships and social life (Alonso et al., 2018).

Our findings on role impairment point out the importance of detecting mental disorders among university students, not only because of their high frequency (as in the case of MDE and GAD) but also because of their substantial role impairment. Mental disorders have an important academic impact on university students (i.e., low academic performance, university attrition) (Auerbach et al., 2016). The deployment of preventive interventions could diminish their potential impact on academic performance.

Regarding the use of **mental health treatment**, in our study only a fifth of university students with mental disorders received treatment. Our finding is consistent with previous international studies among university students reporting treatment between 10% and 36% in the previous year (C. Blanco et al., 2008; Bruffaerts et al., 2019; Eisenberg, Hunt, Speer, & Zivin, 2011; Hunt & Eisenberg, 2010; McLafferty et al., 2017; Verger et al., 2010). Comparing university students and youth of 15-29 years of age in Spain, the publication *Barómetro juvenil de vida y salud* reported slightly higher results, showing a rate of 49.4% (Barómetro juvenil de vida y salud, 2017). Notwithstanding, a study carried out in the US by Blanco et al. (2008) found no differences in treatment rates between university students and non-students with mood and anxiety disorders. In relation to the general population, results were lower than those found in Spain (35%) (Codony et al., 2007) and in international studies in

Europe and the US (Alonso et al., 2004b; Wang et al., 2005). However, the differences could be given by the mode of administration of the surveys (face-to-face interviews) and the questions regarding the use of services.

Treatment rates were higher among students with anxiety disorders, in line with previous findings reported in the US and cross-nationally (Bruffaerts et al., 2019; Eisenberg et al., 2011). In the multivariable regression model, anxiety disorders (panic disorder and GAD) also yielded the highest adjusted odds for treatment. Although in general population (15-year-olds and older) studies have reported mood disorders as the most treated disorders (Wang, Angermeyer, et al., 2007; Wang, Berglund, Olfson, & Kessler, 2004); at disorder-specific level, higher rates on the use of healthcare services have been found previously for panic disorder, which might be partly explained by its physical symptomatology and greater distress (Katon, Von Korff, & Lin, 1992; Mackenzie, Reynolds, Cairney, Streiner, & Sareen, 2012; Roy-Byrne et al., 1999). Regarding treatment rates associated with comorbidity, these were greater according to severity (Katon et al., 1992; Mackenzie et al., 2012; Merikangas et al., 2011; Roy-Byrne et al., 1999) but we found a subadditive effect of multiple disorders associated with mental health treatment, suggesting that the comorbidity of mental disorders does not represent a greatest perceived need for mental health treatment (Bruffaerts et al., 2019).

Several barriers in seeking help have been reported and could be responsible for a low rate of treatment use, such as lack of time, lack of knowledge on available services or perceived stigma (Czyz, Horwitz, Eisenberg, Kramer, & King, 2013; Eisenberg, Golberstein, et al., 2007). Recently, a cross-national study by Ebert et al. (2019) suggested that attitudinal barriers were more important reasons than structural barriers for not seeking help (Ebert, Mortier, et al., 2019). Accordingly, specific programs will be needed to reduce these barriers and at the same time, to increase the use of mental health treatment

(Gulliver, Griffiths, Christensen, & Brewer, 2012) as well as to promote web-based interventions to attract those students who would not use traditional mental health services (Lattie et al., 2019).

4. Risk and protective factors associated with the onset and persistence of major depressive episode and/or generalised anxiety disorder

Summary of findings

Many risk factors were associated with first-onset of MDE-GAD (ORs=1.12–4.85) and persistence of MDE-GAD (ORs=1.31-4.02), with the magnitude of associations being generally higher with the onset of MDE-GAD. The strongest predictors for first-onset of MDE-GAD were childhood/adolescent emotional abuse or neglect, any childhood/adolescent adversity, current severe stress in any area of life; baseline 12-month mania/hypomania, baseline 12-month suicidal ideation and lifetime MDE and GAD symptoms. The strongest predictors for persistence of MDE-GAD were: any 12-month stressful event, baseline 12-month suicidal ideation and lifetime GAD symptoms. Regarding the protective factors examined, significant negative associations were found for perceived support, coping strategies and positive expectations with the onset and persistence of MDE-GAD.

The multivariable baseline prediction models had cross-validated AUCs of 0.76 for predicting first-onset of MDE-GAD, and 0.81 for predicting persistence. Considering the 30% of students at the highest baseline predicted risk for first-onset of MDE-GAD would include 74.9% (SE = 6.34) of all observed cases. On the other hand, the 30% of students at the highest baseline predicted risk of persistent MDE-GAD would include 54.6% (SE=6.23) of all observed cases.

Discussion

MDE and GAD are often comorbid disorders and share common risk factors (Barlow et al., 2016; Garber & Weersing, 2010; Gorman, 1996; Kessler et al., 2008; Kotov, 2011; Moffitt et al., 2007). Given the evidence of commonalities between these disorders, a debate has been raised questioning whether they are in fact empirically separate diagnostic entities. Transdiagnostic approaches have been proposed in the literature, suggesting latent factors underlying the covariance of depression and anxiety as emotional distress disorders (Clark & Watson, 2006; Kotov, 2011; Krueger & Eaton, 2015). According to this framework, our study shows that a wide range of risk and protective factors are associated with MDE and/or GAD including: childhood/adolescent adversities, social support, recent stressful events, psychological factors, prior mental health problems and prior symptomatology (Brackney & Karabenick, 1995; Crockett et al., 2007; Galatzer-Levy et al., 2012; Horwath, 1992; Kessler et al., 2002, 2008; McLafferty et al., 2019; Riskind et al., 1987; Rueter et al., 1999; Spinhoven et al., 2010; van Voorhees et al., 2008).

The results of our study point out that **childhood/adolescent adversities** are a strong predictor for first-onset of MDE-GAD, especially emotional abuse or neglect, as previously found (Gibb, Chelminski, & Zimmerman, 2007; Hammen, 2005; Spinhoven et al., 2010). It has been suggested that negative attributions are supplied by the abuser and then, this cognitive style could contribute to the depression vulnerability (Gibb et al., 2007). On the other hand, less childhood adversities were associated with persistence of MDE-GAD, which is in line with previous findings that report a reduced impact of stressful events on mental disorders according to the increase of the number of previous episodes (Kessler et al., 2008; McLaughlin, Green, et al., 2010). This might be explained by a kindling phenomenon, that is, a progressive neurobiological sensitisation where the occurrence of the disorder might increase the risk of the subsequent episode requiring lower levels of stressful events (Post, 2007). Increasing the

knowledge about the role of childhood adversities on mental disorders could improve interventions. Some proposed interventions, such as home visitation or parenting programs at school should be implemented during childhood and adolescence addressing the prevention of different maltreatment forms (M. Chen & Chan, 2016; Donelan-McCall, Eckenrode, & Olds, 2009; Hutchings, Griffith, Bywater, & Williams, 2017), or otherwise, at university entrance, some interventions could be tailored for university students who suffered childhood adversity experiences (Di Lemma et al., 2019; Korotana, Dobson, Pusch, & Josephson, 2016).

Another risk factor associated with both the onset and the persistence of MDE-GAD was the **lifetime symptoms of MDE and GAD**. Consistently, previous findings that reported a greater risk of developing a mental disorder among those who have had prior symptoms of this mental disorder (Fava & Tossani, 2007; Horwath, 1992; Liu et al., 2019). Regarding the first-onset of MDE-GAD, the majority of previous MDE and GAD symptoms were associated. These may correspond to subclinical syndromes, such as prodromal stages or subthreshold disorders (Murphy et al., 1989; Wolitzky-Taylor et al., 2014). Otherwise, regarding the persistence of MDE-GAD, we found that lifetime GAD symptoms predicted persistence of MDE-GAD with more magnitude than lifetime MDE symptoms. Some authors have argued that GAD would be considered a prodrome or a severity marker of MDE (Kessler et al., 2008; Wittchen, Hoyer, & Friis, 2001). Nevertheless, the reverse pattern has been found to occur with almost the same frequency (Moffitt et al., 2007). **Suicidal ideation** was also a strong common predictor for the onset and persistence of MDE-GAD. This finding could be in line with the above, considering subthreshold disorders or prodromal stages (Murphy et al., 1989; Wolitzky-Taylor et al., 2014). These results suggest that early detection of subclinical symptoms could provide an opportunity to facilitate early interventions before such conditions become fully formed disorders.

Regarding the studied **protective factors**, we found that **social support** (i.e., positive family relationships, supportive peers and connection to school) was negatively associated with both first-onset and persistence of MDE-GAD. This is consistent with previous studies (Davaasambuu, Aira, Hamid, Wainberg, & Witte, 2017; Galatzer-Levy et al., 2012; Peng et al., 2012; van Voorhees et al., 2008). Social support has been considered as a psychosocial resource that buffers against the development of mental disorders when a person is exposed to adverse life events (Dalgard, Bj∅rk, & Tambs, 1995; Hefner & Eisenberg, 2009). On the contrary, a lack of social support is associated with psychological problems (Bruwer, Emsley, Kidd, Lochner, & Seedat, 2008). **Positive coping strategies** were also found associated with the onset and persistence of MDE-GAD in our study. Previous findings have shown better coping associated with lower levels of mental disorders (Crockett et al., 2007; Galatzer-Levy et al., 2012; McLafferty et al., 2019; van Voorhees et al., 2008). Finally, **student expectations** were also found associated with the onset and persistence of MDE-GAD. It has been suggested that those with higher future expectations may believe in their ability to cope with life adversities (Brackney & Karabenick, 1995; Riskind et al., 1987). The identification of modifiable protective factors could guide prevention strategies, beyond a focus on the reduction of potential risk factors and thus, contributing to resilience (Steinhardt & Dolbier, 2008). Beyond the negative associations between protective factors and mental disorders, it would be interesting to study their mediator role (McLafferty et al., 2019; Peterson & Vaidya, 2001), for instance, the role of coping strategies between stressful events and mental disorders, or the buffering effect of perceived social support (Quittner, Glueckauf, & Jackson, 1990).

Regarding the results of **multivariable baseline models**, the accuracy was similar to that obtained separately for MDE and GAD in primary care and general population settings (Bellón et al., 2011; King et al., 2011; Nigatu et al.,

2016; Nigatu & Wang, 2019; van Loo et al., 2014, 2015). Much less evidence exists about predictive models among university students (Ebert et al., 2019; Kiekens et al., 2019; Mortier, Demyttenaere, et al., 2017; Mortier, Kiekens, et al., 2017). According to our models, among the 30% of students at the highest baseline predicted risk, 74.9% of the observed cases would develop first-onset MDE-GAD in the following 12 months. Among those with a history of MDE-GAD, our models determined that 54.6% at the highest baseline predicted risk, will persist as an MDE-GAD case.

These baseline risk profiles could be used as orientation to implement preventive interventions which may increase clinical and cost-effectiveness (Becker et al., 2018; Bremer et al., 2018; Ioannidis & Garber, 2011). Research on effective interventions based on different cut-off points and the use of these threshold values as intervention rules is needed. The use of a single algorithm for MDE-GAD could be a potential tool in the university setting for the early detection of a wide population with symptoms of these frequent mental disorders, and for implementing preventive interventions addressing common underlying factors (Titov et al., 2011). Transdiagnostic interventions have shown to be effective in reducing symptoms of both disorders (Barlow et al., 2016; Ebert, Cuijpers, Muñoz, & Baumeister, 2017; Păsărelu, Andersson, Bergman Nordgren, & Dobrean, 2017; Tulbure, Rusu, Sava, Sălăgean, & Farchione, 2018). Therefore transdiagnostic interventions, deployed more broadly than disorder-specific alternatives— could have a greater impact to improve student mental health (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Păsărelu et al., 2017).

Risk prediction models are relatively new in psychiatry, while other fields of medicine have used it extensively in areas such as coronary heart disease, diabetes or cancer (Bernardini et al., 2017). Further research is needed in terms of developing risk prediction algorithms in the psychiatric field and

external validation of existing models to exploit the use of these tools for the detection of risk groups.

6.2. Limitations

The findings resulting of this thesis should be considered in light of some limitations. The first set of issues could limit the generalizability of results, and include: the analysis of a convenience sample of universities and the low response rates obtained in the baseline and follow-up surveys, as well as the use of monetary incentives. On the other hand, results of this thesis should be considered on the basis that mental disorders' assessment was based on self-reported measures and not in-depth clinical interviews. Also, the assessment of mental disorders was limited to a number of common mental disorders, excluding the assessment of amount of mental disorders desirable to assess. These limitations are discussed below.

The UNIVERSAL project was carried out in a convenience sample of five public universities from five Autonomous Regions of Spain without probabilistic sampling strategy. These five universities represented 8% of all the students enrolled in Spanish public universities in the 2014-15 academic year. Nevertheless, we attempted to represent geographical dispersion. Moreover, comparing basic socio-demographic characteristics in terms of gender, nationality and academic field of the students in the participating universities and the overall Spanish public universities, distributions were very similar.

The low response rate obtained could have made our results a biased representation of the total population of Spanish university students. The final weighted response rate at baseline was 19%, with a range from 9% to 44% depending on the university. This response rate was similar than those

obtained in other studies among university students (Bewick et al., 2008; McLafferty et al., 2017; Oswalt & Wyatt, 2011) but lower than those expected according to a meta-analysis (mean response rate of 40%)(Colleen Cook, Heath, & Thompson, 2000). Comparing distributions of the sample at baseline with the census information available, higher proportions of females, foreign students and students in the field of health sciences were found in the UNIVERSAL sample. Post-stratification weights were applied to restore the distribution of the sample according to the available census information. Post-stratification weights have been shown to be effective in the reduction of bias produced by low participation (Brick, 2013; Dey, 1997).

In terms of efforts to increase participation in the study, economic incentives were offered on a random subsample of non-respondents at the end of the baseline survey (end game strategy). Previous studies have found positive effects on the use of incentives in terms of sample and response distributions (Singer & Ye, 2013). Nevertheless, these incentives could be a possible source of bias (Moyer & Brown, 2008). The responses of the students that participated in the endgame strategy were weighted by the inverse of their probability of selection.

The assessment of mental disorders was based on online screening scales and not in-depth clinical interviews. These screening measures were validated previously in other settings (Army personnel, primary care patients and general population) (Haro et al., 2006; Kessler, Calabrese, et al., 2013; Kessler, Santiago, et al., 2013), showing good concordance with clinical diagnostic interviews. We carried out the clinical reappraisal study to assess the accuracy of these instruments among university population. The online screening instruments showed good concordance with the Mini-International Neuropsychiatric Interview (Ballester et al., 2019), suggesting that might be useful for screening purposes. Therefore, mental disorders should be

considered as possible cases of mental disorder rather than confirmed diagnostic cases.

In addition, also with regard to the assessment of mental disorders, only a limited number of common mental disorders were assessed through the online survey among university students. The set of mental disorders included in the WMH-ICS surveys was selected taking into account those disorders with higher levels of associated role impairment among university students. In addition, although it would be interesting to study other mental disorders among university population (such as social anxiety disorder or specific phobia), the selection of a limited number of mental disorders reduced the duration of the surveys, thus facilitating the completion of the surveys by the participants.

Specifically, regarding the assessment of substance use disorders, alcohol use disorder was assessed using an online version of the AUDIT and drug use disorder was assessed through adapted items from the CIDI and the CIDI-SC (including cannabis, cocaine, any other illegal drug and medication used without prescription or used more than prescribed) without substance-specific assessment for abuse or dependence. In future research, it would be interesting to evaluate the consumption and possible drug use disorder of specific drugs, such as cannabis or cocaine, among university students and also to include the assessment of tobacco as a legal drug. In the same direction, it would also be of interest to conduct an in-depth study focused on the prevalence of alcohol and drug use disorders among university students, in whose population, previous studies have reported a high prevalence of some alcohol consumption patterns (García-Carretero et al., 2016; Gómez et al., 2017; Plan Nacional sobre Drogas, 2019) as well as cannabis and tobacco use (Arria et al., 2017; Caamaño-Isorna et al., 2011; Moreno-Gómez et al., 2012; Varela-Mato, Cancela, Ayan, Martín, & Molina, 2012).

6.3. Implications and future lines of research

This doctoral thesis contributed to the existing evidence about mental disorders among Spanish university students and the role impairment and mental health treatment associated, as well as the risk and protective factors associated with the onset and persistence of depression and/or generalised anxiety disorder. Also, the thesis shows an adequate accuracy of an online survey to assess mental disorders in the university setting. These findings suggest some preventive opportunities in the university context and also, future lines of research based on the results found in this thesis.

a) Implications

Implementation of mental health screening in universities

The high prevalence of mental disorders found in this thesis suggests the need for developing and implementing effective preventive interventions among university students. Screening strategies might be widely deployed in the university context through web-based surveys, in which some advantages have been found, such as the ease of administration, cost reduction and limitation of social desirability bias (Heiervang & Goodman, 2011; Lin et al., 2007) as well as adequate diagnostic concordance with clinical diagnostic interviews (Ballester et al., 2019). Besides it would be interesting the use of online short self-report scales validated among Spanish population to evaluate severity and impairment of anxiety and depression (González-Robles et al., 2018; Mira et al., 2019).

Furthermore, the combination of extensive information on risk and protective factors could be used to create useful risk prediction models to early detect at-risk students for the onset or persistence of mental disorders for planning preventive interventions. Ultimately, these screening strategies might provide useful information for university authorities not only to detect mental

disorders cases, but also to obtain information on the mental health of the university students as a whole.

Interventions to prevent mental disorders and reducing barriers to seek help

One practical implication of our work would be to offer internet-based interventions in addition to the student mental health services already offered by universities. Web-based intervention programs have proven to be effective for reducing symptoms and preventing the onset of mental disorders (Andersson & Cuijpers, 2009; Buntrock et al., 2016; Davies et al., 2014; Josephine et al., 2017; Sander, Rausch, & Baumeister, 2016). Specifically, in Spain, nowadays some studies yet has been proven the effectively of web-based interventions among clinical samples for reducing symptoms of depression, anxiety and adjustment disorders (Barceló-Soler et al., 2019; González-Robles et al., 2020; Mira et al., 2018, 2017; Montero-Marín et al., 2016; Rachyla et al., 2020), and showing positive results in terms of economic costs (Romero-Sanchiz et al., 2017). Offering transdiagnostic interventions could be more effective than disorder-specific alternatives because it might address common underlying factors and cope with high comorbidity, as well as be offered more broadly (Newby et al., 2015; Păsărelu et al., 2017). Concretely, depression and generalised anxiety disorder have been found to be the most frequent and some of the most disabling mental disorders. There are established, effective transdiagnostic internet-based interventions for reducing symptoms of both disorders (Bolinski et al., 2018; González-Robles et al., 2020; Mira et al., 2017; Musiat et al., 2018; Păsărelu et al., 2017). Also, preventive interventions targeting the main risk and protective factors associated with mental disorders could be offered. For instance, preventive interventions directed to reduce the negative effects of childhood adversities or to treat subclinical symptomatology (V. Blanco, Rohde, Vázquez, & Otero, 2014; Musiat et al., 2018) would be especially suitable. Likewise, there is a need for prevention programs that promote protective factors of mental disorders, such as adequate coping

strategies and positive relationships, which could contribute to increasing resilience (R. Herrero et al., 2019; Steinhardt & Dolbier, 2008).

Mental health promotion efforts may also be necessary in the university setting. They must target promoting help-seeking and reducing barriers on the use of mental health treatment through a wide variety of strategies, such as web-based interventions, psychoeducation or peer training, which have been found effective for reducing stigma and also, to increase mental health literacy (Aguirre Velasco, Cruz, Billings, Jimenez, & Rowe, 2020; Ebert et al., 2015).

Lastly but not least, the university setting offers an excellent opportunity for reaching a large number of individuals who might benefit from universal prevention programs (Conley, Durlak, & Kirsch, 2015; Fernández et al., 2016).

b) Future lines of research

Results of this thesis show that mental disorders are common among university students. But results also provide evidence of persisting knowledge gaps about mental health among university students. Although we estimated the frequency of mental disorders using both cross-sectional and longitudinal data, our results offer limited evidence on the long-term course of mental disorders. The longitudinal study of mental disorders with the identification of different patterns across mental disorders as well as the assessment of the risk and protective factors implied, could be necessary to identify university students with high risk and for increasing the effectiveness of preventive interventions (Chen, Haas, Gillmore, & Kopak, 2011; Hale, Raaijmakers, Muris, van Hoof, & Meeus, 2008; Meadows, Brown, & Elder, 2006; Moure-Rodriguez et al., 2018). On one hand, it would be relevant to examine the information collected in the four years of the UNIVERSAL project, coinciding with the period at university, to have a broad vision of the development of mental disorders in this specific period. On the other hand, it could be necessary to link data from different

developmental periods (e.g., adolescence, emerging adulthood and adulthood), to better understand the natural course of mental disorders.

This doctoral thesis has focused on the study of mental disorders among university students in Spain. The results have shown that mental disorders are frequent in this population and a higher prevalence of mental disorders has been found than in the general population, in line with the results reported by other international studies. In addition, studies conducted among university students and non-students have found few differences in the overall prevalence of mental disorders. However, although university students are a group of special interest due to the psychosocial changes inherent to this period of development (i.e., emerging adulthood) and the factors associated with university entrance, perhaps differences in the prevalence of mental disorders would be found in comparison with other young populations, such as young individuals with low socio-economic status or with physical and cognitive disabilities that could act as barriers to access to higher education. For this reason, it might be necessary to study other groups of young people than university students or to study the general young populations in Spain.

In the current study, we examined potential risk and protective factors related to the onset and persistence of mental disorders during the university period, but a better understanding of the underlying mechanisms is required. A better knowledge about the particular role of some variables in mental disorders, such as the role of social support and coping strategies (Asselmann et al., 2018; McLaughlin, Conron, Koenen, & Gilman, 2010; Paykel, 1994; Quittner et al., 1990) could allow that prevention interventions target the specific mediators that contribute to the mental disorder (Mackinnon & Dwyer, 1993; Sutton, 2007).

Our study showed a remarkable level of any role impairment associated with mental disorders. Therefore, there is a need to further study specific domains to implement specific interventions in the most affected areas to reduce the impact of mental disorders (Alonso et al., 2018). In addition, more analysis will be directed to study the specific attributable disability for each disorder, as well as to study disability related to physical and mental disorders in order to understand and respond to the needs of university students.

The low rates of mental health services found in our study call for conducting future research on barriers and help-seeking behaviours among university students. Recently it was discovered that even though treatments are available, students do not access them (Ebert et al., 2019). This finding may help to create specific programs to reduce the barriers and facilitate the use of mental health services (Gulliver et al., 2012).

Finally, there is insufficient evidence on predictive models of mental disorders among university students. In this sense, we have developed a single predictive model for MDE-GAD that could be a potential tool for the early detection of a wide population with symptoms of MDE-GAD. Development and external validation of predictive models for other common mental disorders are needed to facilitate the early identification of students at-risk in the university context.

GENERAL
CONCLUSIONS

7

7. GENERAL CONCLUSIONS

1. **The WMH-ICS online screening survey shows adequate concordance to assess common mental disorders and suicidal thoughts and behaviours among the university population**. **Concordance is good, especially for screening suicidal thoughts and behaviours; and 12-month major depressive episode, generalised anxiety disorder and alcohol dependence.** These results suggest that the online survey might be useful for identifying mental disorders in the university setting as an easy-to-use screening tool.

2. **Mental disorders among Spanish university students are highly prevalent both at lifetime and 12-month periods in comparison to the general Spanish population and similar than results found in other international studies. Major depressive episode and generalised anxiety disorder are the most frequent disorders (both for their lifetime and 12-month prevalence). Also, higher frequencies on incidence and persistence are found for both disorders.** Results highlight the need for monitoring common mental disorders among university students. This information could allow the early identification of those who might benefit from preventive interventions and mental health services.

3. **Comorbidity of mental disorders is common among Spanish university students**, **supporting previous findings among university students and the general population that comorbidity is frequent on mental disorders. Also, comorbidity is related to greater role impairment and higher rates of mental health treatment.** Thus, there is a need for identifying specific profiles and their associated risk factors to develop

prevention strategies targeted to these conditions. Furthermore, it might be recommendable to implement transdiagnostic interventions targeting comorbidity and underlying risk factors across disorders.

4. **Severe role impairment is most frequently reported among students who have mental disorders than those who do not have mental disorders. Particularly, panic disorder, generalised anxiety disorder and major depressive episode are the mental disorders most strongly associated with severe role impairment.** This finding highlights the importance to target specific strategies on mental health among university students, not only for their higher prevalence.

5. Only a **low proportion of university students with mental disorders have received mental health treatment in the last 12 months**, similar than rates found on the Spanish general population. Students with anxiety disorders report the highest treatment rate. The understanding of help-seeking barriers could aid in the development of specific strategies on the university campus to increase the use of mental health treatment.

6. In general, **a wide range of risk and protective factors are associated with the first-onset and persistence of major depressive episode and/or generalised anxiety disorder (MDE-GAD). However, are stronger for the onset of MDE-GAD than for its persistence.** This result suggests the need to identify additional potential factors associated with persistence to allow the identification of a part of students that may not have been previously identified or that remain without effective mental health treatment. Overall, the inclusion of a broad range of risk and protective factors may allow the development of multivariable baseline predictive models as a useful prediction tool in university campuses for an early identification of high-risk students.

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8. REFERENCES

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ANNEX

9

9. ANNEX

9.1.   Annex 1. Supplementary material for article 1

Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià AI, Echeburúa E, et al. (2019) Accuracy of online survey assessment of mental disorders and suicidal thoughts and behaviors in Spanish university students. Results of the WHO World Mental Health- International College Student initiative. *PLoS ONE* 14(9): e0221529.

https://doi.org/10.1371/journal.pone.0221529

S1 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Major Depressive Episode 12-month algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar		AUC
					χ2	p-value	
(>= 1)	97.8	64.6	2.8	0	92.8	<.0001*	0.81
(>= 2)	97.8	64.6	2.8	0	92.8	<.0001*	0.81
(>= 3)	97.8	64.6	2.8	0	92.8	<.0001*	0.81
(>= 4)	97.8	64.6	2.8	0	92.8	<.0001*	0.81
(>= 5)	97.8	65.0	2.8	0	91.7	<.0001*	0.81
(>= 6)	97.8	65.0	2.8	0	91.7	<.0001*	0.81
(>= 7)	97.8	65.0	2.8	0	91.7	<.0001*	0.81
(>= 8)	97.8	65.5	2.8	0	90.4	<.0001*	0.82
(>= 9)	97.8	67.2	3.0	0	86.1	<.0001*	0.83
(>= 10)	97.8	67.2	3.0	0	86.1	<.0001*	0.83
(>= 11)	92.5	69.6	3.0	0.1	77.1	<.0001*	0.81
(>= 12)	92.5	71.7	3.3	0.1	71.5	<.0001*	0.82
(>= 13)	92.5	82.8	5.4	0.1	42.3	<.0001*	0.88
(>= 14)	73.0	87.4	5.8	0.3	22.4	<.0001*	0.80
(>= 15)	70.8	89.6	6.8	0.3	15.9	<.0001*	0.80
(>= 16)	60.3	91.5	7.1	0.4	8.84	0.003*	0.76
(>= 17)	49.8	92.3	6.5	0.5	5.3	0.021*	0.71
(>= 18)	46.9	93.9	7.7	0.6	2.28	0.131	0.70
(>= 19)	43.7	96.9	14.1	0.6	0.04	0.835	0.70
(>= 20)	26.4	97.2	9.4	0.8	1.15	0.283	0.62
(>= 21)	16.1	97.4	6.2	0.9	2.22	0.136	0.57
(>= 22)	5.60	98.0	2.8	1	4.79	0.029*	0.52
(>= 23)	5.60	98.7	4.3	1	7.81	0.005*	0.52
(>= 24)	2.90	99.0	2.9	1	9.53	0.002*	0.51

*P-value statistically significant 0.05.

S2 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Major Depressive Episode lifetime algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar χ^2	p-value	AUC
(>= 1)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 2)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 3)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 4)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 5)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 6)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 7)	99	46.4	1.8	0	122.9	<.0001*	0.73
(>= 8)	99	47.5	1.9	0	120.3	<.0001*	0.73
(>= 9)	99	49.0	1.9	0	116.8	<.0001*	0.74
(>= 10)	97.1	50.1	1.9	0.1	111.1	<.0001*	0.74
(>= 11)	97.1	54.4	2.1	0.1	101.3	<.0001*	0.76
(>= 12)	96.3	57.7	2.3	0.1	92.8	<.0001*	0.77
(>= 13)	95.9	64.9	2.7	0.1	75.5	<.0001*	0.80
(>= 14)	88.9	69.8	2.9	0.2	56.0	<.0001*	0.79
(>= 15)	61.8	73.3	2.3	0.5	24.9	<.0001*	0.68
(>= 16)	53.5	78.1	2.4	0.6	12.2	0.001*	0.66
(>= 17)	48.6	84.0	3.0	0.6	3.09	0.078	0.66
(>= 18)	46.6	86.6	3.5	0.6	0.82	0.365	0.67
(>= 19)	43.5	91.6	5.2	0.6	0.89	0.346	0.68
(>= 20)	33.6	92.5	4.5	0.7	3.43	0.064	0.63
(>= 21)	25.0	94.4	4.5	0.8	9.09	0.003*	0.60
(>= 22)	15.6	95.1	3.2	0.9	14.1	0.0002*	0.55
(>= 23)	12.1	95.9	3.0	0.9	17.9	<.0001*	0.54
(>= 24)	6.60	98.5	4.4	0.9	32.2	<.0001*	0.53

*P-value statistically significant 0.05.

S3 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Mania/Hypomania 12-month algorithm for estimating reference standard (MINI) (weighted values)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar		AUC
					χ^2	p-value	
(>= 2)	33.6	89.2	3.1	0.7	21.7	<.0001*	0.61
(>= 3)	33.6	91.9	4.1	0.7	14.4	0.0001*	0.63
(>= 4)	33.6	97.7	14.6	0.7	1.03	0.310	0.66

*P-value statistically significant 0.05.

S4 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Mania/Hypomania lifetime algorithm for estimating reference standard (MINI) (weighted values)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar		AUC
					χ^2	p-value	
(>= 2)	83.7	77.6	3.7	0.2	57.2	<.0001*	0.81
(>= 3)	63.7	84.3	4.1	0.4	34.4	<.0001*	0.74
(>= 4)	20.9	95.5	4.6	0.8	1.52	0.218	0.58

*P-value statistically significant 0.05.

S5 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Panic Disorder 12-month algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar χ^2	p-value	AUC
(>= 1)	44.8	97.7	19.5	0.6	0.12	0.725	0.71
(>= 2)	44.8	97.7	19.5	0.6	0.12	0.725	0.71
(>= 3)	44.8	97.7	19.5	0.6	0.12	0.725	0.71
(>= 4)	39.8	98.2	22.1	0.6	0.06	0.809	0.69
(>= 5)	17.8	98.7	13.7	0.8	1.55	0.213	0.58
(>= 6)	17.8	99.6	44.5	0.8	5.19	0.023*	0.59
(>= 7)	4.90	100	NA	1	8.74	0.003*	0.52

*P-value statistically significant 0.05.

S6 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Panic Disorder lifetime algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar		AUC
					χ^2	p-value	
(>= 1)	71.1	82.8	4.1	0.3	26.7	<.0001*	0.77
(>= 2)	71.1	82.8	4.1	0.3	26.7	<.0001*	0.77
(>= 3)	71.1	83.2	4.2	0.3	25.7	<.0001*	0.77
(>= 4)	36.1	87.6	2.9	0.7	5.09	0.024*	0.62
(>= 5)	19.8	94.3	3.5	0.9	0.96	0.328	0.57
(>= 6)	6.5	98.4	4.1	1	14.1	0.0002*	0.52
(>= 7)	3.2	99.6	8.0	1	21.9	<.0001*	0.51

*P-value statistically significant 0.05.

S7 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Generalized Anxiety Disorder 12-month algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar χ^2	p-value	AUC
(>= 13)	100	81.1	5.3	0	52.5	<.0001*	0.91
(>= 14)	100	81.1	5.3	0	52.5	<.0001*	0.91
(>= 15)	100	81.3	5.3	0	52.1	<.0001*	0.91
(>= 16)	100	81.6	5.4	0	51.2	<.0001*	0.91
(>= 17)	100	82.5	5.7	0	48.6	<.0001*	0.91
(>= 18)	100	82.5	5.7	0	48.6	<.0001*	0.91
(>= 19)	100	83.4	6.0	0	46.3	<.0001*	0.92
(>= 20)	100	84.8	6.6	0	42.3	<.0001*	0.92
(>= 21)	100	86.2	7.2	0	38.3	<.0001*	0.93
(>= 22)	95.0	88.2	8.1	0.1	32.3	<.0001*	0.92
(>= 23)	95.0	89.1	8.7	0.1	29.9	<.0001*	0.92
(>= 24)	95.0	89.7	9.2	0.1	28.1	<.0001*	0.92
(>= 25)	72.7	91.8	8.9	0.3	20.0	<.0001*	0.82
(>= 26)	63.4	93.3	9.5	0.4	14.9	0.0001*	0.78
(>= 27)	63.4	93.5	9.8	0.4	14.2	0.0002*	0.78
(>= 28)	63.4	94.2	10.9	0.4	12.4	0.0004*	0.79
(>= 29)	63.4	96.1	16.3	0.4	7.24	0.007*	0.80
(>= 30)	63.4	97.2	22.6	0.4	4.31	0.038*	0.80
(>= 31)	41.0	98.6	29.3	0.6	0.42	0.517	0.70
(>= 32)	31.7	98.9	28.8	0.7	0.03	0.862	0.65

*P-value statistically significant 0.05.

S8 Table. Sensitivity, specificity, likelihood ratio positive (LR+), likelihood ratio negative (LR-), McNemar and Area Under the Curve (AUC) for different cut-off points of Generalized Anxiety Disorder lifetime algorithm for estimating reference standard (MINI) (n=287)

Cutpoint	Sensitivity	Specificity	LR+	LR-	McNemar χ^2	p-value	AUC
(>= 13)	100	57.8	2.4	0	115.6	<.0001*	0.79
(>= 14)	100	58.0	2.4	0	114.9	<.0001*	0.79
(>= 15)	100	59.5	2.5	0	110.8	<.0001*	0.80
(>= 16)	100	59.9	2.5	0	109.9	<.0001*	0.80
(>= 17)	100	60.6	2.5	0	107.9	<.0001*	0.80
(>= 18)	100	61.2	2.6	0	106.2	<.0001*	0.81
(>= 19)	100	68.3	3.2	0	86.9	<.0001*	0.84
(>= 20)	100	69.9	3.3	0	82.4	<.0001*	0.85
(>= 21)	100	71.4	3.5	0	78.2	<.0001*	0.86
(>= 22)	97.3	74.8	3.9	0	68.5	<.0001*	0.86
(>= 23)	97.3	77.4	4.3	0	61.3	<.0001*	0.87
(>= 24)	97.3	79.4	4.7	0	55.6	<.0001*	0.88
(>= 25)	85.3	83.4	5.1	0.2	42.2	<.0001*	0.84
(>= 26)	85.3	85.6	5.9	0.2	36.0	<.0001*	0.85
(>= 27)	85.3	86.4	6.3	0.2	34.1	<.0001*	0.86
(>= 28)	64.2	90.4	6.7	0.4	19.5	<.0001*	0.77
(>= 29)	52.6	94.1	8.9	0.5	8.35	0.004*	0.73
(>= 30)	52.6	95.7	12.2	0.5	4.47	0.035*	0.74
(>= 31)	52.6	97.2	18.8	0.5	1.67	0.196	0.75
(>= 32)	35.6	97.8	16.2	0.7	0.19	0.662	0.67

*P-value statistically significant 0.05.

S9 Table. Prevalence estimates of common mental disorders and suicidal thoughts and behaviors in the clinical reappraisal samples recruited at each follow-up, according to the WMH-ICS online survey screeners and the MINI (n= 287) (unweighted values)

| | Baseline (n=45) | | | | 1st Follow-up (n=91) | | | | 2nd Follow-up (n=151) | | | |
| | Online survey screeners | | MINI | | Online survey screeners | | MINI | | Online survey screeners | | MINI | |
	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)
Mental disorders												
Any mood[a]												
12-m	10	22,2 (0,06)	3	6,7 (0,04)	17	18,7 (0,04)	11	12,9 (0,04)	40	26,5 (0,04)	18	11,9 (0,03)
Lifetime	11	24,4 (0,06)	9	23,7 (0,06)	40	44 (0,05)	18	21,2 (0,04)	85	57,0 (0,04)	39	26 (0,04)
Major depressive episode												
12-m	10	22,2 (0,06)	0	0 (0)	16	17,6 (0,04)	10	11,8 (0,03)	34	22,5 (0,03)	16	10,7 (0,03)
Lifetime	11	24,4 (0,06)	5	13,2 (0,05)	37	40,7 (0,05)	17	19,8 (0,04)	81	54,4 (0,04)	36	24 (0,03)
Mania/Hypomania												
12-m	1	2,2 (0,02)	3	6,7 (0,04)	2	2,2 (0,02)	1	1,1 (0,01)	11	7,3 (0,02)	3	2 (0,01)
Lifetime	1	2,2 (0,02)	5	12,2 (0,05)	5	5,5 (0,02)	1	1,1 (0,01)	19	12,8 (0,03)	7	4,6 (0,02)
Any anxiety[b]												
12-m	10	22,2 (0,06)	4	9,5 (0,04)	18	19,8 (0,04)	6	6,6 (0,03)	42	27,8 (0,04)	9	6,1 (0,02)
Lifetime	10	22,2 (0,06)	4	9,8 (0,04)	31	34,1 (0,05)	10	11 (0,03)	88	58,7 (0,04)	18	12,2 (0,03)
Panic disorder												
12-m	2	4,4 (0,03)	3	6,7 (0,04)	1	1,1 (0,01)	5	5,5 (0,02)	2	1,30 (0,01)	9	6 (0,02)
Lifetime	2	4,4 (0,03)	3	6,7 (0,04)	2	2,2 (0,02)	9	9,9 (0,03)	16	10,9 (0,03)	16	10,6 (0,03)
Generalized anxiety disorder												
12-m	9	20 (0,06)	2	4,8 (0,03)	17	18,7 (0,04)	3	3,3 (0,02)	41	27,2 (0,04)	2	1,3 (0,01)
Lifetime	9	20 (0,06)	3	7,3 (0,04)	30	33 (0,05)	4	4,4 (0,02)	84	56 (0,04)	4	2,7 (0,01)

(*Continued*)

S9 Table

(Continued)

Suicidal thoughts and behaviors		n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)
Idea	12-m	5	11,1 (0,05)	4	4,4 (0,02)							19	12,6 (0,03)
	Lifetime	9	20 (0,06)	25	27,5 (0,05)							64	42,4 (0,04)
Plan	12-m	6	13,3 (0,05)	7	7,7 (0,03)							14	9,3 (0,02)
	Lifetime	10	22,2 (0,06)	15	16,5 (0,04)							51	33,8 (0,04)
Attempt	12-m	1	2,2 (0,02)	0	0 (0)							1	0,7 (0,01)
	Lifetime	2	4,4 (0,03)	2	2,2 (0,02)							6	4 (0,02)
Suicidal thoughts and behaviors[c]	12-m	6	13,3 (0,05)	2	4,4 (0,03)	8	8,8 (0,03)	6	6,6 (0,03)	21	13,9 (0,03)	17	12,6 (0,03)
	Lifetime	10	22,2 (0,06)	10	22,2 (0,06)	26	28,6 (0,05)	14	15,4 (0,04)	68	45 (0,03)	47	34,1 (0,04)

a.- Mood include: Major Depression Episode or Mania/Hypomania, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC]; b.- Anxiety include: Panic Disorder or Generalized Anxiety Disorder, assessed with the Composite International Diagnostic Interview Screening Scales [CIDI-SC]; c.- Suicidal thoughts and behaviors based on definition used in Spain suicide prevalence paper (by MJ. Blasco) including: suicidal ideation, suicide plan and suicide attempt (excluding the questions of death wish and non-suicidal self-injury), assessed with question from the Self-Injurious Thoughts and Behaviors Interview [SITBI] and the Columbia-Suicide Severity Rating Scale [C-SSRS]. SE: Standard Error.

S1 STARD checklist for reporting of studies of diagnostic accuracy (2015 version)

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	Page 4
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	Page 4
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	Page 6-7
	4	Study objectives and hypotheses	Page 7
METHODS			
Study design	5	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	Page 8
Participants	6	Eligibility criteria	Page 8-9
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	Page 8-9
	8	Where and when potentially eligible participants were identified (setting, location and dates)	Page 8-9
	9	Whether participants formed a consecutive, random or convenience series	Page 9
Test methods	10a	Index test, in sufficient detail to allow replication	Page 7, 10
	10b	Reference standard, in sufficient detail to allow replication	Page 10-11
	11	Rationale for choosing the reference standard (if alternatives exist)	Page 10-11
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	Page 10, 12
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	Page 11,12
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	Page 9
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	Page 11
Analysis	14	Methods for estimating or comparing measures of diagnostic accuracy	Page 11-12
	15	How indeterminate index test or reference standard results were handled	Page 12-13
	16	How missing data on the index test and reference standard were handled	Page 12
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	Page 12-13
	18	Intended sample size and how it was determined	Page 12
RESULTS			
Participants	19	Flow of participants, using a diagram	Fig 1, page 13
	20	Baseline demographic and clinical characteristics of participants	Table 1, page 14
	21a	Distribution of severity of disease in those with the target condition	---------
	21b	Distribution of alternative diagnoses in those without the target condition	---------
	22	Time interval and any clinical interventions between index test and reference standard	Page 9
Test results	23	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	Table 2, page 16
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DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	Page 29-30
	27	Implications for practice, including the intended use and clinical role of the index test	Page 31
OTHER INFORMATION			
	28	Registration number and name of registry	---------
	29	Where the full study protocol can be accessed	Page 8
	30	Sources of funding and other support; role of funders	Page 3

9.2.   Annex 2. Supplementary material for article 3

Ballester L, Alayo I, Vilagut G, Almenara J, Cebrià AI, Echeburúa E, et al. (2020). Mental disorders in Spanish university students: Prevalence, age-of-onset, severe role impairment and mental health treatment. *Journal of Affective Disorders*, 273, 604-613. https://doi.org/10.1016/j.jad.2020.04.050

Supplementary Table 1. Distribution of the academic field, gender and nationality among all Spanish universities, universities participating in the UNIVERSAL study and eligible students in the UNIVERSAL study.

	All Spanish universities[a]		UNIVERSAL universities[b]		Eligible students UNIVERSAL universities[c]	
	n	%	n	%	n	%
Academic field						
Arts and Humanities	126,081	10.1	7,817	8.8	1,595	9.8
Engineering and Architecture	232,118	18.6	17,568	19.8	3,040	18.6
Health Sciences	227,870	18.2	14,633	16.5	2,574	15.8
Science	75,182	6.0	5,332	6.0	1,362	8.3
Social and Legal Sciences	589,571	47.1	43,305	48.9	7,761	47.5
Gender						
Female	686,555	54.9	48,101	54.3	9,021	55.2
Male	564,267	45.1	40,554	45.7	7,311	44.8
Nationality						
Spain	1,201,047	96.0	86,149	97.2	15,809	96.8
Other	49,775	4.0	2,506	2.8	523	3.2

a.-Total degree students in Spanish universities. Source: https://www.educacion.gob.es/educabase/menu.do?type=pcaxis&path=/Universitaria/Alumnado/Estadistica/2014-2015/1GradoCiclo/CapituloI&file=pcaxis&l=s0 (I1.1; I.1.3)

b.-Total degree students in universities participating in the UNIVERSAL study. Source: https://www.educacion.gob.es/educabase/menu.do?type=pcaxis&path=/Universitaria/Alumnado/Estadistica/2014-2015/1GradoCiclo/CapituloIII/Publicas&file=pcaxis&l=s0 (III.1.1b; III.1.4b)

c.-Eligible students in universities participating in the UNIVERSAL study (data provided by the participating universities)

Supplementary table 2. Age-of-onset of mental disorders by gender in the UNIVERSAL study (n= 2,118)

	Age of onset			
	Total Median [IQR]	Male Median [IQR]	Female Median [IQR]	F (ndf, ddf)[f]
Mental disorders				
Major depressive episode	15 [13-17]	15 [13-16]	16 [13-17]	1.23 (1,195957)
Broad mania	15 [13-16]	16 [14-18]	15 [13-16]	0.43 (1,10368)
Any mood disorder[a]	15 [13-17]	15 [13-16]	15 [13-17]	0.90 (1,66578)
Generalized anxiety disorder	16 [15-17]	16 [15-17]	16 [14-17]	0.02 (1,445819)
Panic Disorder	16 [14-17]	16 [12-19]	16 [14-16]	2.36 (1,7611)
Any anxiety disorder[b]	16 [14-17]	16 [15-17]	16 [14-17]	0.09 (1,76184)
Alcohol abuse or dependence	15 [14-16]	15 [14-16]	15 [14-17]	0.02 (1,870776)
Drug abuse or dependence	16 [15-17]	16 [16-17]	16 [14-17]	0.19 (1,35712)
Any substance use disorder[c]	16 [14-17]	16 [15-17]	15 [14-17]	0.07 (1,180882)
Attention deficit hyperactivity disorder[d]	14 [11-16]	14 [9-15]	14 [11-16]	3.05 (1,4638)
Any mental disorder[e]	15 [13-16]	15 [13-16]	15 [13-16]	4.99 (1,11019)*

a.-Any mood disorder: Major depressive episode or Broad mania; b.-Any anxiety disorder: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.-Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e.- Any mental disorder: Any mental disorder for the lifetime prevalence and 12-month prevalence, with the exception of ADHD with a prevalence of 6-month. f.- F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom. *p-value <.05; **p-value<.01. %: weighted IQR: Interquartile range

Supplementary table 3. Bivariate logistic regression models of 12-month mental disorders as predictors for 12-month of severe role impairment in the UNIVERSAL study (n=2,118)

	Any severe role impairment	
	OR (CI95%)	F (ndf, ddf)[f]
Mental disorders		
Major depressive episode	4.5 (3.5-5.7)	138.4 (1, 2082997)**
Broad mania	4.4 (2.6-7.5)	30.0 (1, 2360)**
Any mood disorder[a]	4.3 (3.3-5.4)	132.4 (1, 387601)**
Generalized anxiety disorder	4.2 (3.2-5.4)	115.1 (1, 171103)**
Panic Disorder	8.4 (4.3-16.5)	39.1 (1, 3452)**
Any anxiety disorder[b]	4.3 (3.3-5.5)	120.3 (1, 101009)**
Alcohol abuse or dependence	1.7 (1.2-2.6)	7.5 (1,1000430)**
Drug abuse or dependence	1.8 (0.9-3.6)	3.1 (1, 26307)
Any substance use disorder[c]	1.6 (1.1-2.3)	5.6 (1,148086)**
Attention deficit hyperactivity disorder[d]	2.5 (1.9-3.4)	36.3 (1, 1530118)**
Any mental disorder[e]	3.7 (2.9-4.6)	115.1 (1, 341483)**
Number of disorders		
One disorder	2.2 (1.6-3.0)	55.1 (3,189354)**
Two disorders	4.5 (3.2-6.2)	
Three or more disorders	9.9 (6.6-14.8)	

a.-Any mood disorder: Major depressive episode or Broad mania; b.-Any anxiety disorder: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.- Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e.- Any mental disorder: Any mental disorder for the 12-month prevalence, with the exception of ADHD with a prevalence of 6-month; f.- F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom. Raw p-value statistically significant after adjustment for multiple comparisons using Benjamini-Hochberg procedure with false discovery rate 0.05. *p-value <.05; **p-value<.01.
OR: odds ratio; CI: confidence interval.

Supplementary table 4. Bivariate logistic regression models of 12-month mental disorders as predictors for 12-month treatment in the UNIVERSAL study (n=2,118)

	Any treatment	
	OR (CI95%)	F (ndf, ddf)[f]
Mental disorders		
Major depressive episode	5.0 (3.4-7.2)	73.0 (1, 1204370)**
Broad mania	3.2 (1.6-6.5)	10.2 (1, 5736)**
Any mood disorder[a]	4.9 (3.4-7.2)	71.3 (1, 64982)**
Generalized anxiety disorder	7.4 (5.0-10.7)	107.2 (1, 36763)**
Panic Disorder	9.6 (4.8-18.9)	42.3 (1, 10127)**
Any anxiety disorder[b]	7.8 (5.3-11.4)	112.2 (1, 29299)**
Alcohol abuse or dependence	1.2 (0.6-2.3)	0.2 (1,34793852)
Drug abuse or dependence	1.9 (0.7-5.0)	1.7 (1, 91307)
Any substance use disorder[c]	1.1 (0.6-2.1)	0.1 (1,670129)
Attention deficit hyperactivity disorder[d]	2 (1.2-3.2)	8.3 (1, 12271383)**
Any mental disorder[e]	6.1 (4.0-9.2)	72.7 (1,390132)**
Number of disorders		
One disorder	3.4 (2.0-5.7)	32.2 (3,75027)**
Two disorders	9.8 (6.0-15.9)	
Three or more disorders	9.3 (5.1-16.9)	

a.-Any mood disorder: Major depressive episode or Broad mania; b.-Any anxiety disorder: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.- Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e.- Any mental disorder: Any mental disorder for the 12-month prevalence, with the exception of ADHD with a prevalence of 6-month; f.- F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom. Raw p-value statistically significant after adjustment for multiple comparisons using Benjamini-Hochberg procedure with false discovery rate 0.05. *p-value <.05; **p-value<.01.
OR: odds ratio; CI: confidence interval.

Supplementary table 5. Multiple logistic regression models of 12-month mental disorders as predictors for 12-month treatment in the UNIVERSAL study (n=2,118)

	Any treatment		Model 1		Model 2		Model 3		Model 4		Model 5	
	%	SE	aOR (95% CI)	F (ndf, ddf)[a]	aOR (95% CI)	F (ndf, ddf)[a]	aOR (95% CI)	F (ndf, ddf)[a]	aOR (95% CI)	F (ndf, ddf)[a]	aOR (95% CI)	F (ndf, ddf)[a]
Mental disorders												
Major depressive episode	16.0	1.83	2.2 (1.4-3.6)	10.7 (1, 80877)**	--	--	--	--	3.7 (2-7)	16.5 (1, 171909)**	3.4 (1.8-6.4)	14.6 (1, 32542)**
Broad mania	16.1	4.69	0.9 (0.4-2.3)	0.0 (1,1504)	--	--	--	--	2.2 (0.7-7)	1.9 (1, 3156)	1.7 (0.6-4.9)	1.1 (1, 1316)
Generalized anxiety disorder	20.1	2.2	5 (3-8.2)	39.0 (1,15657)**	--	--	--	--	8.3 (4.3-16.2)	39.5 (1, 29713)**	7.4 (3.7-14.8)	32.7 (1, 4974)**
Panic Disorder	35.3	7.6	2.8 (1.2-6.6)	5.4 (1, 4913)*	--	--	--	--	5.9 (2-17.1)	10.8 (1, 10067)**	4.3 (1.7-10.8)	9.6 (1, 10790)**
Alcohol abuse or dependence	7.6	2.35	0.8 (0.3-1.7)	0.4 (1, 839627)	--	--	--	--	1.4 (0.6-3.4)	0.5 (1, 680425)	1.1 (0.5-2.5)	0.1 (1, 411338)
Drug abuse or dependence	10.7	4.62	1.7 (0.5-5.5)	0.8 (1, 10322)	--	--	--	--	3.4 (1-12.1)	3.7 (1, 21560)	2.7 (0.8-9.2)	2.4 (1, 11102)
Attention deficit hyperactivity disorder	10.3	1.97	0.9 (0.5-1.6)	0.1 (1, 147247)	--	--	--	--	1.8 (0.8-3.9)	2.1 (1, 163847)	1.7 (0.8-3.4)	2.0 (1, 19327)
Number of disorders (continuous)			--	--	1.9 (1.6-2.3)	62.2 (1,74295)**	--	--	0.4 (0.2-0.9)	5.4 (1, 51184)*	--	--
Number of disorders (categorical)												
One disorder	7.6	1.36	--	--	--	--	3.2 (1.8-5.5)	22.2 (3, 85484)**	--	--	--	--
Two disorders	19.0	2.64	--	--	--	--	8.7 (5-14.9)		--	--	0.6 (0.3-1.5)	3.9 (2, 8786)*
Three or more disorders	18.0	3.61	--	--	--	--	7.5 (3.9-14.4)		--	--	0.2 (0-0.7)	
AUC			0.806		0.786		0.788		0.808		0.805	
AIC			803.1		827.2		819.0		799.7		797.9	

a.-F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom.

*p-value <.05; **p-value<.01.

All models are adjusted for the predictors shown in the rows, socio-demographic (gender, age, parental educational level, parental marital status, religion, place raised, and sexual orientation), university predictors (university, academic field and first-term living location during the university period) and impairment.

%: weighted proportions; SE: Standard error; aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; AIC: Akaike information criterion

Supplementary table 6. Bivariate logistic regression models of socio-demographic correlates of 12-month mental disorders in the UNIVERSAL study (n=2,118)

	Any mood[a]		Any anxiety[b]		Any substance[c]		ADHD[d]		Any disorder[e]			
									1 disorder		≥2 disorders	
	OR	F	OR	F	OR	F	OR	F	OR	F	OR	F
Socio-demographics												
Gender (ref=Female)												
Male	0.5 (0.4-0.7)	30.1 (1,689706)	0.4 (0.3-0.5)	53.7 (1,18165)	2.1 (1.5-2.9)	19.5 (1.31007)**	0.7 (0.5-1)	4.4 (1.37192209)*	0.6 (0.5-0.8)	14.7 (1,35113)**	0.5 (0.4-0.7)	25.6 (1,610240)**
Age (ref=18)												
> 18	0.7 (0.6-0.9)	7.8 (1.368864)**	0.8 (0.6-1)	3.1 (1.63989)	1 (0.8-1.4)	0.8 (1.32036)	0.9 (0.7-1.2)	0.0 (1,23490094)	0.8 (0.6-1.0)	0.6 (1,14801)	0.8 (0.6-1.0)	4.2 (1,518669)*
Country of birth (ref= NonSpain)												
Spain	0.6 (0.3-1.1)	3.2 (1,11200625)	1 (0.5-2)	0.0 (1,2040823)	1.5 (0.5-4.9)	0.6 (1,39576745)	1.1 (0.5-2.5)	0.0 (1,40750358)	1.0 (0.5-1.9)	0.4 (1,111257)	0.8 (0.6-1.0)	0.0 (1,19450810)
Parents University Studies												
At least one	0.7 (0.6-0.9)	7.4 (1,46909)**	0.7 (0.5-0.9)	8.9 (1,18536)**	1.8 (1.6-3.2)	12.6 (1,14881)**	0.9 (0.7-1.2)	0.0 (1,136628)	0.9 (0.7-1.2)	0.4 (1,21743)	0.8 (0.6-1.0)	3.7 (1,28166)
Religion (ref =Christian)												
No religion	1.2 (1-1.6)	1.7 (2,4036)	0.8 (0.6-1)	2.0 (2,1988)	1.0 (0.8-1.7)	0.4 (2,2289)	1.3 (0.9-1.7)	1.3 (2,9250)	1.1 (0.9-1.5)	1.1 (2,7016)	1.1 (0.8-1.4)	0.6 (2,2739)
Another religion	0.8 (0.3-2.2)		0.5 (0.2-1.8)		0.3 (0-4.3)		0.8 (0.2-2.9)		0.8 (0.2-1.8)		0.6 (0.2-2.0)	
Parents separated or divorced	1.5 (1.2-2.1)	8.9 (1,2667590)**	1.4 (1-1.9)	5.1 (1,115484)*	0.6 (0.4-1.1)	3.3 (1,3285)	2.1 (1.5-2.9)	18.1 (1,33235925)**	1.0 (0.7-1.4)	0.0 (1,22638)	1.9 (1.4-2.6)	17.3 (1,765012)**
Place raised (ref=Large city/small city)												
Suburbs	1 (0.6-1.6)	0.7 (2,11665)	1.3 (0.8-2.1)	1.5 (2,830608)	0.9 (0.4-2.2)	0.4 (2,10401)	1.9 (1.2-3.1)	4.7 (2,06461252)**	0.8 (0.4-1.4)	1.1 (2,10084)	1.3 (0.8-2.2)	0.8 (2,283116)
Town/Village/Rural area	1.1 (0.9-1.5)		0.9 (0.7-1.1)		1.2 (0.8-1.7)		0.8 (0.6-1.1)		0.8 (0.6-1.1)		0.9 (0.7-1.2)	
Sexual orientation												
Non-heterosexual	2.8 (2.1-3.8)	46.0 (1,42538)**	1.3 (0.9-1.8)	1.9 (1,24922)	1.3 (0.9-2.4)	1.1 (1,3178)	2.2 (1.5-3.1)	17.3 (1,112868)**	1.6 (1.1-2.3)	6.0 (1,12309)*	2.5 (1.8-3.4)	27.2 (1,46752)**
University socio-demographics												
University (ref=Cadiz University UCA)												
Balearic Islands University (UIB)	1.7 (1.1-2.7)	9.6 (4,747994)**	1.4 (0.9-2.1)	4.6 (4,59051)**	1.3 (0.3-1.4)	4.5 (4,836949)**	1.9 (1.1-3.4)	8.0 (4,67398608)**	1.6 (1.1-2.4)	3.4 (4,121966)**	2.1 (1.3-3.4)	12.2 (4,2339126)**

| | Any mood[a] | | Any anxiety[b] | | Any substance[c] | | ADHD[d] | | Any disorder[e] | | | |
| | | | | | | | | | 1 disorder | | ≥2 disorders | |
	OR	F	OR	F	OR	F	OR	F	OR	F	OR	F
Basque Country University (UPV-EHU)	1.9 (1.4-2.7)		1.3 (0.9-1.8)		1.6 (1-2.5)		2 (1.3-3.3)		1.3 (1.0-1.8)		2.4 (1.6-3.5)	
Miguel Hernandez University (UMH)	2 (1.3-3.1)		1.7 (1.1-2.7)		0.6 (0.3-1.4)		2.7 (1.5-4.8)		1.2 (0.8-1.9)		2..3 (1.4-3.8)	
Pompeu Fabra University (UPF)	3.4 (2.3-5)		2.2 (1.5-3.3)		2.4 (1.4-4.3)		4 (2.4-6.7)		2 (1.4-3.0)		4.8 (3.1-7.5)	
Academic Field(ref=Health)												
Arts and Humanities	2.4 (1.6-3.4)	18.0 (4,1221718)**	1.7 (1.2-2.6)	11.7 (4,644313)**	2.4 (1.2-5.1)	5.6 (4,328086)**	1.4 (0.9-2.4)	3.3 (4, 33852994)**	2.8 (1.8-4.3)	8.9 (4,273363)**	2.6 (1.7-4.0)	14.5 (4,2696295)**
Engineering and Architecture	0.5 (0.3-0.7)		0.4 (0.3-0.7)		3.0 (0.2-1.9)		0.5 (0.3-0.9)		0.9 (0.6-1.4)		0.5 (0.3-0.8)	
Science	0.6 (0.4-1)		0.7 (0.4-1.1)		0.6 (1-3.4)		0.9 (0.5-1.5)		1 (0.6-1.6)		0.5 (0.3-0.9)	
Social and Legal Sciences	0.7 (0.5-1.0)		0.7 (0.5-0.9)		1.7 (1.4-4.9)		1.0 (0.7-1.5)		0.9 (0.7-1.3)		0.8 (0.6-1.1)	
Living at first term (ref= Other)												
Parents' home	1 (0.8-1.3)	0.0 (1, 211190)	1.2 (0.9-1.5)	1.9 (1,96097)	0.5 (0.3-0.7)	14.3 (1,57465)**	1 (0.8-1.3)	0.0 (1, 8406070)	0.8 (0.7-1.1)	2.3 (1,34298)	1 (0.8-1.3)	0.1 (1,417609)

(table continues)

a.- Any mood: Major depressive episode or Broad mania; b.-Any anxiety: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.- Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e. - Any mental disorder: Any mental disorder for the 12-month prevalence, with the exception of ADHD with a prevalence of 6-month; f.- F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom. Raw p-value statistically significant after adjustment for multiple comparisons using Benjamini-Hochberg procedure with false discovery rate 0.05. *p-value <.05; **p-value<.01. ref= reference category; OR: odds ratio; CI: confidence interval.

Supplementary table 7. Multiple logistic regression models of socio-demographic correlates of 12-month mental disorders in the UNIVERSAL study (n=2,118)

	Any mood[a] aOR	Any mood[a] F	Any anxiety[b] aOR	Any anxiety[b] F	Any substance[c] aOR	Any substance[c] F	ADHD[d] aOR	ADHD[d] F	Any disorder[e] — 1 disorder aOR	1 disorder F	Any disorder[e] — ≥2 disorders OR	≥2 disorders F
Socio-demographics												
Gender (ref=Female)												
Male	0.6 (0.4-0.7)	19.0 (1,205542)**	0.4 (0.3-0.5)	38.1 (1,15208)**	2 (1.4-2.9)	13.9 (1,11343)**	0.8 (0.6-1.1)	1.4 (1,263076)	0.6 (0.5-0.8)	12.5 (1,14442)**	0.6 (0.4-0.8)	15.2 (1,190643)**
Age (ref=18)												
> 18	0.8 (0.6-1)	2.5 (1,195783)	0.8 (0.6-1)	1.5 (1,61315)	1.6 (1.1-2.3)	5.9 (1,142269)*	1.2 (0.8-1.6)	0.8 (1,13004245)	1.0 (0.8-1.4)	0.1 (1,13768)	0.9 (0.7-1.2)	1.0 (1, 474562)
Country of birth (ref= NonSpain)												
Spain	0.7 (0.4-1.3)	1.6 (1,611638)	1.2 (0.6-2.4)	0.2 (1,431563)	1.9 (0.6-6.2)	1.2 (1,3885623)	1.4 (0.6-3.4)	0.7 (1,23662370)	0.9 (0.5-1.7)	0.1 (1,550693)	1.3 (0.6-2.9)	0.5 (1,835613)
Parents University Studies (ref=Neither)												
At least one	0.7 (0.5-0.8)	11.5 (1,642113)**	0.6 (0.5-0.8)	11.0 (1,35739)**	1.6 (1.1-2.3)	7.3 (1,15297)**	0.9 (0.7-1.2)	0.3 (1,109597)	0.9 (0.6-1.1)	2.3 (1,32943)	0.7 (0.5-0.9)	6.5 (1,42960)*
Religion (ref =Christian)												
No religion	1 (0.7-1.3)	0.5 (2,2750)	0.7 (0.5-0.9)	3.7 (2,1635)*	0.8 (0.5-1.1)	1.8 (2,2164)	1 (0.7-1.3)	0.3 (2,11859)	1.0 (0.8-1.3)	0.9 (2,5789)	0.8 (0.6-1.1)	1.8 (2,1823)
Another religion	0.6 (0.2-1.7)		0.7 (0.5-0.9)		0.2 (0.0-1.8)		0.6 (0.2-2.2)		0.5 (0.2-1.4)		0.4 (0.1-1.5)	
Parents separated or divorced	1.3 (0.9-1.7)	2.3 (1,645657)	1.8 (1.3-2.6)	1.8 (1,76881)	1.8 (1.3-2.6)	1.8 (1,4940)	0.9 (0.6-1.3)	11.4 (1,1807684)**	0.9 (0.6-1.3)	0.4 (1,19138)	1.6 (1.2-2.3)	8.9 (1,366401)**
Place raised (ref=Large city/small)												
Suburbs	1 (0.6-1.7)	0.0 (2,111980)	1.3 (0.8-2.1)	2.2 (2,619230)	0.9 (0.4-2.0)	0.1 (2,12883)	2 (1.2-3.4)	5.8 (2,32493177)**	0.8 (0.4-1.4)	3.7 (2,11807)*	1.4 (0.8-2.4)	1.7 (2,634034)
Town/Village/Rural area	1 (0.6-1.7)		1.3 (0.8-2.1)		1.0 (0.7-1.5)		0.7 (0.5-1.1)		0.7 (0.5-0.9)		0.8 (0.6-1.1)	
Sexual orientation												
Non-heterosexual	2.5 (1.8-3.5)	31.5 (1,24052)**	1.3 (0.9-1.9)	1.6 (1,14184)	1.3 (0.8-2.3)	1.1 (1,2606)	2 (1.3-2.9)	12.0 (1,19270)**	1.5 (1.0-2.2)	4.0 (1,9189)*	2.4 (1.6-3.4)	20.3 (1,33381)**
University socio-demographics												
University (ref=Cadiz University UCA)												
Balearic Islands University (UIB)	1.7 (1.1-2.7)	7.0 (4,489580)**	1.6 (1-2.5)	4.9 (4,448702)**	1.6 (0.8-3.1)	4.3 (4,487954)**	1.9 (1-3.5)	6.8 (4,22033065)**	1.9 (1.2-2.9)	3.9 (4,116625)**	2.3 (1.4-4.0)	10.1 (4,1950373)*
	1.7		1.5		1.8		2		1.4		2.4	

| | Any mood[a] | | Any anxiety[b] | | Any substance[c] | | ADHD[d] | | Any disorder[e] | | | |
| | | | | | | | | | 1 disorder | | ≥2 disorders | |
	aOR	F	aOR	F	aOR	F	aOR	F	aOR	F	OR	F
Basque Country University	(1.2-2.5)		(1-2.2)		(1.0-3.1)		(1.2-3.4)		(1.0-2.0)		(1.6-3.7)	
												(table continues)
Miguel Hernandez University (UMH)	1.9 (1.2-3.1)		2 (1.2-3.2)		0.6 (0.3-1.4)		2.7 (1.5-4.8)		1.3 (0.8-2.1)		2.3 (1.4-3.9)	
PompeuFabra University (UPF)	3.1 (2-4.8)		2.5 (1.6-4)		2.8 (1.5-5.2)		4 (2.3-6.9)		2.2 (1.4-3.5)		4.9 (3.0-8.0)	
Academic Field(ref=Health Sciences)												
Arts and Humanities	2 (1.3-3)	10.1 (4,807749)**	1.7 (1.1-2.6)	7.2 (4,643582)**	1.8 (0.9-3.6)	206 (4,235987)*	1.2 (0.7-2.1)	1.2 (4,14491217)	2.7 (1.7-4.3)	8.3 (4,195623)**	2.0 (1.2-3.2)	7.0 (4,1527230)*
Engineering and Architecture	0.7 (0.4-1.0)		0.7 (0.4-1.1)		1.9 (1.0-3.5)		0.7 (0.4-1.2)		1.2 (0.8-1.8)		0.7 (0.4-1.1)	
Science	0.7 (0.4-1.1)		0.8 (0.5-1.4)		0.5 (0.2-1.5)		1.1 (0.6-2.0)		1.1 (0.7-1.8)		0.6 (0.4-1.1)	
Social and Legal Sciences	0.7 (0.5-1.0)		0.6 (0.5-0.9)		1.3 (0.7-2.3)		1.1 (0.7-1.6)		0.9 (0.6-1.2)		0.7 (0.5-1.1)	
Living at first term (ref= Other)												
Parents' home	1.1 (0.8-1.3)	0.3 (1,111691)	1.2 (1-1.6)	2.6 (1,95854)	0.5 (0.4-0.7)	16.5 (1,38878)**	0.9 (0.7-1.3)	0.1 (1,6143416)	0.8 (0.6-1.0)	3.1 (1,32783)	1.1 (0.8-1.4)	0.2 (1,323506)
AUC	0.625		0.610		0.616		0.607		0.597		0.636	
AIC	1993.8		1804.2		1118.9		1440.8		1859.9		1619.1	

a.-Any mood: Major depressive episode or Broad mania; b.-Any anxiety: Generalized anxiety disorder or Panic Disorder; c.- Any substance use disorder: Alcohol abuse or dependence or Drug abuse or dependence; d.- Attention deficit hyperactivity disorder (ADHD) only surveyed at last 6 months prevalence; e.- Any mental disorder: Any mental disorder for the 12-month prevalence. with the exception of ADHD with a prevalence of 6-month; f.- F-test to evaluate significant difference in estimates based on multiple imputations. ndf = numerator degrees of freedom; ddf = denominator degrees of freedom.
*p-value <.05; **p-value<.01.

ref= reference category; aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; AIC: Akaike information criterion.

All models are adjusted for the predictors shown in the rows. socio-demographic (gender. age. parental marital status. religion. place raised. and sexual orientation) and university predictors (university. academic field and first-term living location during the university period).

Annex 1. STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Keywords
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-8*
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	Supplementary table 5
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	Supplementary figure 1
		(c) Consider use of a flow diagram	Supplementary figure 1

Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10 & Table 1
		(b) Indicate number of participants with missing data for each variable of interest	8
Outcome data	15*	Report numbers of outcome events or summary measures	11-13 & Tables 2-4
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Supplementary tables: 2, 3, 5
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	20

*Give information separately for exposed and unexposed groups.

9.3.   Annex 3. Supplementary material for article 4

Ballester L, Alayo I, Vilagut G, Mortier P, Almenara J, Cebrià AI, et al. Predictive models for first-onset and persistence of depression and anxiety among university students. Article submitted to the *Journal of Affective Disorders* (September 2020).

Supplementary table 1. Characteristics of the 12-month follow-up sample (n=1,253).

	12-month follow-up sample		
	n	%	SE
Socio-demographics			
Gender			
Male	305	44.0	1.4
Female	948	56.0	1.4
Age			
18	930	68.0	1.4
>18	323	32.0	1.4
Country of birth			
Spain	1160	94.9	0.7
Other	93	5.1	0.7
Parents University Studies			
At least one	591	42.4	1.6
Neither	662	57.6	1.6
Religion			
Christian	445	35.5	1.6
No religion	780	62.8	1.6
Another religion	28	1.7	0.4
Place raised			
Large/Small city	826	66.5	1.5
Suburbs	55	4.7	0.8
Town/village/ rural area	372	28.9	1.4
Sexual orientation			
Heterosexual	1102	86.3	1.1
Non-heterosexual	151	13.7	1.1
University socio-demographics			
University			
Balearic Islands University (UIB)	169	12.3	0.9
Basque Country University (UPV-	419	43.9	1.4
Cadiz University (UCA)	150	19.7	1.1
Miguel Hernandez University	143	10.6	0.9
Pompeu Fabra University (UPF)	372	13.5	1.0
Academic Field			
Arts and Humanities	150	9.8	0.8
Engineering and Architecture	159	18.6	1.1
Health Sciences	340	15.7	1
Science	121	8.4	0.8
Social and Legal Sciences	483	47.6	1.4
Living at first term			
Parent's home	874	73.3	1.4
Other	379	26.7	1.4
Childhood-Adolescent experiences			
Adversities			
Breakdown of family structure	252	19.0	1.4
Family maladaptation	444	36.4	1.6
Physical or sexual abuse	145	12.6	1.1
Emotional abuse or neglect	310	25.2	1.4
Dating violence	53	3.5	0.6
Bully victimization	415	35.9	1.6
Any adversity	757	61.7	1.6
Perceived support[a]			
Family			
High	489	35.0	1.5
Middle	407	33.2	1.5
Low	357	31.8	1.5
Peers/others			

	12-month follow-up sample		
	n	%	SE
High	326	25.4	1.4
Middle	495	38.0	1.6
Low	431	36.6	1.5
School			
High	381	27.5	1.4
Middle	478	38.5	1.5
Low	393	33.9	1.5
Recent stressful events			
12-month stressful events			
Death illness injury or accident	683	53.2	1.6
Breakup or betrayal arguments	710	56.5	1.6
Seriously physically or sexually	46	5.0	0.7
Trouble with the police or serious	29	5.2	0.8
Another stressful event	94	7.2	0.8
Any stressful event	1003	80.9	1.3
Current stress			
Severe stress in any area of life	338	27.4	1.4
Psychological factors		Mean	SD
Personality			
Extraversion		4.28	1.64
Agreeableness		4.31	0.93
Conscientiousness		5.20	1.27
Neuroticism		3.62	1.46
Openness to new experiences		5.19	1.22
Coping strategies			
Positive coping strategies		25.9	5.22
Student expectations			
Positive expectations		5.64	1.04
Impairment and mental health	n	%	SE
12-month role impairment			
Any severe role impairment	225	19.1	1.3
12-month mental health problems			
Bipolar spectrum disorder	43	3.8	0.6
Panic disorder	37	2.6	0.5
Alcohol abuse or dependence	43	4.6	0.7
Substance abuse or dependence	24	2.4	0.5
Adult Attention deficit	162	13.2	1.1
Suicidal ideation	138	10.7	0.9
Lifetime symptoms			
Lifetime MDE symptoms			
Sadness or depressed	539	42.2	1.6
Discouraged	575	45.4	1.6
Diminished interest or pleasure	424	33.6	1.5
Worthlessness, feel down on	478	36.0	1.5
Thoughts of death	182	15.1	1.1
Diminished concentration	265	22.0	1.3
Number of symptoms			
0	472	38.3	1.5
1	150	12.0	1
2	138	11.2	1
3	164	13.3	1.1
4	159	11.3	1
5	113	9.1	0.9
6	57	4.9	0.7
Lifetime GAD symptoms			
Anxiety or nervousness	483	38.8	1.5

	12-month follow-up sample		
	n	%	SE
Worry about a number of different things or about everything	597	47.4	1.5
More anxious, nervous or worried than other people	367	26.2	1.4
Worry or anxiety about things other people wouldn't worry about	338	27.1	1.4
Difficulty to control the worry or anxiety	364	28.8	1.4
Restlessness or feeling keyed up or on edge	420	30.6	1.4
Irritability	479	34.9	1.4
Number of symptoms			
0	426	35.4	1.5
1	140	11.1	1
2	116	9.4	0.9
3	122	10.3	0.9
4	103	8.1	0.9
5	99	7.4	0.8
6	96	6.7	0.8
7	89	6.5	0.8
8	61	5.1	0.7

a.-Family: lowest tertile [1–3.75], middle tertile [3.75–4.5], highest tertile [4.5–5.0]; Peers/others: lowest tertile [1–2.75], middle tertile (2.75–3.5], highest tertile (3.5–5.0]; School: lowest tertile [1–3.33], middle tertile [3.33–4.17], highest tertile [4.17–5.0].

n unweighted; % weighted; SE: standard error; SD: standard deviation.

Supplementary table 2. Bivariate associations of sociodemographic and university-related variables with first-onset and persistence of MDE-GAD at 12-month follow-up.

	First-onset				Persistence			
			Bivariate model				Bivariate model	
	%	SE	OR	95%CI	%	SE	OR	95%CI
Socio-demographics								
Gender (ref= Male)								
Female	49.6	1.8	1.02	(0.64-1.61)	67.9	2.4	1.06	(0.66-1.71)
Age (ref= >18)								
18	68.9	1.8	0.86	(0.53-1.42)	66.3	2.4	0.88	(0.56-1.38)
Country of birth (ref= Spain)								
Non Spain	4.2	0.7	0.9	(0.31-2.60)	6.9	1.4	1.56	(0.65-3.78)
Parents University Studies (ref= Neither)								
At least one	44.2	2.0	1.35	(0.86-2.12)	38.9	2.5	0.66	(0.43-1.02)
Religion (ref=Christian)								
No religion	61.6	2.0	1.8	(1.04-3.13)	65	2.8	1.0	(0.63-1.59)
Another religion	2.0	0.6	3.05	(0.77-12.0)	1.1	0.6	1.05	(0.13-8.57)
Place raised (ref= Large/Small City)								
Suburbs	5.5	1.1	0.84	(0.30-2.34)	3.1	0.9	1.52	(0.46-5.02)
Town/village/ rural area	28.5	1.8	0.73	(0.42-1.26)	29.5	2.4	1.06	(0.67-1.68)
Sexual orientation (ref= Heterosexual)								
Non-heterosexual	10.8	1.2	1.63	(0.83-3.21)	19.3	2.0	**2.10**	(1.22-3.63)
University socio-demographics								
University (ref= Balearic Islands University (UIB))								
Basque Country University (UPV-EHU)	46.7	1.8	0.77	(0.37-1.59)	38.6	2.4	0.95	(0.50-1.78)
Cadiz University (UCA)	20.0	1.5	1.18	(0.52-2.63)	19	2.0	0.84	(0.40-1.76)
Miguel Hernandez University (UMH)	9.4	1.1	0.99	(0.39-2.50)	13	1.7	0.8	(0.36-1.78)
Pompeu Fabra University (UPF)	12.5	1.2	1.09	(0.47-2.57)	15.5	1.7	0.94	(0.45-1.98)
Academic Field (ref= Arts and Humanities)								
Engineering and Architecture	23.0	1.5	0.69	(0.29-1.69)	10.2	1.6	0.54	(0.23-1.26)
Health Sciences	14.9	1.3	0.58	(0.23-1.47)	17.1	1.8	0.76	(0.37-1.54)
Science	8.3	1	0.55	(0.18-1.65)	8.5	1.4	0.81	(0.34-1.95)
Social and Legal Sciences	46.0	1.8	0.94	(0.43-2.06)	50.5	2.4	0.84	(0.45-1.56)
Living at first term(ref= Other)								
Parent's home	72.4	1.7	0.72	(0.45-1.16)	74.9	2.3	1.37	(0.86-2.20)

Significant odds ratios are shown in bold (Raw p-value statistically significant after adjustment for multiple comparisons using Benjamini-Hochberg procedure with false discovery rate 0.05). P-value obtained from F-test to evaluate significant difference in estimates based on multiple imputations.

% weighted. SE: Standard Error; OR: odds ratio; CI: confidence interval; ref: Reference category.

Supplementary table 3. Multivariable logistic regression model including predictors for first-onset of MDE-GAD at 12-month follow-up.

	First-onset		
	aOR	95%CI	p-value[a]
Socio-demographics			
Gender (ref= Male)			
Female	1.0	(0.5-1.7)	0.892
Age (ref= >18)			
18	0.5	(0.3-1.0)	0.033
Parents University Studies (ref= Neither)			
At least one	1.4	(0.8-2.3)	0.246
Living at first term(ref= Other)			
Parent's home	0.7	(0.4-1.1)	0.127
Childhood-Adolescent experiences			
Adversities			
Breakdown of family structure	0.9	(0.4-1.8)	0.719
Family maladaptation	1.3	(0.7-2.4)	0.372
Emotional abuse or neglect	3.2	(1.7-5.7)	<0.01
Perceived support [b]			
Family (ref= Low)			
High	1.0	(0.5-2.1)	0.446
Middle	1.4	(0.8-2.7)	
Peers/others (ref= Low)			
High	0.5	(0.2-1.1)	0.198
Middle	0.8	(0.4-1.5)	
Recent stressful events			
12-month stressful events			
Death illness injury or accident	1.4	(0.8-2.4)	0.201
Current stress			
Severe stress in any area of life	3.0	(1.7-5.3)	<0.01
Psychological factors			
Personality			
Extraversion	0.9	(0.6-1.2)	0.321
Agreeableness	0.9	(0.7-1.2)	0.430
Neuroticism	1.7	(1.3-2.3)	<0.01
Openness to new experiences	1.2	(0.9-1.7)	0.150
Coping strategies			
Positive coping strategies	0.8	(0.6-1.1)	0.143
Student expectations			
Positive expectations	0.9	(0.7-1.2)	0.462
Lifetime symptoms			
Lifetime MDE symptoms			
Sadness or depressed	1.9	(1.0-3.7)	0.047
Discouraged	1.1	(0.6-2.1)	0.829
Diminished interest or pleasure	1.3	(0.6-2.5)	0.494
Diminished concentration	0.8	(0.3-1.9)	0.608
Lifetime GAD symptoms			
Worry about a number of different things or about everything	2.4	(1.4-4.0)	<0.01
AUC			*0.76*

a.-P-value obtained from F-test to evaluate significant difference in estimates based on multiple imputations.

b.-Family: lowest tertile [1–3.75], middle tertile [3.75–4.5], highest tertile [4.5–5.0]; Peers/others: lowest tertile [1–2.75], middle tertile [2.75–3.5], highest tertile [3.5–5.0]; School: lowest tertile [1–3.33], middle tertile [3.33–4.17], highest tertile [4.17–5.0].

aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; Ref: reference category.

Supplementary table 4. Multivariable logistic regression model including predictors for persistence of MDE-GAD at 12-month follow-up.

	Persistence		
	aOR	95%CI	p-value[a]
Socio-demographics			
Gender (ref= Male)			
Female	0.7	(0.3-1.3)	0.216
Parents University Studies (ref= Neither)			
At least one	0.6	(0.4-1.1)	0.095
Sexual orientation (ref= Heterosexual)			
Non-heterosexual	2.1	(1.0-4.3)	0.057
Childhood-Adolescent experiences			
Adversities			
Family maladaptation	1.4	(0.8-2.4)	0.211
Bully victimization	1.8	(1.0-3.2)	0.054
Perceived support[b]			
Family (ref= Low)			
High	2.8	(1.3-5.9)	0.021
Middle	1.7	(0.9-3.3)	
Peers/others (ref= Low)			
High	1.1	(0.5-2.3)	0.220
Middle	0.6	(0.3-1.2)	
Recent stressful events			
12-month stressful events			
Death illness injury or accident	1.2	(0.7-2.2)	0.447
Breakup or betrayal arguments	1.3	(0.7-2.4)	0.372
Psychological factors			
Personality			
Extraversion	0.8	(0.6-1.1)	0.108
Agreeableness	1.2	(0.9-1.5)	0.293
Conscientiousness	0.8	(0.6-1.1)	0.144
Neuroticism	1.5	(1.1-2.1)	0.015
Openness to new experiences	1.4	(1.0-1.8)	0.032
Coping strategies			
Positive coping strategies	0.8	(0.6-1.0)	0.080
Student expectations			
Positive expectations	0.9	(0.7-1.2)	0.435
Impairment and mental health problems			
12-month mental health problems			
Adult Attention deficit hyperactivity disorder	1.6	(0.8-3.0)	0.150
Suicidal ideation	2.0	(1.0-3.8)	0.043
Lifetime symptoms			
Lifetime MDE symptoms			
Diminished interest or pleasure	2.1	(1.2-3.9)	0.014
Diminished concentration	1.3	(0.7-2.3)	0.392
Lifetime GAD symptoms			
More anxious, nervous or worried than other people	1.9	(1.1-3.6)	0.034
Worry or anxiety about things other people wouldn't worry about	1.9	(1.1-3.5)	0.024
Difficulty to control the worry or anxiety	1.5	(0.8-2.9)	0.167
Restlessness or feeling keyed up or on edge	2.2	(1.2-4.2)	0.017
AUC			*0.81*

a.- P-value obtained from F-test to evaluate significant difference in estimates based on multiple imputations.

b.- Family: lowest tertile [1–3.75], middle tertile [3.75–4.5], highest tertile [4.5–5.0]; Peers/others: lowest tertile [1–2.75], middle tertile [2.75–3.5], highest tertile [3.5–5.0].

aOR: odds ratio adjusted; CI: confidence interval; AUC: Area under the curve; Ref: reference category.

Edited by
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