Estudi dels trastorns mentals a Europa mitjançant variables latents. Una aplicació sobre la comorbiditat mental

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Contingut

Introducció general

A. Resum

En aquesta tesi s'apliquen i desenvolupen models estadístics amb variables latents per a l'anàlisi conjunt (multivariant) de trastorns mentals, com a instrument de mesura en estudis epidemiològics. En l'anàlisi multivariat dels trastorns mentals no només es mesura la presència dels trastorns, sinó que també es té en compte les seves associacions, ajustant directament la comorbiditat mental, i permetent quantificar estats de salut psíquica individuals que no es poden observar directament. L'estructura de comorbiditat es construeix a partir d'estudis psiquiàtrics conceptuals previs. S'utilitzen models de tipus IRT (Item Response Theory) per construir les mesures dimensionals de salut mental que no es poden observar directament (les variables latents) a partir de la informació observada, categòrica, sobre els trastorns mentals. Els models de variables latents modelitzen simultàniament les variables observades i els individus.

Al llarg d'aquesta tesi es demostra que els trastorns mentals definits categòricament segons el manual DSM-IV responen a fenòmens dimensionals. Els trastorns mentals més rellevants poden agrupar-se en un nombre petit de dimensions, i dins de cada dimensió existeix una gradació dels nivells de salut. Aquests models poden utilitzar-se per descriure nivells de salut mental d'una població en un moment determinat (utilitzant informació sobre trastorns patits en aquell moment) o per a estimar la predisposició a patir trastorns mentals en algun moment de la vida (trastorns vida).

En aquesta tesi es realitzen estudis epidemiològics de la salut mental, enfocats en considerar la comorbiditat mental i l'estimació de les dimensions subjacents als trastorns observats, i modelant l'existència d'una classe sense trastorn ('sana') i 'malalta' dins la població. Les dades consisteixen en una mostra representativa de la població europea (ESEMeD). S'analitza l'estat 'actual' de la població per mitjà dels trastorns patits en l'últim any i es desenvolupa una metodologia per analitzar els trastorns vida tenint en compte que es disposa de mesures retrospectives, en les quals la informació sobre aparició de trastorns es troba censurada per la dreta (la gent sense trastorn observat fins al moment de la recollida de dades pot estar encara a risc de patir-lo en el futur). També es formulen i apliquen models on la dimensionalitat latent es mesura de manera discreta-ordinal, en comptes de l'assumpció contínua utilitzada habitualment. Cadascun d'aquests models descriuen diferents aspectes del la salut mental en la població europea.

B. Importància dels models de variables latents en la recerca psiquiàtrica

Moltes de les dades utilitzades en la investigació mèdica són factibles d'obtenir directament, com per exemple els marcadors biològics. D'altres, però, no es poden obtenir directament, sinó que estan basades en instruments que s'apropen a la realitat dels individus de manera indirecta. A aquest tipus de dades no observables directament se'ls anomena variables latents. Les variables latents són variables aleatòries no observades que, sota certes assumpcions estadístiques (distribució de probabilitat) i conceptuals (coneixement teòric previ de les dades), es poden incloure en un model estadístic. Tot i que les variables latents no poden ser mesurades directament, sí que observem d'altres variables que recullen els efectes de la variable latent subjacent (Bollen, 2002). L'ús de variables latents és especialment freqüent en molts camps de recerca com, per exemple, estudis sobre la qualitat de vida relacionada amb la salut i en l'àmbit de psicologia i de les ciències del comportament.

L'estudi de la salut mental és un camp de recerca on l'ús de variables latents és especialment convenient. El nivell de salut mental no es pot mesurar directament, però sí que es pot observar quin efecte té sobre determinats símptomes. Sota el supòsit que un cert nivell de salut (o malaltia) mental pot provocar l'aparició de certs símptomes (o trastorns), es pot construir un model estadístic capaç de quantificar el nivell de salut subjacent no-observable.

Els models de variables latents no són una tècnica recent dins de l'estadística. Charles E. Spearman, psicòleg britànic, va suggerir per primer cop un model d'anàlisi factorial per mesurar la intel·ligència (Spearman, 1904), on el factor no directament observable (en aquest cas la intel·ligència) és la causa comuna que afecta a la resposta d'una sèrie de tasques intel·lectuals (les variables observades). Aquest model recull dos tipus de factors: un factor d'habilitat intel·lectual comú a totes les tasques, i un factor (residual) específic de cada tasca (el que posteriorment s'anomenarà *comunalitats* i *unicitats* en l'anàlisi factorial). Estadísticament, el factor és una variable latent contínua.

Paul Lazarsfeld va ser també un dels pioners en el desenvolupament de models de variables latents. Lazarsfeld va desenvolupar models de classes latents com a anàlisi de clústers des d'un punt de vista probabilístic (Lazarsfeld & Henry, 1968). En concret,

el Latent Class Analysis (LCA) parteix de variables observades categòriques i classifica patrons de resposta en un nombre finit de classes "prototip", latents. La classe latent en els models LCA és una variable categòrica no-observada. No obstant, els mètodes d'estimació proposats per Lazarsfeld no estaven encara adequadament definits. No va ser fins a mitjans de la dècada dels 70 que els models de classes latents van donar un salt qualitatiu gràcies a què Leo Goodman va proposar un algorisme iteratiu d'estimació màxim versemblant (Goodman, 1974), donant una utilitat pràctica a les idees metodològiques de Lazarsfeld.

De manera molt genèrica, els models bàsics de variables latents es poden agrupar segons el caràcter mètric de les variables observades i latents (Bartholomew & Knott, 1999): anàlisi factorial (FA), anàlisi de trets latents (LTA), anàlisi de perfils latents (LPA), and anàlisi de classes latents (LCA).

	Variable(s) latent(s)	
Variables Observades	*Continues*	*Categòriques*
Continues	Anàlisi factorial	Anàlisi de perfils latents
Categòriques	Anàlisi de trets latents	Anàlisi de classes latents

Taula 1. Tipus bàsics de models amb variables latents. [Font: Bartholomew and Knott (1999)]

En la actualitat, els models de variables latents poden incloure una combinació de variables observades i latents continues i categòriques, donant lloc a famílies de models més complexes com els Factor Mixture Models (Lubke & Muthen, 2005), Latent Growth Models (Muthen & Khoo, 1998), Structural Equation Mixture Modeling (Bauer & Curran, 2004), entre d'altres. Els models de regressió multinivell es poden entendre també com un tipus de models amb variables latents, on els efectes aleatoris fan el paper de les variables latents.

En l'àmbit de la epidemiologia de la salut mental, les dades bàsiques són la presència i gravetat de certs trastorns o d'un conjunt de símptomes. Per exemple, la informació disponible per a aquesta tesi consta de la informació sobre trastorns mentals. En estudis d'epidemiologia psiquiàtrica usualment no es recull directament la informació sobre els trastorns mentals, sinó que es captura informació de símptomes, i mitjançant una heurística establerta s'infereix l'existència o no dels trastorns mentals. Aquesta heurística s'ajusta a les definicions de trastorns mentals internacionalment reconegudes – per exemple, el DSM-IV (American Psychiatric Association, 2000) –,

donant com a resultat variables de tipus categòric (dicotòmiques): els individus tenen o no un determinat trastorn. Amb aquestes dades no es pot mesurar el grau de severitat ni la duració dels trastorns. El DSM-IV assumeix que els trastorns són entitats diferents (es poden avaluar de manera independent) i de naturalesa dicotòmica.

Existeixen qüestionaris estructurats per avaluar l'existència de trastorns mentals en la població. En el nostre cas, es va fer ús de l'instrument CIDI 3.0 (Kessler & Ustun, 2004; Haro et al., 2006), en el qual la creació de variables que indiquen la presència de trastorns mentals segueix un procés heurístic basat en la definició dels trastorns segons el manual psiquiàtric DSM-IV (American Psychiatric Association, 2000).

El DSM es un sistema classificatori i diagnòstic dels trastorns mentals en diferents àmbits funcionals. El diagnòstic està basat en l'acompliment d'un cert nombre de criteris propis de cada trastorn. Aquests criteris són categorials i poden ser classificats, a grans trets, en criteris de discapacitat funcional, simptomatològics i de malestar subjectiu. La classificació de trastorns mentals DSM-IV ha rebut crítiques importants. Per exemple, First (2005) va destacar la dificultat de delimitar correctament les definicions de trastorns mentals. Així, és difícil saber fins a quin punt alguns trastorn del DSM-IV defineixen realment entitats mentals diferents, degut a què diversos trastorns es construeixen a partir de símptomes similars. Per tant, quan s'observen dos trastorns mentals en un mateix individu no està clar que pateixi realment dues malalties mentals o que existeixi solapament en la definició dels dos trastorns. També s'ha qüestionat la seva naturalesa dicotòmica, considerant millor mesures graduals de nivells de salut mental, així com considerar que les definicions dels trastorns no són entitats totalment diferenciades, sinó que entre elles poden existir associacions inherents (Watson et al., 1988; Clark & Watson, 1991; Krueger & Finger, 2001; Watson, 2005; Krueger et al., 2005a; Krueger et al., 2005b; Clark & Watson, 2006; Slade & Watson, 2006; Livesley, 2007).

La comorbiditat mental es defineix com la co-ocurrència de trastorns psiquiàtrics. L'estudi de la comorbiditat ha esdevingut un tema popular en psiquiatria i psicologia clínica. Entre d'altres qüestions, l'estudi de la comorbiditat mental tracta de trobar quins trastorns estan fortament associats i per què. Estudis previs han posat de manifest importants aspectes relacionats amb la comorbiditat: la comorbiditat està associada amb un increment de la gravetat dels trastorns (Vollrath & Angst, 1989; Andrade et al., 1994; Roy-Byrne et al., 2000b; Andrews et al., 2002), major durada del trastorn (Wittchen et al., 1991; Kessler et al., 1994a), major discapacitat funcional

(Hecht et al., 1990; Roy-Byrne et al., 2000a; Bijl & Ravelli, 2000b), i un increment en l'ús de serveis sanitaris (Kessler et al., 1994b; Bijl & Ravelli, 2000a). La comorbiditat també està associada a diferents perfils de factors de risc en comparació als trastorns purs (Blazer et al., 1994; de Graaf et al., 2002). L'existència de comorbiditat és útil per a entendre millor la situació d'un pacient i identificar possibles situacions de risc.

De Groot et al. (2003) mostra diversos índexs que tracten de resumir en un sol valor l'efecte de la comorbiditat sobre els pacients. L'índex més quantitatiu mostrat en l'article de De Groot et al. (2003) consisteix en una suma ponderada de les patologies observades –sense tenir en compte els possibles efectes de les interaccions–, on el pes de cada patologia estava determinat per tal de maximitzar la predicció de mortalitat. Aquests índexs estaven enfocats principalment en malalties físiques amb alta mortalitat. A més a més, mitjançant la seva manera d'avaluar la comorbiditat es perd el coneixement de la seva naturalesa: tipus de comorbiditat molt diferents poden donar resultats molt similars. Aquesta manera de mesurar la comorbiditat no és apropiada per a l'estudi de la salut mental perquè no s'associa fortament amb la mortalitat (o a cap altre únic indicador). A més a més, les diferents malalties mentals comparteixen molt més símptomes en comú que les físiques, sent necessari incloure les seves associacions.

Els models de variables latents poden modelitzar de manera multivariant la presència simultània de trastorns mentals, assignant-hi una determinada estructura definida per un model conceptual previ. La mesura latent té en compte la presència i associació dels trastorns de manera intrínseca, sense necessitat d'una mesura externa (com la mortalitat en el cas de malalties físiques). Un model conceptual determina quines associacions existeixen entre els trastorns observats i com es relacionen aquests amb la mesures d'interès no-observables (les variables latents). Un exemple senzill de model conceptual va ser estudiat per Krueger i Finger (2001), qui explica tota l'associació existent entre els trastorns d'estat d'ànim i d'ansietat perquè tots ells comparteixen una causa comuna: un factor (no observable) que determina el nivell de salut mental de tipus *internalitzant* (Figura 1). Segons aquest model conceptual, el factor (latent) *internalitzant* explica per sí sol tots els trastorns de tipus ansietat i depressió, i no existeix cap altre relació significativa entre les variables observades un cop ajustades pel factor.

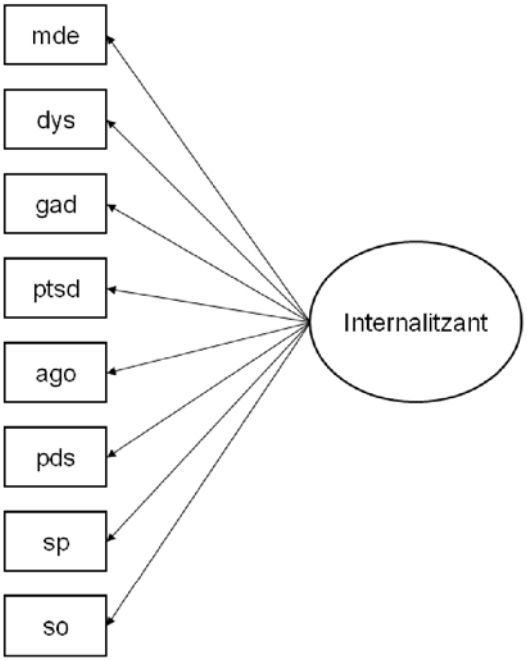

Figura 1. Model conceptual dels trastorns *internalitzant*. Trastorns observats: depressió major (mde), distímia (dys), ansietat generalitzada (gad), estrès posttraumàtic (ptsd), agorafòbia (ago), trastorn de pànic (pds), fòbia específica (sp) i fòbia social (so).

Tots els models conceptuals psiquiàtrics inclouen mesures latents subjacents als trastorns observats. Els models de variables latents juguen un paper important, ja que poden capturar tot allò que és comú a un conjunt de trastorns, ja sigui per la naturalesa pròpia dels trastorns o per un solapament en la construcció de les seves definicions segons el DSM. Per tant, els models amb variables latents poden salvar les limitacions d'una possible definició incorrecte (solapada) dels trastorns mentals, podent estimar nivells de salut de manera més robusta i precisa que la simple mesura de presència o absència de trastorns. No obstant, també permeten predir l'existència de trastorns a nivell individual quan aquesta informació sigui mancant (a partir de la resta de variables observades i de la seva puntuació latent estimada), la qual cosa permet estimar les prevalences de qualsevol patró de trastorns.

Recentment s'han establert les normes directives que hauran de donar lloc a una nova classificació de trastorns mentals: DSM-5 (American Psychiatric Association, 2010). Aquestes emfatitzen una gradació de la gravetat dels trastorns, assumint una dimensionalitat subjacent, i no només indicant la presència o absència d'un trastorn mental (Clark, 2005). Per tal d'assolir aquesta nova classificació dels trastorns mentals es necessita reformular el models conceptuals de cada trastorn, determinar quina és l'estructura subjacent a un conjunt de símptomes i quin pes té cada símptoma en la

definició dels trastorns. Els models de variables latents poden utilitzar-se per validar models conceptuals i seleccionar els símptomes més adients per a la definició de cada trastorn, així com desenvolupar una nova heurística que maximitzi la probabilitat d'assignar un valor de trastorn correcte.

En resum, els models amb variables latents són útils en recerca psiquiàtrica tant per examinar las relacions entre trastorns, com per a testar nous models de definició de trastorns. A més a més, permeten predir l'existència de trastorns a nivell individual a partir de les variables observades i estimar quantitativament nivells de salut mental (no-observable) directament segons un model conceptual. Finalment, una gran avantatge que tenen els models (multivariants) amb variables latents és la seva capacitat de modelar variables (trastorns) i descriure els individus simultàniament.

C. Models de variables latents

Un model estadístic especifica la distribució de probabilitat conjunta d'un grup de variables. En el cas que algunes d'aquestes variables no siguin observables tindrem un model de variables latents. No podem mesurar directament la variable d'interès (latent), però sí que observem variables que recullen els efectes de la variable latent no observada.

De manera molt genèrica, la distribució conjunta de les variables observades $f\left(\mathbf{y}\right)$ en un model amb variables latents $\boldsymbol{\theta}$, es formula de la següent manera:

$$f\left(\mathbf{y}\right)=\int h\left(\boldsymbol{\theta}\right)\cdot g\left(\mathbf{y}\middle|\boldsymbol{\theta}\right)d\boldsymbol{\theta} \tag{1}$$

on $h\left(\theta\right)$ és la distribució *a priori* (assumida) de les variables latents $\boldsymbol{\theta}$, i $g\left(\mathbf{y}\middle|\theta\right)$ és la distribució condicional conjunta de les dades observades, donades les variables latents. Per tant, per estimar aquests tipus de models estadístics és necessari definir un model per a les nostres dades, en el qual s'estableixi el tipus de relació existent entre les variables latents i les observades, $g\left(\mathbf{y}\middle|\theta\right)$, i, a més a més, assumir una distribució de probabilitat en les variables latents $h\left(\theta\right)$.

Dins del marc dels models de variables latents generalment s'assumeix que un conjunt reduït de variables latents expliquen totes les associacions existents entre les variables observades. Per tant, si tenim un total de J variables observades $\left(j=1,2,..,J\right)$, les distribucions condicionals de les variables observades $g_j\left(y_j\middle|\theta\right)$ són mútuament independents. Aquest concepte es coneix com a *independència local forta*. En aquest cas, les variables latents són suficients per determinar la distribució de probabilitat conjunta de les variables observades. La *independència local feble* només requereix que la correlació entre les variables observades sigui zero en condicionar-les a la les variables latents. L'assumpció de *independència local forta* facilita la construcció de la funció multivariant de la versemblança, com a producte de les distribucions univariants condicionades. Així doncs, l'equació (1) pot expressar-se com

$$f\left(\mathbf{y}\right)=\int h\left(\theta\right)\cdot\prod_{j}^{J}g_{j}\left(y_{j}\middle|\theta\right) \tag{2}$$

Els models estadístics de variables latents permeten estimar puntuacions d'aquestes variables latents no observades. Per tant, tots els possibles patrons de resposta d'un cert grup de variables observades poden ser resumits en un nombre petit de variables latents. Com a model multivariant, $f\left(\mathbf{y}\right)$, un dels seus objectius pot ser la reducció de la dimensionalitat. Si s'acompleix el principi d'independència local forta es pot arribar a una reducció de la dimensionalitat sense pèrdua significativa d'informació.

L'estimació de puntuacions de les variables latents es factible quan es coneix la seva distribució (*a posteriori*) a partir de les dades observades, $h\left(\theta\middle|\mathbf{y}\right)$.

$$h\left(\boldsymbol{\theta}\middle|\mathbf{y}\right)=h\left(\boldsymbol{\theta}\right)g\left(\mathbf{y}\middle|\boldsymbol{\theta}\right)\Big/f\left(\mathbf{y}\right) \tag{3}$$

Coneixent $h\left(\theta\middle|\mathbf{y}\right)$ es poden estimar valors latents per a cada individu, per exemple, assignant-li a cada individu i el valor més probable segons $h\left(\boldsymbol{\theta}\middle|\mathbf{y}_{i}\right)$. Aquest mètode d'estimació de les puntuacions latents s'anomena *modal a posteriori* (MAP). Bartholomew i Knott (1999) demostren que per a funcions $g\left(\mathbf{y}\middle|\boldsymbol{\theta}\right)$ de la família exponencial $\mathbf{y}$ és un estadístic suficient per a $\boldsymbol{\theta}$, independentment de la distribució *a priori* de les variables latents $h\left(\boldsymbol{\theta}\middle|\mathbf{y}\right)$. En sentit bayesià, $\mathbf{y}$ és un *estadístic suficient mínim* per a $\boldsymbol{\theta}$.

Les variables latents poden ser tant continues com discretes. Les variables latents continues, per exemple, donen lloc a l'anàlisi de trets latents. Pot ser aquest el cas de mesurar la intel·ligència per mitjà de les respostes obtingudes en un conjunt de tests. Les variables latents categòriques donen lloc a models de classes latents, on cada categoria de la variable latent es correspon amb una subpoblació (o classe). Cadascuna de les classes segueix la seva pròpia distribució de probabilitat. La distribució conjunta de tota la població és una mixtura de les distribucions de cadascuna de les classes latents. Si X és la variable latent categòrica, la distribució de probabilitat de les dades observades seria $f\left(\mathbf{y}\right)=\sum_{x}f_{x}\left(\mathbf{y}\middle|x\right)\cdot P\left[X=x\right]$.

C.1. Models IRT amb mixtures

Els models utilitzats en aquesta tesi són majoritàriament de tipus IRT (Item Response Theory) amb mixtures. Els models de IRT són una família de models de trets latents que van ser desenvolupats dins l'entorn educatiu per a mesurar el nivell d'aptitud (*ability*) davant d'un test (Lord & Novick, 1968). Els models IRT són un conjunt de models estadístics amb variables latents, on les variables observades Y_{ij} són categòriques i la variable latent θ_i subjacent és contínua. Segons Bartholomew i Knott (1999), els IRT seria un tipus d'anàlisi de trets latents, on l'aptitud és només el tipus de tret considerat a l'entorn educatiu. Conceptualment, el tipus de tret depèn del constructe que es pretén mesurar. Així, els trets latents són anomenats de manera diferent depenent de l'àrea de mesura, com ara *trets* a l'entorn de la mesura de disposicions personals. O, com en els casos que ens ocupa en aquests treball *gravetats* (quan es tracta de trastorns) o *vulnerabilitats* (quan es tracta de variables que predisposen al trastorn mental).

En aquesta tesi les variables observades Y_{ij} són binàries, prenen valor 1 quan l'individu i ha manifestat el trastorn j. La formulació del model IRT de dos paràmetres usat en aquesta tesi és el següent:

$$g\left(\hat{P}\left[Y_{ij}=1\middle|\theta_i\right]\right)=\alpha_j+\lambda_j\theta_i \qquad (4)$$

La funció $g\left(\cdot\right)$ relaciona linealment les dades observades amb la variable latent, sent usualment de tipus *logit* o *probit,* i θ_i és l'estat de salut mental o vulnerabilitat latent, no-observable, per a l'individu i. El model IRT assumeix que a majors nivells de gravetat o vulnerabilitat mental, major serà la probabilitat d'observar un trastorn, de manera que Y_{ij} prendrà el valor 1 quan la variable latent $\theta_{i|x}$ per a aquest individu superi un cert llindar (Agresti, 2002). El paràmetres d'aquest model IRT són α_j i λ_j, els quals són anàlogs al *intercept* i *càrrega factorial* de l'anàlisi factorial, respectivament. No obstant, existeixen moltes parametritzacions alternatives per expressar els models de IRT de dos paràmetres (Lord & Novick, 1968; Hambleton et al., 1991; De Boeck, 2004).

Les mixtures es refereixen a diferents subpoblacions no observades (classes latents), cadascuna de les quals tenen una distribució de probabilitat pròpia, definida segons diferents paràmetres dins del model IRT. Un exemple de modelització IRT amb mixtures pot ser el següent. Suposem que tenim un conjunt de variables binàries Y_j que recullen l'efecte una variable latent continua θ, i que la distribució de probabilitat de la variable latent és normal amb mitjana i variància diferents per a cada classe latent $\left(\mu_x, \sigma_x\right)$, sent $\theta_{i|x}$ la puntuació de l'individu i condicionat a la pertinença a la classe latent x:

$$\begin{aligned} & g\left(\hat{P}\left[Y_{ij}=1\middle|\theta_{i|x}\right]\right)=\alpha_j+\lambda_j\theta_{i|x} \\ & \theta\middle|x \sim N\left(\mu_x, \sigma_x\right) \end{aligned} \tag{5}$$

Donat que la pertinença a la classe latent no és coneguda, també s'estima la seva distribució de probabilitat, considerant X una variable multinomial:

$$\operatorname{logit}\left(\hat{P}\left[X=x\right]\right)=\tau_x \tag{6}$$

Aquest és el tipus de model IRT que s'ha utilitzat com a base de les anàlisis d'aquesta tesi. La classe latent s'ha fet servir per a distingir dos grups diferenciats dins de la població que podriem anomenar com a 'sans' i 'malalts'. És assumible que no tota la població pateix trastorns mentals, per tant, un model capaç de modelar aquestes dues classes (o subpoblacions) simultàniament donarà un millor ajust estadístic i una millor descripció de la població. Considerant que la variable latent pren valors elevats per a descriure estats de salut positius i valors baixos en cas de malaltia, s'han construït les classes latents de manera que la distribució latent per als malalts té una mitjana igual a zero $\theta\middle|x=1 \sim N\left(0, \sigma_1\right)$, i la classe de sans es troba degenerada en un valor elevat $\theta\middle|x=2 \sim N\left(10, 0\right)$.

D. Descripció de les dades: Projecte ESEMeD

Les anàlisis d'aquesta tesi s'han dut a terme sobre una mostra representativa de la població europea, recollida en el marc d'un gran projecte internacional: European Study of the Epidemiology of Mental Disorders / Mental Health Disability: a European Assessment in year 2000 (ESEMeD/MHEDEA 2000), d'aquí en endavant referit com a ESEMeD, com a part d'un projecte de la OMS - WHO World MentalHealth (WMH) Survey Initiative (Alonso et al., 2002). L'estudi ESEMeD tenia per objectius mesurar la prevalença dels trastorns mentals en Europa i trobar els factors associats als trastorns, mesurar l'impacte que tenen sobre la qualitat de vida i l'ús que se'n fa dels serveis mèdics i de fàrmacs. Les dades van ser recollides representativament en 6 països d'Europa: Alemanya, Bèlgica, Espanya, França, Holanda i Itàlia, amb una mostra total de 21.425 individus majors de 18 anys i no institucionalitzats. Les entrevistes van ser realitzades entre Gener del 2001 i Agost del 2003 per empreses contractades a cada país, mitjançant l'assistència d'ordinadors que facilitaven l'administració i la recollida de les dades (Computer Assisted Personal Interview – CAPI) programada amb el software Blaise (Statistics Netherlands, 1999). Es va seleccionar una mostra aleatòria estratificada, multietàpica, sense reemplaçament dins de cada país. La taxa de resposta global va ser del 61.2%. Els individus de la base de dades tenen assignats pesos per tal d'obtenir estimacions representatives de tota la població. Una descripció més detallada de com es va seleccionar la mostra es troba en Alonso et al. (2004c).

Específicament, l'estudi ESEMeD tenia per objectiu l'estimació en els 6 països d'Europa de:

(i) prevalences 1-mes, 12-mesos i vida (en algun moment de la vida) dels trastorns mentals més comuns en la població general

(ii) l'associació dels trastorns de l'estat d'ànim i d'ansietat amb factors socio-demogràfics i d'altres factors de risc (com ara l'historial familiar)

(iii) la qualitat de vida de gent amb trastorns de l'estat d'ànim i d'ansietat i l'anàlisi d'altres factors que hi poden influir

(iv) tractaments mèdics rebuts pels individus que compleixen criteris de diagnòstic, la cobertura o manca de cobertura segons les seves necessitats, i la qualitat del tractament rebut.

Per tal d'optimitzar el temps d'entrevista es va dur a terme un procés d'enquesta de 2 fases. La primera fase la contestava tothom i hi conté l'avaluació dels trastorns més

comuns, mesures de qualitat de vida, ús de serveis sanitaris i informació demogràfica. Només aquells que excedien d'un cert nombre de símptomes (en una primera secció de cribatge) i una selecció aleatòria del 25% de la resta de la mostra van realitzar la segona fase del qüestionari, que inclou l'avaluació de trastorns mentals addicionals, trastorns físics crònics, i factors de risc. A aquesta submostra se li va assignar pesos per tal de garantir la representativitat poblacional (Alonso et al., 2004c).

La base de dades ESEMeD és en l'actualitat una de les fonts d'informació més grans, comparable i exhaustiva sobre la prevalença de gent amb trastorns mentals, la discapacitat i les necessitats mèdiques no cobertes, a Europa.

Les anàlisis d'aquesta tesi s'han basat en aquells individus que han contestat la segona fase del qüestionari (8.796 casos), ja que aquests tenen mesurats un nombre major de trastorns mentals, i conserven encara la representativitat poblacional.

Les dades bàsiques sobre les quals s'ha dut a terme les anàlisis d'aquesta tesi són variables binàries, indicant la presència o absència de trastorns mentals DSM-IV en l'últim any (12-mesos) o en algun moment de la vida. L'anàlisi dels trastorns 12-mesos dóna una descripció del nivell de salut mental actual. L'anàlisi dels trastorns vida descriuen la predisposició (intrínseca) dels individus a patir trastorns mentals al llarg de la vida. La comorbiditat 12-mesos estudia la co-ocurrència de trastorns mentals durant l'últim any, i la comorbiditat de trastorns vida mesura l'aparició de diferents trastorns en algun moment de la vida, sense necessitat d'haver aparegut simultàniament ni de què hi hagi solapament temporal entre ells - només es considera que hagin aparegut en la mateixa persona. Tant les mesures 12-mesos com les de tipus vida, són descriptors útils per a entendre quina és la situació de la salut mental en l'àmbit poblacional. A partir d'aquestes mesures es poden determinar factors de risc i suggerir polítiques preventives o que permetrin apropar els serveis sanitaris adients en aquelles subpoblacions que més ho requereixin, així com servir de base per a futurs estudis cost-efectivitat de intervenció pública.

Aquestes dades ESEMeD jan han estat analitzades anteriorment i han donat com a resultat un gran nombre de publicacions. La gran majoria d'estudis enfocats en l'avaluació dels trastorns mentals consistien en descripcions univariants i bivariants, sense considerar estructures (multivariants) subjacents als trastorns. Per exemple, estudis sobre la prevalença dels trastorns mentals (Alonso et al., 2004a; Bonnewyn et al., 2007) i comorbiditat (Alonso et al., 2004b).

La informació poblacional psiquiàtrica que prové d'estudis epidemiològics amb mostres transversals, com és el cas de les dades ESEMeD, té la peculiaritat de basar-se en mesures vida incompletes, ja que en no es poden observar els individus al llarg de tota la vida: només es pot obtenir informació retrospectiva fins al moment de l'entrevista. Els individus que fins a aquell moment no hagin patit cap trastorn mental encara estan a risc de patir-lo en el futur. Tot i aquesta limitació, estudis epidemiològics sobre prevalences de tipus vida majoritàriament han fet estimacions en base a les dades observades, sense tenir en compte les censures, per exemple: Alonso et al. (2004a), donant lloc a resultats esbiaixats (infra-estimats). Recentment s'estan aplicant models actuarials de supervivència per millorar l'estimació de la prevalença de trastorns vida (Kessler et al., 2005; Kessler et al., 2007). No obstant, entre d'altres limitacions, aquest mètode no modela la comorbiditat mental.

És necessari, doncs, donar un pas més enllà en l'estudi de les dades ESEMeD, desenvolupant models que tinguin en compte el patró de trastorns observat en els individus (considerant simultàniament tots els trastorns mentals), que estimin sense biaix les prevalnces vida i que aportin nous tipus d'informació, com nivells quantitatius de la salut mental.

E. La comorbiditat mental mitjançant variables latents

Usualment, en epidemiologia psiquiàtrica s'han analitzat la presència de trastorns mentals separadament, donant estimacions de prevalences de cada trastorn, o agregades segons determinades tipologies – per exemple (Alonso et al., 2004a; Alonso et al., 2004b). Implícitament s'ha assumit que no existeix cap patró de correlació inherent als trastorns observats; i en agregar diferents trastorns s'assumeix que cadascun d'ells té el mateix pes a l'hora de definir la variable agregada. Aquest mètode és adequat quan l'interès de l'estudi es centra en els trastorns individuals, però no s'en poden inferir nivells de salut mental. En cas de voler estimar nivells de salut mental a partir dels trastorns observats, és necessari aplicar models multivariants, que analitzin simultàniament la presència conjunta de les variables psiquiàtriques observades, considerant que cada trastorn observat reflecteix un nivell de salut diferent, així com l'efecte conjunt de diversos trastorns presents.

Ja es troben publicats diferents models conceptuals on es proposen com es relacionen els trastorns mentals entre ells, i quines possibles estructures subjeuen als trastorns mentals observats (Watson et al., 1988; Clark & Watson, 1991; Krueger & Finger, 2001; Watson, 2005; Krueger et al., 2005a; Krueger et al., 2005b; Clark & Watson, 2006; Slade & Watson, 2006; Livesley, 2007). Els models de variables latents són adequats per avaluar l'estructura de comorbiditat subjacent als trastorns mentals, validant els models conceptuals, així com per estimar estats de salut mental que no són observables directament. Per tant, els models de resposta multivariants amb variables latents són capaços de modelar la comorbiditat mental. Aquests models estadístics també permeten estimar puntuacions individuals de les variables latents, no-observades. En aquest cas estimem nivells de salut mental. Aquestes puntuacions seran d'utilitat per descriure l'estat de salut mental en la població i, alhora, trobar quins factors socio-demogràfics estan associats amb els diferents nivells de salut mental. Aquesta característica dels models multivariants de variables latents és molt convenient, ja que es pot mesurar quin impacte tenen altres variables directament sobre els nivells de la salut mental, en comptes d'inferir el seu impacte observant els efectes trastorn per trastorn, resultant molt més parsimoniós i rellevant.

A diferència de la definició categòrica (binària) de trastorn mental segons el DSM-IV, les variables latents estimen quantitativament nivells subjacents de salut mental, on s'assumeix una gradació amb múltiples valors possibles, i on cada variable observada

té un pes diferent en la construcció i l'estimació de la variable latent. Aquesta gradació de valors latents pot considerar-se com a un conjunt infinit (variable latent contínua) o finit (variable latent discreta ordinal).

Tot i què ja hi ha estudis publicats on es testen estadísticament els models psiquiàtrics conceptuals de trastorns mentals DSM-IV, es va observar que aquests models estadístics molt poques vegades han estat utilitzats com a instruments de mesura: estimant puntuacions latents per a cada individu. Al 1988, ja fa més de 20 anys, Clifford Clogg ja mencionava l'escàs ús que se'n feia d'aquesta propietat dels models de variables latents (Clogg, 1988), i encara avui en dia no s'utilitza de manera generalitzada en el camp de l'epidemiologia.

La modelització de la comorbiditat mental analitza el grau d'associació entre els trastorns mentals. És evident que no tota la població pateix aquest tipus de malalties, i per tant, es podrien estimar models on una part de la mostra tingui una probabilitat pràcticament nul·la de patir trasotorns mentals, mentre que la resta de la població segueixi un determinat model de comorbiditat mental. Amb aquest model de dues classes d'individus es podria arribar a una descripció més refinada de la població, així com de les associacions entre els trastorns. A efectes pràctics, podriem denominar aquestes classes com 'sana' i 'malalta' respectivament. Quan a priori desconeixem quins individus es troben en cadascun dels grups, aquest fenòmen es pot modelitzar mitjançant classes latents. La classe latent és una variable categòrica no-observada. La pertinença a cadascuna d'aquestes classes és també estimada pel model, probabilísticament. La modelització conjunta d'aquestes dues subpoblacions és una aportació nova dins la metodologia en recerca epidemiològica, ja que, segons el meu coneixement, no existeixen publicacions (al menys en el camp de l'epidemiologia psiquiàtrica) on s'avaluïn malalties a nivell poblacional distingint entre població 'sana' i 'malalta'. Els models de classes latents permeten estimar un model estadístic on els seus paràmetres són diferents entre classes. D'aquesta manera, un sol model pot ajustar correctament tota la població.

Objectius

L'objectiu principal d'aquesta tesi és desenvolupar i aplicar models estadístics per analitzar de manera multivariant la presència i associació dels trastorns mentals més freqüents en població general. Es busca establir models multivariants capaços de modelar la comorbiditat mental, estimar puntuacions de salut mental individual i, alhora, trobar quins factors socio-demogràfics estan associats amb els diferents nivells de salut mental. Aquests models inclouen el fenomen de la comorbiditat mental de manera més completa, compacta i precisa del que es ve realitzant en epidemiologia.

En primer lloc, es planteja una revisió de models psiquiàtrics conceptuals que defineixen les associacions (estructures subjacents) entre símptomes o trastorns mentals. Es vol explorar la possibilitat de construir instruments de mesura de la salut mental a partir de models conceptuals per, posteriorment, realitzar una descripció epidemiològica de l'estat (actual) de la salut mental de la població europea, utilitzant com a instruments de mesura models estadístics basats en models conceptuals i dades de trastorns 12-mesos. Donat que els trastorns de salut mental clarament no afecten a tota la població, es planteja la modelització explícita de dos subpoblacions ben diferenciades: 'sans' i 'malalts'.

Un altre objectiu d'aquesta tesi és provar de modelar la dimensionalitat mental mitjançant factors discrets ordinals, com alternativa als factors continus. Es provaran algunes propietats des models de factors ordinals com els tests d'invariància (Mellenbergh, 1989), afegir covariables i modelitzar classes latents definint 'sans' i 'malalts'. Finalment s'avaluarà quines avantatges poden tenir respecte de models amb factors continus.

Finalment, i com a major aportació d'aquesta tesi, es desenvoluparà una metodologia per modelitzar correctament dades de trastorns al llarg de la vida, tenint en compte les censures d'aquest tipus de dades. En concret, es pretén desenvolupar un model estadístic que mesuri sense biaix les prevalences vida dels trastorns mentals, així com les comorbiditats i, més en general, la prevalença de qualsevol patró de trastorns mentals. A més a més, aquest model permet estimar la predisposició subjacent individual de patir trastorns mentals i descriure la població europea en aquest aspecte, tenint en compte l'efecte que puguin tenir variables socio-demogràfiques. Bàsicament, es tracta d'estendre els models de IRT utilitzats amb èxit en trastorns 12-mesos, per modelar correctament trastorns vida.

Informe del director del factor d'impacte dels articles

Amb data de 28 Agost 2010, les publicacions que formen part d'aquesta tesi es troben en la situació que es mostra a continuació.

Primer article

Autors	Almansa J, Vermunt JK, Forero CG, Vilagut G, Ormel J, Haro JM, Girolamo G, Alonso J
Títol	Exploring conceptual Comorbidity models as measurement instruments for Mental Health Epidemiology Research
Revista	*Quality of Life Research* Factor d'Impacte (2009): 2.376 Secció "Health Care Sciences & Services": Ranking 20 de 69 Secció "Public, Environmental & Occupational Health": Ranking 37 de 122
Estat	·Enviada una segona revisió el 4 de Març 2010, actualitzant algunes parts del manuscrit segons suggeriments de propi editor de la revista.

Segon article

Autors	Almansa J, Vermunt JK, Forero CG, Vilagut G, De Graaf R, Girolamo G, Alonso J
Títol	Measurement and description of underlying dimensions of comorbid mental disorders using Factor Mixture Models: results on the ESEMeD project.
Revista	*International Journal of Methods in Psychiatric Research* Factor d'Impacte (2009): 3.030 Secció "Psychiatry": Ranking 40 de 117.
Estat	·Enviat a la revista el 28 Gener 2010. ·Enviat una segona versió el 25 d'Agost 2010, després de rebre els comentaris de l'editor i dels revisors anònims.

Tercer article

Autors	Almansa J, Vermunt JK, Forero CG, Alonso J
Títol	Mental-heatlh assessment using discrete factor models.
Revista	Psychometrika Factor d'Impacte (2009): 1.205 Secció "Mathematical Psychology": Ranking 5 de 11. Secció "Social Sciences, Mathematical Methods": Ranking 15 de 38.
Estat	En preparació

Quart article

Autors	Almansa J, Vermunt JK, Forero CG, Vilagut G, De Graaf R, Haro JM, Alonso J
Títol	IRT models with censored binary indicators. Application to lifetime mental health comorbidity, assessed in the ESEMeD project.
Revista	Multivariate Behavioral Research Factor d'Impacte (2009): 2.328 Secció "Social Sciences, Mathematical Methods": Ranking 4 de 38.
Estat	Enviat el 28 Juny 2010

Signat pel directors de la Tesi:

Dr. Jordi Alonso

Dr. Jeroen K. Vermunt

Discussió global dels resultats obtinguts, de la discussió d'aquests resultats i de les conclusions finals

A. Dimensionalitat psiquiàtrica i modelització estadística

Com ja s'ha mencionat en la introducció de la tesi, hi ha evidència científica, tant en estudis conceptuals com en aplicacions estadístiques, de què els trastorns mentals definits segons el DSM-IV no són entitats independents, sinó que segueixen un patró de comportament determinat per dimensions (o factors) no observades. A pesar de la quantitat de recerca realitzada sobre models de comorbiditat mental, aquests models han estat usats principalment per validar estructures subjacents a la classificació de trastorns mentals segons el manual diagnòstic i estadístic dels trastorns mentals (DSM), però no s'han utilitzat de manera generalitzada com a instruments de mesura clínica o epidemiològica. Al llarg dels articles d'aquesta tesi queda demostrat que es poden construir models estadístics com a instruments de mesura per estimar nivells de salut mental que provenen directament de models conceptuals. Aquestes puntuacions estimades tenen en compte la presència i associació dels trastorns mentals, els diferents pesos que cada trastorn té sobre la seva dimensió (factor) mental, l'efecte de covariables socio-demogràfiques i, en definitiva, tot allò que pugi ser inclòs dins d'un model conceptual psiquiàtric. Per tant, recullen directament l'efecte de la comorbiditat mental. Aquestes puntuacions estimades permeten fer inferència directament sobre nivells de salut mental, anant molt més enllà que la simple descripció de l'existència o no de trastorns en la població.

Usualment s'han fet servir descriptives univariants i bivariants de les variables de trastorns mentals, i d'agrupacions d'aquestes variables, per fer descriptives poblacionals. Aquesta metodologia és correcte quan l'interès de la recerca es focalitza en trastorns concrets, analitzant-los separadament, però no és adequada per estimar estats de salut mental. No té en compte el patró de comportament (i correlació) subjacent a les variables psiquiàtriques, i no és capaç de donar una puntuació individual del nivell de salut mental. Els models estadístics amb variables latents ja recullen en la puntuació estimada per a cada factor no-observable tot allò que afecta a

la salut mental dels individus, mesurat quantitativament en un únic valor per a cada factor psiquiàtric; a diferència de les comparacions de presència de trastorns (o tipus de trastorn) que habitualment es fa en epidemiologia psiquiàtrica, on a partir de diverses comparacions s'interpreten de manera genèrica els nivells de salut mental poblacional. Les puntuacions latents, per tant, aporten una major precisió en la comparació psiquiàtrica individual i entre subpoblacions.

Els resultats d'aquests articles també confirmen l'estructura dimensional dels trastorns mentals, en comparació amb la classificació categòrica actual del DSM. Molts investigadors psiquiàtrics ja han suggerit en el passat avaluar els trastorns mentals com una gradació de diferents nivells de salut, en comptes de la simple presència o absència del trastorn (Watson et al., 1988; Clark & Watson, 1991; Krueger & Finger, 2001; Watson, 2005; Krueger et al., 2005a; Krueger et al., 2005b; Clark & Watson, 2006; Slade & Watson, 2006; Livesley, 2007).

Així doncs, els trastorn mentals més comuns en població general (com són els de tipus depressió, ansietat, fòbies, trastorns de substàncies i del comportament) no es donen de manera independent, sinó que existeix una estructura subjacent que explica la presència i associacions dels trastorns. Aquests es poden agrupar en dos dimensions principals: *internalitzant* i *externalitzant* (Krueger, 1999; Khan et al., 2005; Cerda et al., 2008). La dimensió *internalitzant* mesura la predisposició a expressar internament l'estat mental, que es reflecteix en trastorns de tipus depressió i ansietat. La dimensió *externalitzant* mesura la predisposició a expressar l'estat mental cap a l'exterior de la persona, i inclou trastorns de substàncies i del comportament. La dimensió *internalitzant* pot modelitzar-se mitjançant dues subdimensions: *distress* (trastorns de l'estat d'ànim) i *fear* (trastorns d'ansietat). Ambdues subdimensions defineixen entitats diferents, tot i que comparteixen una mateixa causa comuna (Joiner, Jr., 1996; Krueger, 1999; Watson, 2005). Els resultats demostren que la separació en aquestes 2 subdimensions millora l'ajust de les dades, tot i que un únic factor *internalitzant* té encara un ajust acceptable i és més parsimoniós. Per això, els models on el factor *internalitzant* estigui subdividit en les subdimensions *distress* i *fear* només seria recomanable quan aquestes subdimensions siguin realment les dimensions mentals d'interès. En tots aquets models conceptuals explorats, basats en trastorns mentals del DSM, no existeix cap tipus de causalitat entre els trastorns, sinó que tots els trastorns són conseqüència directe de nivells de salut mental no-observable, subjacent als trastorns mentals.

Tots aquests resultats troben coherència amb les directives recentment plantejades per a la realització d'una nova classificació dels trastorns mentals: el DSM-5 (American Psychiatric Association, 2010). Per a la construcció d'aquesta nova classificació es considerarà una estimació gradual dels estats mentals, en comptes de la classificació dicotòmica que proveeix el DSM-IV (American Psychiatric Association, 2000). També considera depressió i ansietat com a dos dimensions dels trastorns de tipus *internalitzant*, on la subdimensió de depressió inclou tant els trastorns depressius (distímia i depressió major) com l'ansietat relacionada amb la depressió (ansietat generalitzada), mentre que la subdimensió ansietat es centra més en el trastorns de tipus fòbia (agorafòbia, fòbia social, fòbia específica i pànic).

Els models basats en dades de trastorns mentals només proveeixen puntuacions precises en el rang latent corresponent a la zona 'malalta'. L'aparició de trastorns mentals es donen en llindars extrems de la dimensió latent, mentre que aquells que no mostren un cert trastorn poden estar situats en una rang molt ampli, desde nivells de trastorns sub-llindar fins a estats positius de la salut mental. Incloent la mixtura de les classes 'sans' i 'malalts', la precisió de les puntuacions en la zona més elevada arriba també a una precisió acceptable, però en el rang intermedi segueix tenint un error estàndard força elevat. Es necessitaria d'altres tipus de variables que mesurin estats de salut lleus (o fins i tot positius, referits a salut en comptes de mesurar només nivells de malaltia) per a obtenir un instrument de mesura precís al llarg de tot el rang latent. Això també permetria explorar l'existència de més de dos classes en la població (per exemple, una possible descripció d'un model de 3 classes podria ser: malalt-greu, malalt-lleu i sa).

La modelització discreta-ordinal de les dimensions latents de salut mental pot ser una alternativa eficaç a la molt habitual assumpció de normalitat en la distribució de la variable latent. Donat que la distribució discreta-ordinal no assumeix cap tipus de forma *a priori* pot ajustar-se millor a la distribució latent no-observada. Els factors discrets permeten explorar quins són el nombre de punts (latents) més rellevants i quina distància hi ha entre ells, podent "etiquetar" cada punt segons la seva gravetat (molt-greu, lleu, sa, etc.). Aquesta podria ser una manera d'avaluar la gradació de la gravetat dels trastorns mentals en la nova classificació DSM-5. A més a més, la flexibilitat de la distribució de probabilitat discreta permet situar els punts de diferent manera per a diferent subpoblacions, podent comparar (gràficament) les distribucions de freqüències 'típiques' per a cada subpoblació. Això facilita la interpretació i podria millorar l'estimació de la distribució latent.

Les anàlisis realitzades amb factors discrets han mostrat que la distribució del factor *distress* dins la població 'malalta' pot tenir una forma lleugerament asimètrica. No obstant, encara no s'ha explorat en profunditat fins a quin grau de no-normalitat el model normal comença a donar resultats incorrectes, i quan seria estadísticament recomanable utilitzar variables latents discretes en detriment de les contínues-normals. El models aquí ajustats amb factors discrets i continus donen resultats generals força similars, i només varien de manera rellevant en la forma d'interpretar les dimensions latents.

B. Classes latents

La modelització de classes latents és una metodologia molt útil en recerca epidemiològica. És possible comprovar que no tota la població segueixi un mateix patró de comportament respecte d'algunes malalties. En el cas estudiat en aquesta tesis, s'ha trobat clarament una separació entre població 'sana' i 'malalta' referent a trastorns mentals. Aquesta classificació és coherent amb la realitat, ja que no tota la població es veu afectada per trastorns mentals.

Els models amb classes latents defineixen subpoblacions no-observades, cadascuna de les quals segueix una distribució de probabilitat diferent. En la majoria dels casos, la població segueix un mateix tipus de distribució, però amb paràmetres diferents per a cada classe. En aquesta tesi s'ha classificat la població en 'sana' i 'malalta' segons el tipus de puntuació en els factors latents. S'ha demostrat que els factors lantents són invariants, i per tant, ambdues classes només es diferencien en la seva puntuació lantent. La modelització de la comorbiditat es única per a tota la població. Els 'sans' tenen una puntuació fixa elevada, de manera que la probabilitat d'observar-se qualsevol trastorn és pràcticament nul·la. Els 'malats', en canvi, segueixen una distribució latent amb mitjana zero. Aquesta modelització de classes (o mixtures) ha resultat en una millor bondat d'ajust i interpretabilitat de les dades que el model d'una classe.

Les covariables en un model de IRT amb classes latents poden afectar a les variables latents d'interès de dues maneres diferents. Primerament, les covariables poden tenir un efecte sobre la probabilitat de pertànyer a cadascuna de les classes latents. En

segon lloc, les covariables poden mesurar diferents graus de gravetat dins de cada classe latent. Per exemple, en l'anàlisi dels trastorns mentals en els últims 12 mesos (en el segon article d'aquesta tesi), s'ha trobat que la proporció de sans i malats difereix entre homes i dones, però dins de la classe de malalts no hi ha diferències de gravetat entre gèneres. En canvi, no s'han trobat diferències en la probabilitat de pertànyer a ambdues classes segons l'estat civil, però dins de la classe de malalts els casats amb anterioritat (vidus i separats) tenen un grau de gravetat major que els no s'ha casat mai, i aquells que estan casats (o cohabitant) són els que tenen menor gravetat. D'aquesta manera, les diferències observades en les dades poden ser explicades per mitjà d'aquestes dues causes diferenciades.

Una conclusió principal d'aquesta tesi és la recomanació de plantejar més sovint incloure aquesta separació latent en 'sans' i 'malalts' en estudis epidemiològics. Permetrà detectar amb més precisió poblacions de risc o quina subpoblació necessita una intervenció més intensa, de manera que es podran administrar els recursos sanitaris de manera més eficient. Suposar que tota la població segueix un mateix patró de comportament pot ser massa simplista i pot emmascarar efectes significatius rellevants. Però també d'altres aplicacions podrien beneficiar-se en ser modelades per mitjà de classes latents, per exemple: modelar els usos de serveis sanitaris (per a una determinada patologia, quan una gran part de la població mai no fa ús de serveis sanitaris), estudis basats en l'índex de massa corporal (classifica la població en sana i obesa), etc.

C. Descripció de la població Europea segons la salut mental

La modelització factorial permet avaluar l'impacte de covariables directament sobre el nivell de salut de cada dimensió (factor) mental – de forma més clara, directe i parsimoniosa que, per exemple, comparant l'efecte trastorn a trastorn (o grups de trastorns). L'efecte de les covariables sobre la puntuació de les dimensions mentals poden descriure la salut mental en la població segons les característiques socio-demogràfiques. A continuació es presenten els resultats generals més significatius.

Les dones i la gent jove presenten un major risc de malaltia mental (tot i que en trastorns vida l'efecte edat podria ser degut a un biaix de memòria). La presència de trastorns físics crònics també té un cert efecte a favor de patir trastorns mentals de tipus *internalitzant*.

Respecte de l'estat civil, els casats (o vivint en parella) tenen en general una salut mental millor que els que no estan casats en la dimensió *internalitzant*, i el grup de casats anteriorment (separats o vidus) són els que han mostrat un pitjor nivell de salut. En analitzar la dimensió *internalitzant* com a un únic factor, l'estat civil només afecta al nivell de gravetat dins de la classes de 'malalts'. Mirant-ho amb més detall, quan s'analitzen les dues subdimensions (*distress* i *fear*) per separat, s'ha trobat que l'estat civil només té efecte sobre la subdimensió relativa als trastorns depressius (*distress*) com a covariable de la classe latent, i no com a covariable de gravetat del factor dins de la classe de 'malalts'. Aquests efectes de l'estat civil sobre els trastorns de tipus *internalitzant* s'han trobat tant en models amb factors discrets com continus. No obstant això, la diferència entre les bondats d'ajust dels models amb estat civil com covariable de classe o de factor (mantenint la resta del model igual) han estat petites.

També s'ha trobat un efecte geogràfic. Els països del sud d'Europa (Espanya i Itàlia) presenten en global una millor salut mental que els països del nord d'Europa. Bèlgica es troba en la mitjana europea en la dimensió *internalitzant*, França és el país amb pitjors nivells de la dimensió *internalitzant*, Països Baixos i Bèlgica mostren els pitjors nivells de salut mental en la dimensió *externalitzant*. Alemanya mostra bons nivells de salut en trastorns d'ansietat, però dolents en trastorns depressius, mentre que els Països baixos és a l'inrevés.

D. Models per a trastorns al llarg de la vida

Un indicador important en epidemiologia psiquiàtrica és la prevalença vida desl trastorns mentals: la proporció d'individus que pateixen un trastorn mental en algun moment de la seva vida. Aquesta informació, però, no és possible estimar-la directament ja que habitualment només es disposa de mostres transversals amb dades retrospectives. Aquest fet fa que les dades observades estiguin censurades, de manera que els individus sense trastorn observat fins a la data de recollida de dades encara estan a risc de patir el trastorn en el futur. Tot i aquesta limitació, en molts estudis s'han estimat prevalences vida directament sobre les dades observades, obtenint una infra-estimació de les prevalences (Alonso et al., 2004a; Khan et al., 2005; Kovess-Masfety et al., 2007; Herman et al., 2009; Wells et al., 2009). En els estudis d'epidemiologia psiquiàtrica realitzats en el marc de la secció "World MentalHealth" (WMH) de la OMS, s'han estimat les prevalences vida mitjançant models actuarials de supervivència (Kessler et al., 2007), els quals tenien en compte les censures de les dades. No obstant, aquests models de supervivència estimen cada trastorn per separat i no de manera multivariant, sense considerar les associacions entre els trastorns – l'estructura latent subjacent als trastorns – i per tant, poden tendir a infra-estimar lleugerament les prevalences. Tampoc poden estimar un valor de predisposició individual a patir trastorns mentals associats a una dimensió mental. En aquesta tesi s'ha proposat un model IRT que té en compte l'associació dels trastorns per mitjà d'estructures latents definides en models conceptuals, i també considera que les dades es troben censurades. Bàsicament, es pretén estendre els models de IRT utilitzats amb èxit amb trastorns 12-mesos, per modelar correctament trastorns vida.

Les variable binàries indiquen la presència o absència de trastorn en algun moment de la vida (valors 1 o 0). En aquest cas, en fet de no tenir trastorn observat no implica que no el pugui manifestar en un futur, aquesta informació està censurada. En el model IRT proposat s'inclou tota la informació observada de les dades, de manera que els individus sense trastorn observat només aporten informació al model proporcionalment al temps del qual es disposa informació, és a dir, en proporció a la seva edat en el moment de la recollida de dades. S'inclou en el model el temps d'exposició al trastorn durant el qual aquest no s'ha manifestat. Específicament, s'ha definit una edat-límit fins a la qual seria possible patir els trastorns mentals quan aquests no s'ha observat. Cada trastorn té la seva edat-límit. Els individus sense un trastorn observat i amb edat superior a l'edat-límit d'aquest trastorn no es consideren com a censurats, sinó que

s'assumeix que ja no patiran el trastorn en el futur. Per a la resta d'individus sense trastorn, es té en compte la seva censura introduint en el model el temps d'exposició com a proporció de temps en el qual no s'ha observat, respecte de l'edat-límit del trastorn. Aquesta edat-límit s'ha estimat com el màxim valor mostral d'inici de trastorn. També es planteja la selecció d'un valor més robust en cas que la distribució sigui molt asimètrica (per exemple, el percentil 99). En el futur es podria plantejar un estudi de simulació per tal de buscar un mètode de càlcul de l'edat-límit vàlid per a qualsevol tipus de distribució de l'edat d'inici de trastorn.

Les estimacions de les prevalences vida resultants del model IRT proposat són significativament majors a les observades (sense tenir en compte les censures) i també lleugerament superiors a les estimades amb els models actuarials de supervivència (univariants). Les prevalença estimada per a fòbia específica segons la selecció de l'edat-límit com a percentil 99 resulta més creïble que usant el valor màxim (fòbia específica és el trastorn amb major asimetria en la distribució de l'edat d'inici de trastorn).

A diferència dels estudis epidemiològics clàssics, aquest model de tipus IRT per a modelar dades binàries censurades té la gran avantatge de poder capturar tota la informació mèdica rellevant. És a dir, un sol model permet estimar les prevalences vida, la prevalença de qualsevol patró específic de trastorns mentals, les associacions entre trastorns, l'efecte que tenen els factors de risc sobre el nivell de predisposició a patir trastorns mentals, etc. Tots aquells valors i associacions que en epidemiologia usualment es calculen separadament, en aquest cas es poden obtenir de l'ajust d'un únic model estadístic. Per tant, tots els valors estimats d'aquest model ja estan apropiadament ajustats per totes les variables que tenen un efecte significatiu sobre la salut mental, segons el model conceptual.

Una assumpció important dels models de IRT és que per a cada patró de resposta (i covariables) estima una puntuació del factor latent, independentment de l'edat d'inici dels trastorns observats. Aquesta assumpció concorda amb la definició conceptual de "predisposició mental" donada per Clark (2005), on l'edat d'aparició dels trastorn només depèn dels factors ambientals que es presentin en els individus en cada moment, i l'existència del trastorn només depèn del nivell de predisposició individual. S'assumeix en el model IRT que els factors ambientals que donen lloc als trastorns són independents de la predisposició mental. No obstant, diferents assumpcions sobre com la predisposició a patir trastorns i els factors ambientals interactuen entre ells

poden portar a construir diferents tipus de models estadístics. Per exemple, es podria assumir que la predisposició (latent) a patir un trastorn està relacionada amb l'edat de la primera aparició: una major predisposició implicarà una edat d'inici de trastorn menor. En aquest cas, però, implícitament s'assumeix que l'efecte de l'entorn ambiental sobre l'aparició de cada trastorn al llarg de la vida de les persones de tota la població és similar, en terme mig.

D.1. Nova proposta per modelar trastorns vida

Si assumim que la predisposició a patir trastorns mentals (el factor latent del nostre model) no només afecta al fet de tenir o no tenir el trastorn en algun moment de la vida, sinó que també té un efecte significatiu sobre l'edat d'aparició dels trastorns, es requerirà un altre tipus de model estadístic diferent al model IRT presentat amb anterioritat. En aquest cas serà necessari plantejar un model de supervivència multivariant, en el qual l'associació entre les funcions de supervivència dels trastorns ve definida pel factor latent (p.ex. predisposició a patir trastorns de tipus *internalitzants* en algun moment de la vida). D'aquesta manera, la puntuació latent estimada per a un individu tindrà en compte quina és la probabilitat de donar-se el trastorn per primer cop en el període (edat) en el qual s'ha donat el trastorn en aquell individu. És raonable pensar que les persones de major predisposició patiran un trastorn abans que les que tenen una menor predisposició envers la patologia mental. En aquest cas, però, estem assumint que l'efecte dels factors ambientals depenen majoritàriament de l'edat (o al menys una part significativa), obviant l'efecte d'altres factors ambientals importants (no observats) no relacionats amb l'edat. No obstant, té cert sentit assumir que hi ha molts fenòmens en la vida que tendeixen a succeir amb dependència de l'edat (com situacions laborals, familiars o les pròpies de l'adolescència) que poden estar relacionats amb l'aparició de trastorns mentas.

Donat que l'aparició dels trastorns estan recollides en anys (edat) es modela el risc d'aparició de trastorns mentals mitjançant funcions de supervivència discreta. L'estructura latent es defineix de manera que prengui un únic valor per individu, mentre que el risc de trastorn varia segons l'edat (Vermunt, 2009). Condicionat a les variables latents de nivell individual, les funcions de supervivència són mútuament independents.

Una possible formulació d'aquest tipus de model és la següent. Considerem T_j una variable discreta, que pren valor t quan es dóna per primer cop el trastorn j dins del període t ($t = 1,2,...,t^{\max}$). La probabilitat de que en un individu i aparegui per primer cop el trastorn y_j en un interval de temps t (per tant, sabent que no a ha aparegut per a temps anteriors), i condicionat a la seva puntuació latent de predisposició mental $\theta_{i|x}$, es calcula com

$$g\left(\hat{P}\left(y_{ijt}=1\middle|T_{ij}\geq t,\theta_{i|x}\right)\right)=\alpha_j+\beta_{jt}+\lambda_j\theta_{i|x} \tag{7}$$

Cal remarcar que, amb aquesta notació, les expressions $y_{ijt}=1$ i $T_{ij}=t$ són equivalents.

Suposant que tenim dos classes latents (x) que defineixen les subpoblacions 'sana' i 'malalta' tal com s'ha modelat en el quart article d'aquesta tesi, amb covariables de gravetat dins de les classe 'malalta' ($\mathbf{z}^F$) i covariables predictores de la pertinença a les classes ($\mathbf{z}^C$), es pot estimar el risc de trastorn en un temps t com

$$\begin{aligned}&\hat{P}\left(y_{jt}=1\middle|T_j\geq t\right)=\\&N^{-1}\sum\nolimits_{i=1}^{N}w_i\left\{\begin{array}{r}\int\hat{P}\left(y_{ijt}=1\middle|\theta,x=1,T_{ij}\geq t\right)f\left(\theta\middle|x=1,\mathbf{z}_i^F\right)d\theta\cdot\hat{P}\left(x=1\middle|\mathbf{z}_i^C\right)+\\+\hat{P}\left(y_{ijt}=1\middle|\theta=10,x=2,T_{ij}\geq t\right)\hat{P}\left(x=2\middle|\mathbf{z}_i^C\right)\end{array}\right\}\end{aligned} \tag{8}$$

L'equació (7) estima la probabilitat de què un trastorn es doni per primer cop un interval en de temps, condicionat a que no s'ha donat prèviament. Estima, per tant, el risc d'aparició de trastorn en un temps determinat, de vagades també anomenat com a *hazard*. L'equació (8) estima la funció *hazard* marginal respecte de les variables latents. Aquesta formulació difereix del model IRT proposat per analitzar dades binàries censurades en el quart article d'aquesta tesi, on l'equació del model estimava directament les probabilitats de tenir un determinat trastorn en algun moment de la vida (prevalences vida). En aquest nou model, però, es requereix d'un pas addicional per transformar la funció de risc en prevalences. Les prevalences s'han d'estimar mitjançant la projecció del risc fins a un determinada edat. La probabilitat d'haver patit un trastorn (projectada) fins a un temps t s'estimaria de la següent manera:

$$\hat{P}\left(T_j \leq t\right) = 1 - \prod_{l=1}^{t}\left(1 - \hat{P}\left(y_{jl} = 1 \middle| T_j \geq l\right)\right) \quad (9)$$

Per a t igual al valor de temps màxim ($t^{\max}$) s'obtindrien les estimacions de les prevalences vida. Utilitzant la propietat d'independència local, (condicionant a la variable latent la distribució les funcions de risc/supervivència són independents), es poden estimar prevalences de qualsevol patró de comorbiditats mentals vida.

Donat que el model (7) no estima directament la probabilitat de patir trastorns vida, pot plantejar-se si seria més adient el càlcul de la distribució marginal respecte les variables latents en l'equació (9), un cop transformat el risc individual de trastorn en funció de distribució, en comptes d'estimar les prevalences en (9) a partir dels riscs agregats segons l'equació (8).

Degut al baix nombre de trastorns en població general, el nombre de valors discrets de la funció de risc ($t^{\max}$) no pot ser molt elevat. En el nostre cas, models amb $t^{\max}$=5 períodes de 20 anys cadascun han resultat satisfactoris (amb intervals de temps de menor tamany el nombre d'inici de trastorns no resulta suficient per estimar la funció de risc en alguns intervals). Els models de supervivència discreta lliguen de manera exacta el temps d'exposició amb els intervals de temps amb els quals es construeix de la funció de risc. No obstant, utilitzant l'estructura de variables binomial, de manera similar a com s'ha realitzat en el quart article, es poden separar ambdues mesures de temps. En l'últim interval de temps observat, el "nombre d'intents" en cas de censura serà la proporció de temps dins d'aquest interval en el qual s'ha observat l'individu. Aquesta modelització binomial presenta una major precisió en l'estimació de les puntuacions latents, tenint en compte el temps exacte d'exposició al trastorn, independentment del nombre de punts en els que es subdivideixi la funció de risc.

La següent taula mostra un exemple de com quedaria l'estructura de dades per a un individu amb trastorn aparegut als 34 anys i un altre sense trastorn amb 56 anys en el moment de l'entrevista. La columna *Esdeveniment* s'inclouria en el model com a "nombre d'esdeveniments" i la columna *Exposició* com a "nombre d'intents". La columna *Exposició parcial* s'utilitzaria per tenir en compte el temps d'exposició exacte, amb independència de la codificació de temps requerida per a la funció de risc.

Id	Trastorn	Edat	Periode[1]	Esdeveniment	Exposició	Expos. parcial
1	1	34	1	0	1	1
1	1	34	2	1	1	1
1	1	34	3	0	0	0
1	1	34	4	0	0	0
1	1	34	5	0	0	0
2	0	56	1	0	1	1
2	0	56	2	0	1	1
2	0	56	3	0	1	0.35
2	0	56	4	0	0	0
2	0	56	5	0	0	0

[1] Períodes d'edat: 1=0-19; 2=20-39; 3=40-59; 4=60-79; 5=80-99.

En el nostre cas tenim múltiples trastorns, i es necessita una columna diferent d'*Esdeveniment* i *Exposició* per a cadascun dels trastorns i definir cada trastorn mitjançant l'estructura de dades binomial. Vermunt (2009) explica una manera diferent (i equivalent) d'ordenació de les dades i definició de variables per modelar funcions supervivència multivariant.

Un model de supervivència amb modelització continua del temps ja té en compte tot el temps d'exposició dels individus. L'avantatge d'utilitzar funcions de risc discretes és que són fàcils d'ajustar mitjançant rutines de regressió logística i aquestes poden tenir una distribució del risc (*hazard*) flexible, que possiblement no s'ajustarien adequadament a les formes de les funcions de risc contínues paramètriques usuals. Les funcions de supervivència no-paramètriques de temps continu (com la regressió de Cox) tampoc assumeixen cap forma distribucional prèvia, però requereixen que no existeixi empats en els temps d'esdeveniments – en el nostre cas els inicis de trastorn dades estan agrupats en anys. La supervivència discreta també permet modelar fàcilment l'existència de no proporcionalitat en les funcions de risc.

Aquest nou model proposat donarà lloc a un altre article, un cop aplicat en profunditat en les dades ESEMeD, que serà presentat a la *Royal Statistical Society Special Conference on "Statistical Challenged in Lifecourse Research"* (hosted by the Division of Biostatistics at the University of Leeds – July 2010), i serà enviat a la revista *Journal of the Royal Statistical Society: Series C (Applied Statistics)*.

D.2. Limitacions de les dades vida retrospectives

No obstant, els models desenvolupats no poden realitzar estimacions correctes si les dades no poden obtenir-se de manera totalment representativa. La informació poblacional sobre trastorns mentals s'obté en la gran majoria dels casos a partir de mostres transversals. La informació vida s'obté, doncs, de manera retrospectiva. Aquest tipus d'informació ha rebut sèries crítiques. Recentment, Strainer et al. (2009) ha emfatitzat clarament les limitacions i problemes de la informació vida sobre salut mental. Aquestes limitacions estan basades en la metodologia retrospectiva per mitjà de la qual es recullen les dades. Els principals problemes que tenen aquest tipus de dades són deguts principalment a l'efecte memòria: el record d'un episodi de trastorn mental disminueix a mesura l'edat de l'entrevista s'allunya de l'edat de trastorn. En menor mesura, també existeix una relació entre trastorns afectius i mortalitat, de manera que existeix un truncament informatiu en la mostra seleccionada. En les anàlisi d'aquesta tesi s'ha trobat que la gent gran ha patit menys trastorns mentals, tot i que amb major severitat. Altres estudis també han trobat un decreixent risc de trastorns mentals respecte l'edat (Kessler et al., 2003; Kessler et al., 2005; Bonnewyn et al., 2007; Lee et al., 2007; Medina-Mora et al., 2007; Stein et al., 2008). Però donades les limitacions de les dades retrospectives, no es pot concloure amb claredat que existeixi un augment en els últims anys de les prevalences de trastorns mentals. Els models estadístics proposats assumeixen que tant les censures com els truncaments són no-informatius. En cas que hi hagi censures i truncaments relacionats amb trastorns mentals i que existeixi error de mesura degut al biaix de memòria, les estimacions de qualsevol model estadístic seguiran estan en certa manera esbiaixades. Arribar al coneixement de quin és el comportament del biaix de memòria pot ser realment complicat.

Tot i les limitacions d'obtenir dades vida de qualitat, les mesures de prevalences mentals al llarg de la vida ofereixen informació epidemiològica rellevant. És necessari, per tant, seguir desenvolupant models estadístics i millorar l'estratègia de recollida de dades per tal d'obtenir estimacions el menys esbiaixades possible.

E. Dades binàries incompletes

Les dades de tipus binari prenen 2 possibles valors, indicant la presència o absència d'un determinat esdeveniment d'interès. Quan aquesta informació no es refereix a un moment puntual i allò que ens interessa és veure si l'esdeveniment succeeix en algun moment d'un interval de temps, s'ha d'incloure en el model no només el nombre d'esdeveniments i d'individus a risc, sinó també el temps individual d'exposició. A més a més, en les dades binàries observades es poden donar censures (per la dreta) quan l'esdeveniment no s'ha donat en un individu però no s'ha observat tot l'interval de temps complet. En general, quan la informació binària respon a un fenomen puntual dins d'un el temps d'exposició més ampli, tindrem dades binàries incompletes: les dades binàries no aporten tota la informació necessària per analitzar correctament l'esdeveniment d'interès. Si en aquest cas només s'analitzen les dades binàries s'obtindran estimacions esbiaixades, ja que implícitament s'estarà assumint que s'ha observat l'interval de temps complet, ignorant les censures.

Usualment aquest tipus de dades s'han analitzat amb models que lligaven completament el temps d'exposició amb l'interval de temps sobre el qual es feia inferència. Per exemple, amb les dades de trastorn vida ajustades amb els models habituals de IRT s'assumeix implícitament que el temps d'exposició observat era el mateix que el temps total de vida. Això mateix succeeix en les estimacions de prevalences simplement com a percentatge d'individus amb trastorn observat en algun moment de la seva vida. En models de supervivència discreta, la funció de risc estima un nombre finit (petit) de valors per a cada individu i trastorn, com es mostra en l'equació (7), i per defecte el temps d'exposició resulta discretitzat exactament de la mateixa manera.

En aquesta tesi es proposa analitzar les dades binàries incompletes com a variables de tipus binomial, indicant per a cada variable el "nombre d'esdeveniments" i "nombre d'intents", on el "nombre d'esdeveniments" és 1 si aquest s'ha observat (i 0 altrament) i el "nombre d'intents" és la proporció de temps observat dins de l'interval sobre el qual es fa inferència. L'ús d'estructures de dades binomials deslliga el temps d'exposició observat i el temps sobre el qual es fa inferència en els models. En models de IRT només és rellevant el patró de trastorns observat, però no quan han aparegut aquests. Per això, si ja s'ha observat un trastorn en algun moment de la vida d'un individu es considera que la informació és completa, i amb l'estructura de dades binomials tant el

"nombre d'esdeveniments" com el "nombre d'intents" prenen ambdós valor 1. Però quan no s'ha observat el trastorn, aquesta dada es troba censurada si es considera que l'edat de l'individu observat encara està dins del període de risc d'aparició del trastorn. Llavors el "nombre d'esdeveniments" val 0 i el "nombre d'intents" s'imputa amb la proporció de temps observat dins de l'interval on pugui aparèixer el trastorn mental. En models de supervivència discreta es pot incloure el temps exacte d'exposició a l'esdeveniment d'interès (o a la censura), independentment de com es discretitzi la funció de risc, incloent "nombre d'intents" en l'últim interval de temps observat com a proporció de temps observat fins a la censura o a l'esdeveniment (i 1 per als intervals anteriors).

De vegades només es disposa de dades per intervals, sabent que els esdeveniments o les censures s'han donat en algun moment dins de l'interval, però sense poder saber el moment exacte. En aquests casos se sol imputar el valor mig de l'interval com a temps d'exposició, per intentar corregir la manca d'informació exacte del temps d'exposició (altrament s'assumeix que l'esdeveniment sempre succeeix al final de l'interval). En el nostre cas, però, tenim el temps exacte (en anys) d'aparició del trastorn o de censura, i per tant hem pogut definir amb més precisió el valor de l'exposició (els intervals de les funcions de risc no poden fer-se més petits per problemes d'estimació degut al baix nombre de trastorns en la població general). Ordenant la base de dades adequadament, els models de supervivència discreta es poden estimar mitjançant el mateix procediment que per estimar una regressió logística (Efron, 1988; Singer & Willett, 1993; Vermunt, 2009).

Per tant, s'ha mostrat que és possible desvincular l'estructura discreta que té la distribució de les variables resposta del model respecte del seu temps d'exposició, podent incloure el temps d'exposició exacte, aportant més informació al model ajustat i corregint el biaix que existiria si s'ignorés el temps exacte d'exposició.

F. Resum de les conclusions

- Els trastorns mentals DSM-IV poden agrupar-se en dimensions (per exemple, internalitzant i externalitzant). Els models estadístics de variables latents poden modelar la comorbiditat mental, segons les dimensions psiquiàtriques definides en models conceptuals.

- Els models estadístics de variables latents basats en models conceptuals també poden utilitzar-se com a instruments de mesura en estudis epidemiològics, estimant puntuacions de les dimensions mentals (latents). Aquestes puntuacions provenen directament del model conceptual psiquiàtric utilitzat.

- Les puntuacions latents han servit com a eina per descriure la població Europea segons nivells de salut mental de les diferents dimensions. Aquestes puntuacions descriuen de manera resumida i rellevant la informació present en el conjunt de trastorns mentals (i covariables) observats, aportant un nou tipus d'informació epidemiològica.

- La població pot classificar-se en dos classes o subpoblacions clarament diferenciades, segons les puntuacions latents: una classe amb puntuació de salut mental positiva (en la qual la probabilitat de patir trastorns mentals és pràcticament nul·la), i una altre amb puntuacions de baixa salut mental.

- Mitjançant els models de variables latents, a partir d'un sol model estadístic es pot: modelar la comorbiditat mental, descriure la població segons les puntuacions latents, estimar prevalences i associacions entre trastorns, i avaluar els factors de risc associats als nivells de salut mental.

- Els factor ordinals són una alternativa als factors continus per modelar la dimensionalitat latent, tot i que en ambdós casos el grau d'ajust és força similar.

- L'anàlisi dels trastorns mentals al llarg de la vida pot fer-se definint les variables de trastorn com a binomials, indicant per a cada individu la proporció de temps que ha estat observat.

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Publicacions

A. Còpia de les publicacions

A continuació s'annexen les publicacions científiques que formen part d'aquesta tesi, en el següent ordre:

Article 1

Exploring conceptual Comorbidity models as measurement instruments for Mental Health Epidemiology Research.

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TITLE:

Exploring conceptual Comorbidity models as measurement instruments for Mental Health Epidemiology Research

ABSTRACT:

Purpose

Despite of numerous proposals, models of mental-health disorder co-occurrence have been scarcely used in epidemiological research, and comorbidity issues are frequently described as pattern-less correlations. In this paper, we show how to build and compare comorbidity models using an IRT latent variable framework to measure quantitatively mental health states.

Methods

Diagnostics for internalising and externalising psychiatric disorders were established using the WHO-CIDI interview as gathered in the ESEMeD study: a representative dataset in 6 European countries (part 2 sample, N=8,796). Using this data, IRT models of comorbidity were tested and compared via information-based goodness-of-fit indexes.

Results

A two-factor comorbidity model of internalising disorders (including “distress” and “fear” factors) yielded the best fit among competitive models. When accounting for externalising disorders, hierarchical and non-hierarchical factor structures were statistically indistinguishable, and models had to be conceptually compared. On these grounds, hierarchical structure was deemed more adequate due to its explicative power.

Conclusion

IRT modelling serves as a general method to assess model applicability and is useful for mental health descriptions at the population and individual levels. Latent trait models of internalising and externalizing disorders provide scores that come straight from psychiatric conceptual models. Scores can be used for either epidemiological descriptions or clinical assessments.

KEY WORDS:

Mental health epidemiology ; Psychiatric comorbidity; Internalising disorders ; Externalising disorders; Factor analysis ; IRT .

Background and aims

Studies on mental comorbidity generally assume that a non observable psychic state serves as a dispositional factor -or diathesis- from which individuals develop psychopathology in response to a sufficiently stressful environment [1]. Given that previous studies have shown that mental disorders are not independent, their correlation can be modelled through the use of latent (unobserved) variables capturing the predisposition to some kind of mental health illness. In this fashion, mental health states can be measured indirectly through their effect on observed symptoms or disorders. Several statistical models have been proposed in order to relate psychiatric symptoms or disorders to latent measures, but so far these models have rarely been used to describe large population samples, i.e. by estimating latent scores for each subject. Most usually, comorbid disorder associations are tackled from mere bivariate correlations.

Although previous studies have established various models as a basis for understanding the structure and dimensionality of the co-occurrence of mental disorders (describing relationships and comorbidity structures), they have been seldom used for mental-health measurement. Their use for individual scoring has been overlooked. This is an important omission, given that conceptually-driven measures could be very useful for epidemiologic research purposes. Moreover, such a scoring method would allow inferences regarding the individual's mental-health state.

Mental-health conceptual models have been developed from two approaches: based on symptom information [2-12] and based on disorder information. This article discusses how conceptual disorder comorbidity models can be assessed and how individuals can be scored with these models by means of latent trait modelling. In particular, we test disorder-comorbidity models for the most commonly assessed disorders in general population (mood, anxiety, substance and behavioural disorders). Krueger and Finger [13] have proposed models with acceptable fit for an internalising factor that captures the co-variation among internalising (mood and anxiety) disorders. Krueger [14] proposed a model where the internalising factor is a second order factor (with *Anxious-Misery* and *Fear* as first order factors) correlated with an externalising factor (substance and behavioural disorders). Watson [15] proposed a hierarchical disorder structure, where the emotional disorders give rise to a higher order factor for *distress*, *fear* and *bipolar* factors. Slade and Watson [16] fitted a similar model to that of Krueger [14], but adding the posttraumatic stress disorder (ptsd) as a distress disorder.

Vollebergh et al. [17] tested the longitudinal stability of a three factor model (*Anxious-Misery*, *Fear* and *Externalising*) model. Krueger et al. [18] and Markon and Krueger [19] studied the externalising factor, and found that a single factor could be sufficient to explain several substance dependence disorders and antisocial personality.

A variety of instruments exist which may be used for assessment, for instance, Inventory of Depression and Anxiety Symptoms (IDAS) [20] is an example of a symptom based instrument, while for disorder analysis one valid instrument is the CIDI [21, 22].

The main objective of this paper is to demonstrate the feasibility of using latent-trait models of IRT-type for mental-health comorbidity modelling, scoring and assessment. The aims are: 1) to test several previously proposed disorder-based comorbidity models on the ESEMeD data – a representative European general population sample – , according to their (jointly) observed disorders in the last 12 months; 2) to compare them statistically and conceptually, in order to decide which models can be suitable for being integrated within a more complex epidemiological or clinical mental-health research model; 3) and to show how the estimation of latent scores can describe mental health states.

Statistical Methods

Data

The ESEMeD Project was a cross-sectional survey. Individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population was the non-institutionalized adult population (aged 18 years or older) of Belgium, France, Germany, Italy, the Netherlands and Spain. A stratified, multistage, area-clustered, probability sample design was used. In total 21,425 respondents provided data for the project between January 2001 and August 2003. The overall response rate in the six countries investigated was 61.2%, with the highest rates in Spain (78.6%) and Italy (71.3%), and lower rates in Germany (57.8%), the Netherlands (56.4%), Belgium (50.6%) and France (45.9%). A two-phase interview procedure was used. The first phase contained the diagnostic assessment of the most common mood and anxiety disorders, health related quality of life, health services utilization and main demographic characteristics. Those who exceeded a predetermined number of

symptoms of specific mood or anxiety disorders, and a random sample of 25% of the rest, were administered the second phase of the interview (part 2 respondents, N=8,796), that included an in-depth interview about additional mental disorders (ptsd and externalising disorders) and chronic physical conditions, as well as other information. The assessment of mental disorders was based on version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI 3.0), a fully structured lay administered diagnostic interview that generates diagnoses of main mental disorders according to both the ICD-10 and DSM-IV criteria. Individuals were weighted to adjust for the differential probabilities of selection for the second phase, differential probabilities within household. Additional post-stratification weights were applied to restore age and gender distribution of the population within each country and the relative dimension of the population across countries [23].

The data used in this paper come from the ESEMeD part-2 sample (N=8,796). Twelve disorders were coded as dichotomous variables each reflecting whether the subject showed the disorder during the last 12 months according to DSM-IV criteria [24], without hierarchy rules. These disorders are: major depression episode (mde), dysthymia (dys), generalized anxiety disorder (gad), posttraumatic stress disorder (ptsd), agoraphobia –with or without panic– (ago), specific phobia (sp), social phobia (so), panic disorder (pd), alcohol disorders (alcohol abuse and alcohol dependence) and behavioural disorders (conduct disorder (cd), oppositional defiant disorder (odd) and attention deficit disorder (add)). Alcohol and behavioural disorders are externalising disorders, and the rest are internalising ones [25].

Due to the low prevalence of alcohol dependence disorder, alcohol disorders (abuse and dependence) were collapsed into one variable (alc); both abuse and dependence have already been reported to be indicators of a single latent dimension [26].

Confirmatory Factor Analysis

All the conceptual models have been estimated through Confirmatory Factor Analysis (CFA). The CFA groups variables into previously defined factors, or latent dimensions, where the observed variables are indicators of the unobserved factors [27]. Given the dichotomous nature of our data (either having the disorder or not) a probit link was used to relate the continuous latent factor with the binary observed variables - leading to an IRT model: probit 2-PL [28, 29]. Nevertheless, similar results would be expected if a logistic link had been used instead.

Analyses

Given that most of the existing epidemiological studies have focused only on the internalising disorders, we firstly considered models for them. Two IRT models were estimated for the assessment of the internalising factor: (model 1) one internalising factor where all the eight disorders are indicators of the internalising latent factor, as used in Krueger and Finger [13] and McGlinchey and Zimmerman [30]; (model 2) two correlated factors: *distress* (mde, dys, gad, pts) and *fear* (so, sp, pds, ago) [14, 16]. In accordance with the analyses by Slade and Watson [16], ptsd has been included in the *distress* factor. Moreover, Watson [7] detected a substantial overlap between ptsd and major depression. Figures 1-2 show the graphical representation of the models with internalising disorders.

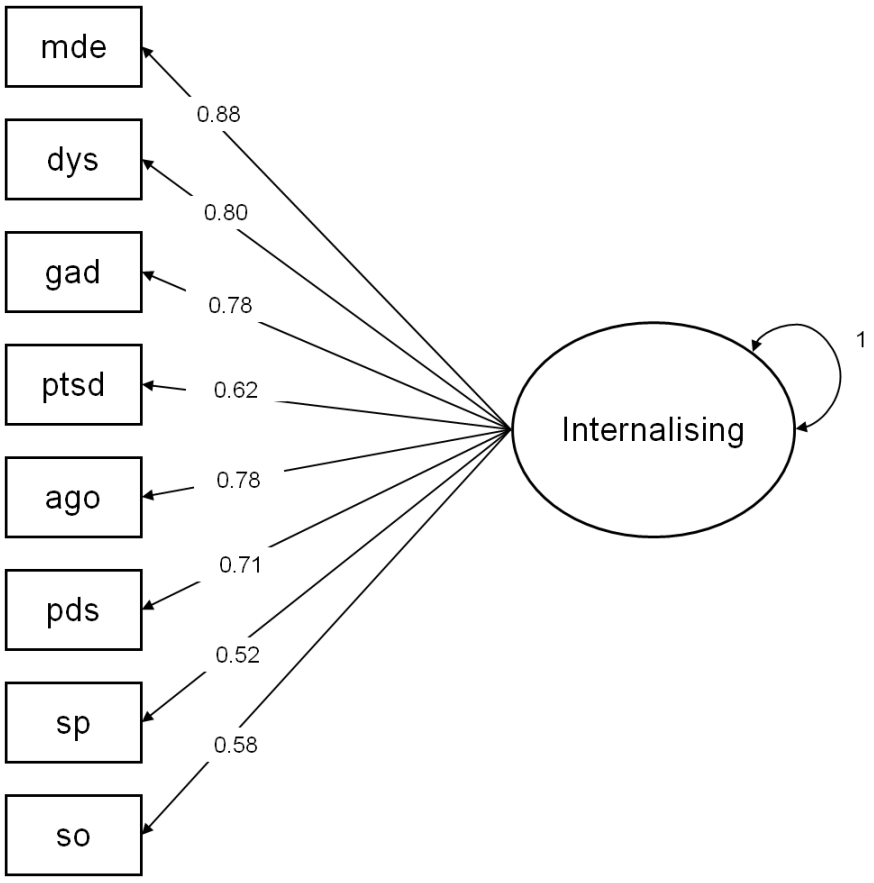

Figure 1. Single-factor internalising model

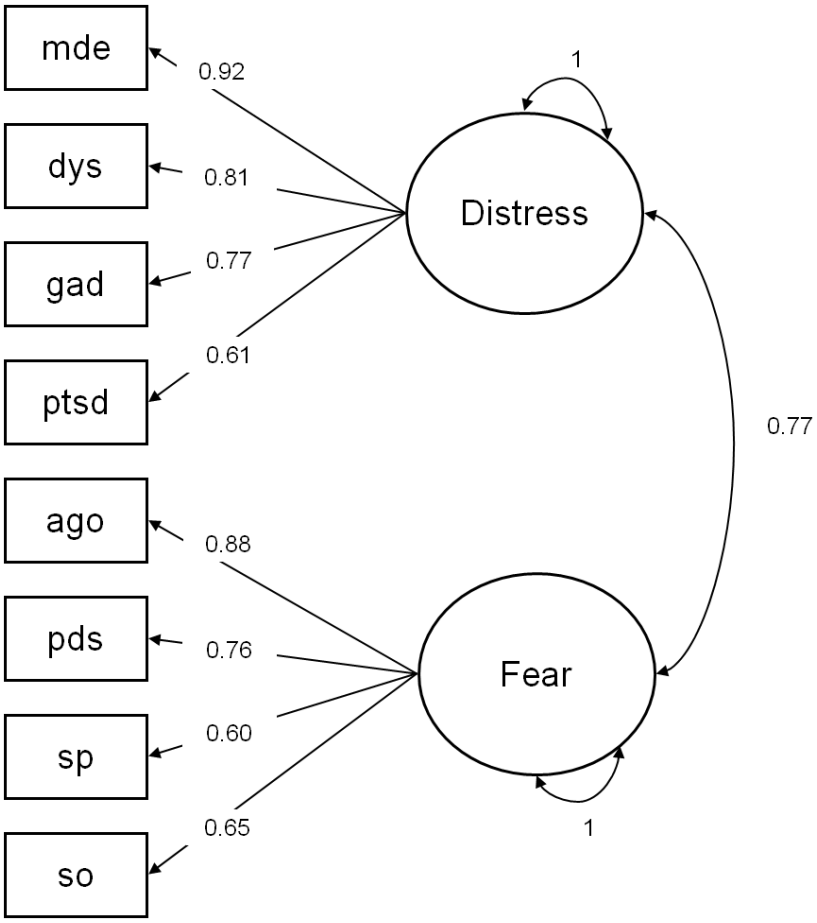

Figure 2. Two-factor internalising model

Secondly, three models including the externalising factor were tested, adding alcohol disorders, conduct disorder, oppositional defiant disorder and attention deficit disorder as indicators of the externalising factor: (model 3) one internalising factor, as described in model 1, correlated with the externalising factor; (model 4) one internalising factor constructed as a (hierarchical) second order factor correlated with the externalising factor, where the internalising first-order factors are *distress* and *fear*, as described in Krueger [14] and Slade and Watson [16]; and (model 5) internalising disorders split into *distress* and *fear* factors, and all the 3 factors (distress, fear and externalising) mutually correlated [17]. Figures 3-5 show the graphical representation of the models with internalising and externalising disorders.

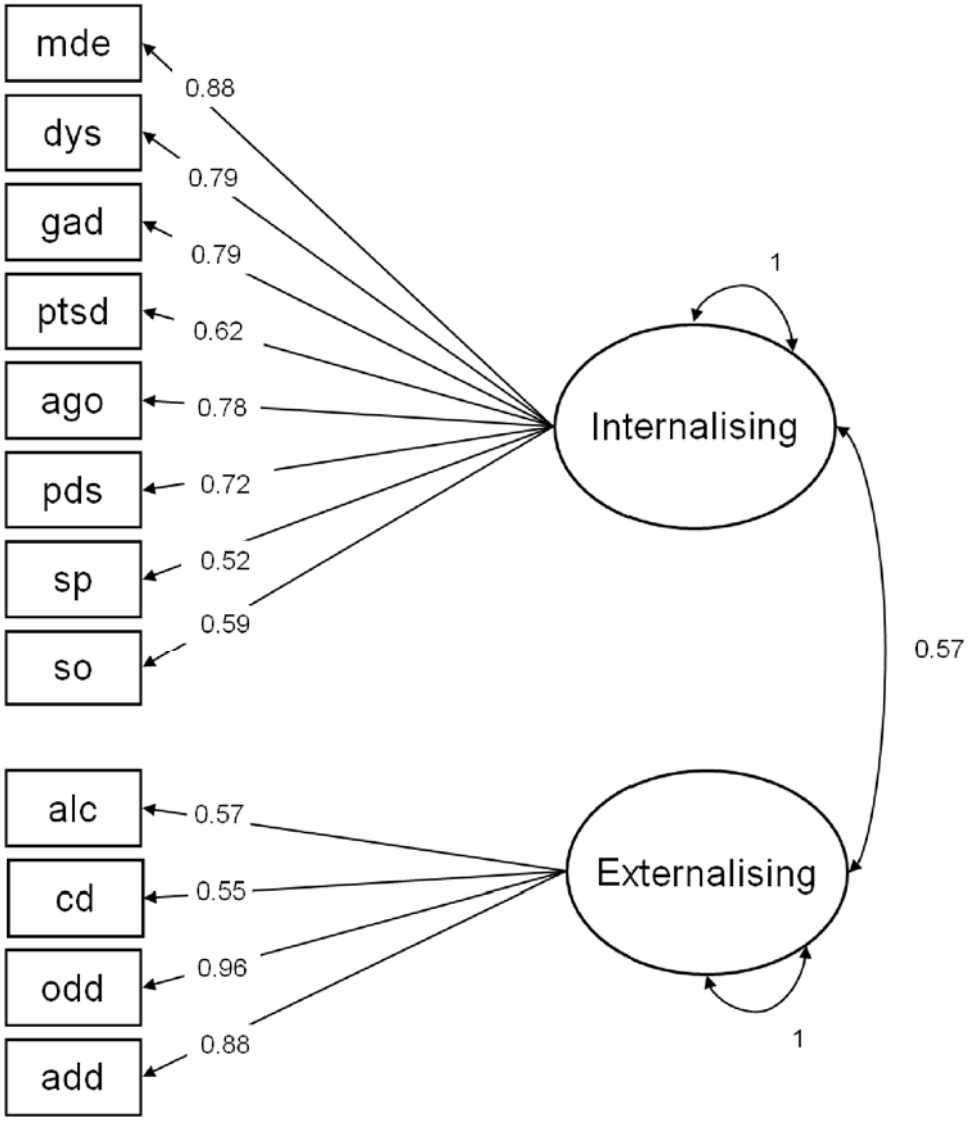

Figure 3. Single-factor internalising correlated with externalising

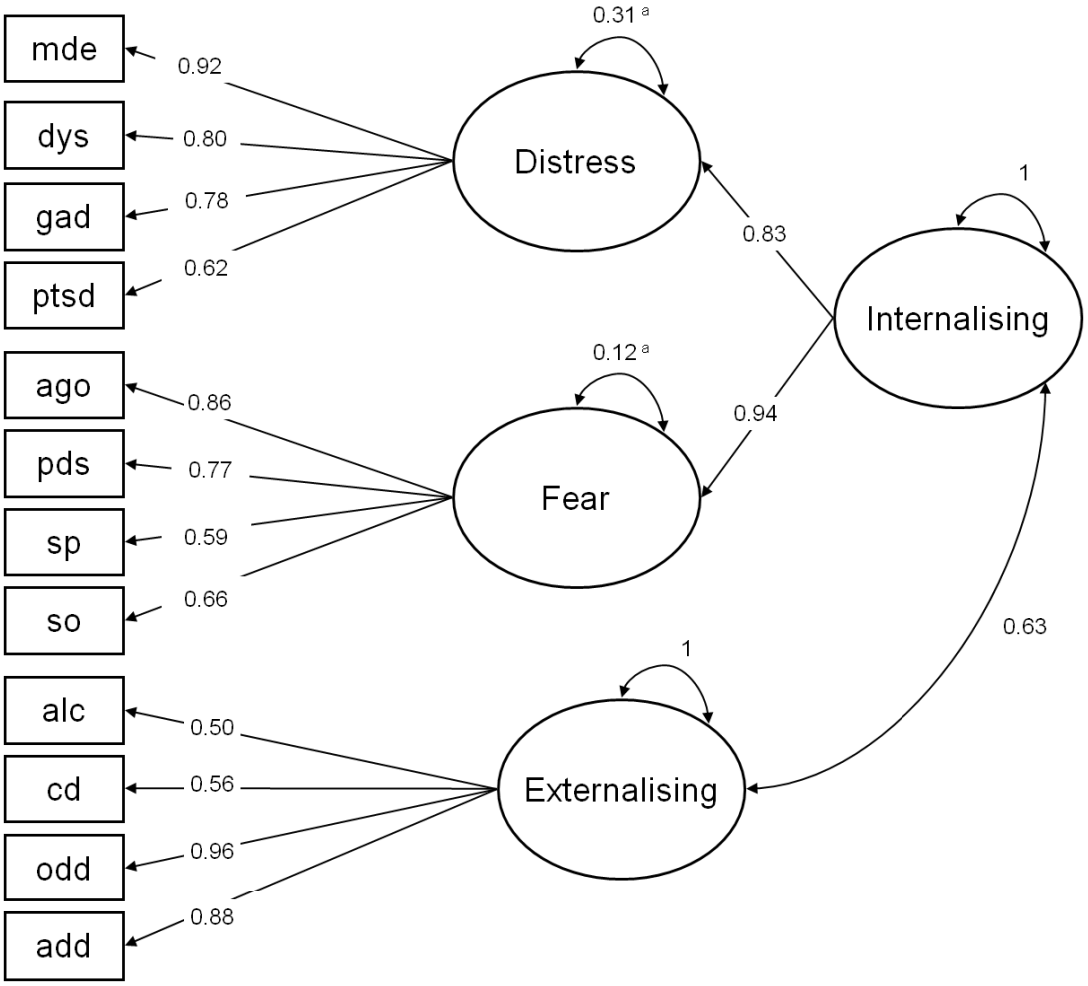

Figure 4. Two-factor hierarchical internalising correlated with externalising
[a] Residual variance (distress and fear variance not explained by the internalising factor).

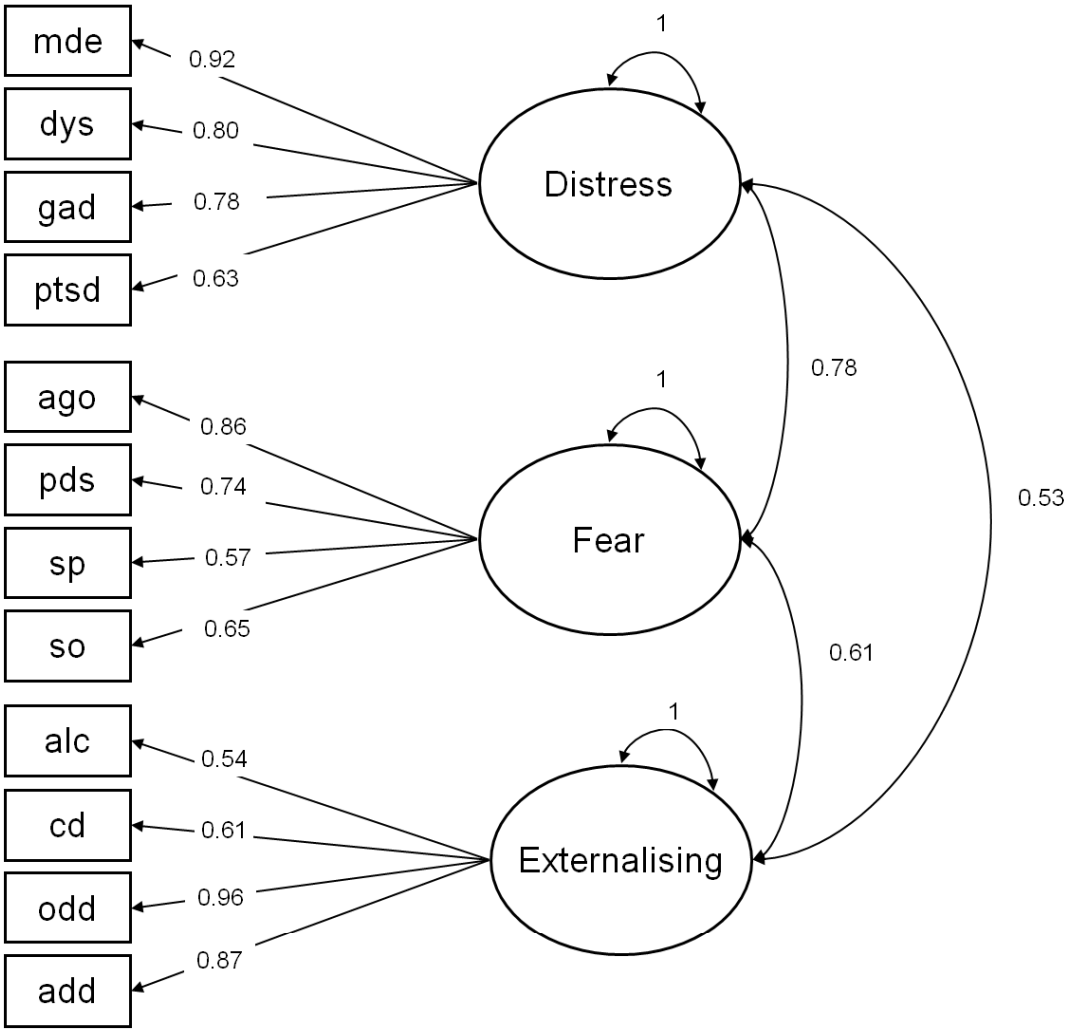

Figure 5. Three-factor model.

Second-order factor models are not identified when estimated from just two first-order factors, unless the second-order factor is correlated with other variables or further constraints are imposed. For this reason, a second-order internalising factor has not been tested in model number 2.

Models were statistically compared using the BIC index, where a lower BIC value indicates a better fit of the model [31]. Other comparison indices such as AIC and AIC3 were also considered. The AIC and BIC indexes balance the fit of the data (logLikelihood) and the number of parameters used in the model, and lead to the selection of a parsimonious model.

Another measure of goodness of fit is the Bivariate Residuals (BVR). Once the model is fitted the BVR checks if there is still some association among any pair of variables that is left unexplained by the model. The CFA/IRT model aims to explain all the associations among the observed variables, so a large BVR in any pair of variables implies that the model is not capturing all their information. It was considered that a BVR cut-off value for misfit was 10.

All the analyses have been conducted through maximum likelihood estimation method, using the software LatentGold 4.5, with the exception of the hierarchical (second order) factor model (model number 4) which was estimated with Mplus 5.2.

In all the analyses we took into consideration the complex design of the sample [1], in order to obtain unbiased estimates and standard errors [32].

Results

The most prevalent 12-month disorder was specific phobia followed by major depression episode (Table 1).

Table 1. Sample weighted 12-month prevalences

Disorder	N	Prevalence (%)	95% CI
Dysthymia	283	1.23	1.03 - 1.47
Major Depression	905	4.09	3.72 - 4.49
Agoraphobia	110	0.69	0.50 - 0.93
Genear Anxiety Disorder	196	0.94	0.75 - 1.17
Panic disorder	174	0.80	0.65 - 0.98
Post-traumatic Stress	214	1.13	0.93 - 1.38
Social Phobia	228	1.62	1.31 - 2.00
Specific Phobia	679	5.77	5.10 - 6.51
Alcohol Disorders	93	0.77	0.52 - 1.13
Conduct disorder	11	0.07	0.03 - 0.14
Oppositional Defiant Disorder	21	0.17	0.09 - 0.30
Attention Deficit Disorder	59	0.39	0.24 - 0.63

Internalising disorders

Model 1 (a single factor for the internalising disorders) had a few somewhat large BVR between some *fear* disorders: specific phobia with agoraphobia (a BVR value of 12.1), and specific phobia with social phobia (14.3). According to the BIC, model 2 showed better fit than the one-factor internalising model (model 1). Additionally, no significant BVR were found. Table 2 shows the comparative goodness of fit for all the fitted models.

Table 2. Model fit indices

	Model	LL	BIC	AIC	AIC3	Npar
1	Internalising 1F	-5896.3	11938.0	11824.7	11840.7	16
2	Internalising 2F	-5871.0	11896.4	11776.0	11793.0	17
3	Intern.1F & Extern.	-6591.8	13410.6	13233.6	13258.6	23
4	Intern.2F(Hierarch) & Extern.	-6565.8	13376.8	13185.6	13212.6	25
5	Intern.2F & Extern.	-6565.8	13376.8	13185.6	13212.6	25

Internalising and externalising disorders

Regarding models with internalising and externalising disorders, model 3 exhibited worse fit than models where the internalising factor is split into *distress* and *fear* (models 4 and 5). Model 3 also showed two significant BVR among *fear* disorders: specific phobia with agoraphobia (12.3), and specific phobia with social phobia (13.6). This result indicates that fear disorders are not entirely captured by a single internalising factor.

Models 4 and 5 are algebraically indistinguishable [33]. Thus, the hierarchical structure of model 4 and the simpler correlated-factor model 5 are statistically equivalent. Both of them have the same numbers of parameters, because including the second order factor eliminates the estimation of two correlations between factors (fear with externalising, and distress with externalising) but needs to estimate two new parameters: one factor loading and the variance of the second order factor.

Figures (1-5) show the most important result estimates: standardized factor loadings and factor correlations.

Scoring

As an example of the feasibility of individual scoring in latent variable models, we took model 3 to estimate the internalising and externalising subject scores. The scoring procedure assigns each individual the most probable value on the scale represented by the latent variable. Table 3 shows the mean scores of the most frequent comorbidity patterns. Factor scores were scaled in order to obtain high values for good mental-health level and low scores for mentally diseased individuals.

The highest scores were obtained from those without any disorder. The pattern with mde, dys and gad disorders had a very low score in the internalising factor (-2.41), much lower than the score of the patterns were these disorders appeared alone (-1.56, -1.44 and -1.47 respectively). Presence of both odd and add (-3.99) had also lower score than add alone (-2.75). Thus, the model provides a quantitative indicator of comorbidity impact on mental-health severity.

Patterns with only internalising disorders were assigned a low score in the externalising factor (and the other way round), because the model assumed factor correlation. According to the conceptual model, the presence of any internalising (or externalising) disorders implies an unhealthy state in the externalising (or internalising) dimension, even when no externalising (or internalising) disorders were present.

Table 3. Estimated mean scores in most frequent observed comorbidity patterns (model 3).

dys	mde	ago	gad	pds	pts	so	sp	alc	cd	odd	add	N[a]	Internalising Mean (sd)	Externalising Mean (sd)
												7723.8	0.17 (0.89)	0.14 (1.19)
							●					367.6	-0.69 (0.70)	-0.49 (1.10)
	●											156.6	-1.56 (0.45)	-1.11 (0.99)
						●						68.5	-0.95 (0.62)	-0.68 (1.07)
					●							43.8	-1.07 (0.59)	-0.76 (1.05)
								●				43.7	-0.50 (0.75)	-1.59 (0.92)
●	●											30.3	-2.03 (0.41)	-1.42 (0.96)
●												27.2	-1.44 (0.47)	-1.03 (1.00)
	●						●					25.9	-1.77 (0.43)	-1.25 (0.98)
				●								22.2	-1.32 (0.51)	-0.94 (1.02)
			●									19.8	-1.47 (0.46)	-1.05 (1.00)
						●	●					16.1	-1.34 (0.53)	-0.95 (1.02)
	●		●									15.2	-2.05 (0.41)	-1.43 (0.96)
											●	14.5	-0.87 (0.63)	-2.75 (0.52)
	●				●							14.1	-1.88 (0.42)	-1.32 (0.97)
		●										11.8	-1.48 (0.46)	-1.05 (1.00)
●	●						●					9.1	-2.20 (0.41)	-1.54 (0.95)
	●					●						7.1	-1.84 (0.43)	-1.30 (0.98)
	●			●								7.0	-1.98 (0.42)	-1.39 (0.97)
●	●	●										5.7	-2.41 (0.37)	-1.67 (0.93)
		●				●	●					5.6	-1.93 (0.41)	-1.36 (0.97)
	●					●	●					5.6	-2.03 (0.42)	-1.42 (0.96)
					●		●					5.6	-1.41 (0.51)	-1.00 (1.02)
		●					●					5.2	-1.69 (0.42)	-1.19 (0.98)
						●		●				4.9	-1.24 (0.55)	-1.96 (0.82)
●	●		●									4.4	-2.41 (0.38)	-1.67 (0.93)
										●	●	3.8	-1.32 (0.52)	-3.99 (0.28)
	●			●			●					3.8	-2.15 (0.41)	-1.50 (0.96)
●							●					3.8	-1.66 (0.43)	-1.18 (0.99)

[a] Weighted sample size

Discussion

The measurement of mental illness is still an active field of research. First [34] discussed the problems that arise when classifying symptoms to get diagnostic information in accordance with the DSM (Diagnostic and Statistical Manual of Mental Disorders). In the DSM, the relationship between a comprehensive list of disorder definitions and the risk of symptom overlap is not yet well balanced. This situation leads to a discussion between "splitters" and "lumpers" criteria. Broadly speaking, "lumpers" aggregate symptoms into a small number of non-overlapping disorders, at the risk of creating too broad, heterogeneous categories. In contrast, "splitters" define large sets of disorders, but run the risk of considering entities that share much symptom information as different disorders because of their partial overlap. Furthermore, splitters must face the difficulty of finding the appropriate cut-point to discriminate disorders, a sensitive decision which is frequently attained in terms of symptom duration or severity. For example, most important difference between depression and dysthymia is the duration and severity of their symptoms. "Lumpers" may underestimate comorbidity, whereas co-occurrence of disorders identified by "splitters" may be an artifact [3, 34].

Latent variable models, like IRT, offer considerable advantages for dealing with this problem. They allow summarizing that information shared by the disorders, either because symptoms overlap between disorders or due to the co-existence of symptoms caused by the same underlying factor. Scores can be estimated from the unobserved factors according to the conceptual model, as mental health-state descriptors. In this fashion, latent variable models can overcome these current limitations when analysing mental-health comorbidity DSM-IV data, giving more meaningful results that the usual bivariate disorder association. Moreover, psychiatric researchers already mentioned the necessity of including some kind of dimensionality in the assessment of mental health and to include this aspect in future reviews of the DSM [16, 18, 35, 36].

Model results

The two-factor (*distress* and *fear*) internalising model (model 2) presented a better fit compared with the one-factor model (model 1). Mineka et al. [3] showed that anxiety disorders themselves are genetically heterogeneous and a single factor could be insufficient to account fully for the diversity of symptoms subsumed by the anxiety disorders. However, the two-factor model showed that the fear disorders can be explained by a single factor. To what extent fear symptoms are well captured in their disorder variables is beyond the scope of the present paper.

The single factor model for internalising disorders capture most of the internalising disorders' association, is more general and will remain more stable when integrated into larger models – but with the disadvantage that some associations among anxiety (fear) disorders are not yet well explained by a single internalising factor, although their BVR were not high. Fergusson et al. [37] also found that a single factor was not capturing all the common information of internalising disorders. On the other hand, including the two-factor internalising model within a more complex model would considerably increase the computational cost of Maximum-Likelihood estimation – models with more than 3 continuous latent factors are computationally very demanding.

When externalising disorders are also available the hierarchical model (model 4) and the three-factor model (model 5) are statistically equivalent [33], so these models cannot be compared in terms of goodness of fit. From a conceptual point of view, the hierarchical structure implies that *fear* and *distress* share a common source of variability, but they also have their own non-correlated specific variability in form of residual variance. Model 4 also assumes that the association between *distress* or *fear* with the externalising factor is achieved through the internalising higher-order factor. The three-factor model (model 5) allows for direct correlation between the three factor disorders and assumes that they are equally distinguishable entities. According to the reviewed conceptual research, the hierarchical model, with a second-order internalising factor, seems to be closer to the nature of the disorders. Evidence in favour of the conceptual hierarchical model has been reported by Brown et al. [9], who conclude that despite the differentiation among anxiety and mood disorders, they share a common diatheses; Clark and Watson [38] and Mineka et al. [3] remarked that mood-anxiety comorbidity shows a higher level of *negative affect* (internalising) than pure mood or anxiety; and Joiner [12] also concluded that depression and anxiety are distinguishable disorders despite their considerable overlap. Given that it is widely accepted the existence of the internalising dimension, the hierarchical model (model 4) may be preferred over the three-factor model (model 5) because it allows the estimation of the internalising scores, as well as the *distress* and *fear* subdimensions. Nevertheless, this hierarchical model suffers a statistical shortcoming given that the second-order factor was poorly measured using only two fist-order indicators: it is not identifiable unless it is correlated with another factor of further constrains are imposed. Even so, the existence of the internalising second-order factor is in accordance with psychiatric theory. The required estimation time is also larger for model 4 compared to model 5.

Just as we have discussed subdimensions within the internalising factor, it is also feasible to explore the existence of subdimensions within the externalising disorders. For example, it is open to discussion whether *substance disorders* and *disruptive behaviour* constitute separate dimensions or whether they can be modelled under the umbrella of a single high-order externalising factor. A single externalising factor is in line with the findings of Markon and Krueger [19]. Alternative externalising structures cannot be tested with the ESEMeD data because only a small number of externalising disorders were assessed and they showed low 12-month prevalence.

Overall, most of the models showed low residuals (BVR) indicating that they can explain the greater part of their relationship by means of latent variables (factors).

Dimensionality assessment of Mental Health

Our results lend support to the idea of dimensionality in mental health assessment, in which some mental health characteristics can be allocated in a continuum, rather than using the discrete classification of DSM-IV and ICD-10 [3, 13-15, 17]. Another aspect in favour of dimensionality in mental health is the fact that a variety of DSM disorders respond similarly to the same drug or psychosocial treatment [9]. Watson [15] defends the idea of dimensionality, highlighting the main advantages of a dimensional system: it allows the measurement of severity, not simply presence versus absence, and continuous scores tend to be more stable over time, displaying higher levels of reliability than dichotomous measures, as well as being virtually unaffected by relatively minor shifts in psychopathology.

Factor loadings indicate the strength association between the observed variables and the latent dimensions. These estimates obtained here were quite similar to those found in previous models tested over general population [14, 16, 17]. The fact that our results are similar to these previous results speaks in favour to the stability of these conceptual models (the meaning of the dimensions are equivalent across these studies), and implies that they are not dependent on the data.

An important limitation of these analyses is that all models were fitted using 12-month disorders, whereas the individual diathesis [1] has life-course implications. The statistical analysis of lifetime disorders involves methodological challenges, due to samples are right-censored (an individual is still at risk of suffering some disorder in the remainder of their life). For this reason, lifetime comorbidity assessment in cross-

sectional mixed-age samples is likely to be biased [39]. This methodological limitation has not been overcome so far in comorbid psychiatric assessment. Research in this direction is already under way by the authors. Kueger [14] and Krueger and Finger [13] used lifetime disorders, ignoring this methodological limitation, whereas Vollebergh et al. [17], Slade and Watson [16] and McGlinchey and Zimmerman [30] analysed 12-month disorders. However, the similarity found in the factor loadings between the 12-month and lifetime models goes in favour to the stability of the factor conceptual meaning, not depending on any time framework.

Scoring

The CFA/IRT models provide the means to estimate continuous factor scores for each individual, but at present the technique is scarcely used in epidemiological research. Clifford C. Clogg [40] already mentioned this lack of use of the latent variable models more than twenty years ago. From the reviewed literature, only McGlinchey and Zimmerman [30] used this technique to score each internalising comorbidity pattern in a clinical sample, and Krueger and Finger [13] to assess external correlates of internalising factor.

Once the model is estimated and validated, it is possible to use the estimated parameter to compute factor scores of new observations. Most important advantage of this methodology is that it is possible to compute the score (and its standard deviation) of an individual with a comorbidity pattern different from those existent in our data, so all possible disorders' combinations can be described from the estimated parameters. This scoring methodology allows ordering all possible comorbidity patterns according to their mental-health severity.

Given the factor associations in the conceptual model, the estimated model can predict dimensions scores for a missing dimension (that is, variables of that dimension were not measured). For example, in the case of model 3, when an externalising score can be provided with internalising information only, using the shared information quantified in their correlated. The statistical model also allows factor inferences even if the information on any disorder is missing.

The scores capture the effect of the number of disorders and the different weight that each disorder have on its factor. This methodology models the comorbidity directly:

scores come straight from the psychiatric conceptual model. Scores, then, can be used by clinicians to understand the impact of comorbidity on the patients, and by epidemiologist, to describe mental health in general population.

Symptoms vs disorders

Our analyses focused on disorder information provided by the CIDI 3.0 instrument, used in the ESEMeD project. However, models based on symptom information are a promising line of research. Watson [7, 15] suggested using the analysis of psychiatric symptoms instead of DSM diagnoses in order to avoid problems associated with the DSM diagnostic data: (i) heterogeneity between the disorder definition rules applied to different datasets; (ii) very low prevalence of several disorders; (iii) heterogeneity between raters' assessments, and (iv) heterogeneity between symptoms within a given disorder – for example, ptsd [7]. Using symptom information could also provide more indicator variables for the measurement of latent factors, which would probably result in more stable model estimation [41]. Additionally, we could choose a set of symptoms closer to the measured dimension, thus avoiding the inclusion of heterogeneous variables as indicators of the same factor.

In spite of these drawbacks, and unlike symptom-based models, the various disorder-based conceptual models share many features that make them more satisfactory for latent variable modelling. Symptom-based analyses were very heterogeneous with respect to their measured symptoms. None of the reviewed articles analysing mental health symptoms were based on exactly the same set of symptom variables, nor were they using the same scoring procedure. Using different variables makes it doubtful whether they are measuring exactly the same latent dimensions. Furthermore, some latent constructs are conceptually heterogeneous across the different models. These important limitations imply that these studies are not comparable. Nonetheless, there is as yet insufficient research on a consolidated conceptual structure for symptom-based models.

Conclusion

As long as a general internalising assessment is intended, and for the sake of parsimony, researchers may well consider using only one factor to describe the internalising disorders. But perhaps the two-factor internalising model seems closer to the reality of mental health, at the cost of increasing the computational demands if maximum-likelihood is used as the estimation method. A potential drawback is that a single internalising (second order) factor is not identifiable alone – unless it is correlated with other mental dimensions. Hence, the two-factor internalising model should be used when *fear* and *distress* are the dimensions of interest.

If externalising disorders are also available, they can be analysed as a single factor correlated with the internalising factor. This internalising-externalising factor model can serve as a basis for more complex clinical or epidemiological model, aiming to describe mental-health status.

Once the nosology is established, clinical or epidemiological researchers would like to describe samples based on these conceptual models. The possibility of factor scoring, as provided by latent variable models (such as CFA/IRT), should be preferred for the description of mental health status.

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Article 2

Measurement and description of underlying dimensions of comorbid mental disorders using Factor Mixture Models: results on the ESEMeD project.

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Title

Measurement and description of underlying dimensions of comorbid mental disorders using Factor Mixture Models: results on the ESEMeD project.

Abstract

Epidemiological studies on mental health and mental comorbidity are usually based on prevalences and correlations between disorders, or some other form of bivariate clustering of disorders. In this paper, we propose a factor mixture modeling (FMM) methodology based on conceptual models aiming to measure and summarize distinctive disorder information in the internalising and externalising dimensions. This methodology includes explicit modelling of subpopulations with and without 12month disorders ('ill' and 'healthy') by means of latent classes, as well as assessment of model invariance and estimation of dimensional scores. We applied this methodology with an internalising/externalising 2-factor model, to describe the European internalising/externalising disorder scores using a representative sample gathered in the ESEMeD study - which includes 8,796 individuals from 6 countries, and used the CIDI 3.0 instrument for the disorder assessment. Results revealed

that Southern European countries have significantly higher mental health levels concerning internalising/externalising disorders than northern countries; males suffered more externalising disorders than women did, and conversely, internalising disorders were more frequent in women. Differences in mental-health level between socio-demographic groups were due to different proportions of healthy and ill individuals and, noticeably, to the ameliorating influence of marital status on severity. An advantage of latent model-based scores is that the inclusion of additional mental-health dimensional information - other than diagnostic data - allows providing greater precision within a target range of scores.

Keywords

Internalising disorders, externalising disorders, measurement invariance, mental comorbidity, latent classes.

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Background and aims

Several authors have improved the conceptual framework of mental health with proposals that aim to explain the co-occurrence of mental disorders. Statistically, these models involve explaining the joint presence of psychiatric disorders by modelling their inherent correlations (Krueger, 1999; Krueger et al., 2001; Markon et al., 2005; Slade et al., 2006; Watson, 2005). In spite of these theoretical developments, univariate and bivariate analysis of descriptive information have been the norm in mental health epidemiology when approaching the study of disorder comorbidity. Although these analysis might be appropriate when the interest resides on specific disorders, such approaches ignore much of the information shared by observed disorders, and thus overlook individual health state. Multivariate models might provide better accounts of mental health description in the population as long as they allow for the joint presence of disorders (i.e. the comorbidity pattern) according to the existent psychiatric knowledge.

Multivariate modelling strategies comprise an additional benefit. A dimensional definition of mental health beyond the classical classification system as ICD or DSM (American Psychiatric Association, 2000; World Health Organization, 1993) is gaining strength among psychiatric researchers. In the study of mental comorbidity it is assumed that individuals' non-observable "psychic state" determines their vulnerability to suffering certain disorders. This vulnerability is also known as diathesis (Clark, 2005). By means of latent variable modelling, it is possible to capture common information shared by the disorders, based on previous psychiatric conceptual research (for example, see Krueger (1999), Mineka et al. (1998) and Vollebergh et al. (2001)). Moreover, this information is of dimensional nature. Along these lines, conceptual models of mental health have proposed two broad factors for the expression of this vulnerability: Internalising (depression and anxiety) and Externalising (behavioural and substance disorders) (Cerda et al., 2008).

Most desirably, scoring values on the dimensions should allow for fair comparisons between individuals, regardless of their population of origin. Then, group comparisons would be immediate. This property of the scores is known in psychometrics as measurement invariance (MI), and it warrants that the observed variables measure the latent dimension in the same way, regardless of sampled characteristics in each subpopulation (Mellenbergh, 1989; Meredith, 1993). Although MI is a crucial property for any measurement instrument, it has seldom been tested on the mental-health conceptual models. Non-invariance in a disorder outcome would imply that individuals with the same actual mental-health level would have a differential

probability of endorsing the disorder depending on their subpopulation group they belong to. MI only exists if measurement parameters hold equal for any subpopulation. This is clearly the most desirable case, because individuals can be compared based on factor scores only, regardless of their subpopulation of origin. Then, group comparisons based on factor scores are immediate.

Latent variable modelling as a scoring method would allow describing populations from a conceptual model, because they provide the means to compute individual scores. In the present study we propose the use of latent variable models to answer to the requirements of epidemiological studies on mental health models of comorbidity. We emphasise the usefulness of latent modelling not just for conceptual model testing, but also to provide the means to estimate scores of non-observable dimensions of mental health and to contrast whether the measures are invariant. This article also includes a very new approach to the epidemiologic mental-health assessment, consisting on the assumption that there exists a 'healthy' subpopulation, that is, that the population includes a proportion of individuals who would not endorse any (12-month) disorder, through a Factor Mixture Model.

Especially when dealing with observational studies, so common in epidemiology research, the population may display excessive heterogeneity. On certain instances the source of variance might be known, observed and conveniently coded as part of the data gathering process. But in numerous other occasions it is impossible to identify the source of heterogeneity. Extensions of latent variable (factor) models allow estimating individual probabilities of pertaining to different, non-observed groups or *latent classes*. These models are known as Factor Mixture Models (FMM) because they combine continuous latent variables (factors) with discrete latent variables (mixtures or classes). Model parameters in FMM differ according to the class membership (Lubke et al., 2005; Lubke et al., 2006; Lubke et al., 2007), and thus, individual scores can be qualified depending on a group of membership (for instance, disorder severity). An important feature is that classes are estimated, and so, instead of using variables to indicate group membership, the mixture models estimate individual probabilities of pertaining to each latent class. Differently from stratified or multigroup analysis, where the grouping variable is explicitly observed, a FMM grouping variable is also latent (i.e. unobserved). This approach has two main advantages. Firstly, they allow taking into account unknown sources of variability. Secondly, it is possible to estimate factor scores along with the probability of class membership. Class characteristics can be then explained with covariates such as demographics. It is important to remark that these covariates might be related with the latent class, but the latent class is not defined by them, but by model specifications. Thus, class covariates allow for posterior

epidemiologic inferences on class characteristics to identify the source of variability, but the model has already taken those sources into account.

To sum up, FMM allows a) obtaining continuous scores based on categorical information (such as a pattern of disorders or symptoms); b) controlling confounding sources of heterogeneity; c) introducing covariates into the model to explain the latent classes, which is a practical method for epidemiologic inferences and d) model-based invariance contrasts.

In the following sections we exemplify how to conduct such analysis using data from the European Study of the Epidemiology of Mental Disorders (ESEMeD), addressing the following goals: a) to describe the mental health related with internalising/externalising disorders of the European population according to their (jointly) observed disorders in the last 12 months, based on the Internalising-Externalising conceptual model; b) to assess model invariance across socio-demographic groups; and c) to explicitly model the healthy and ill subpopulations jointly.

The Internalising-Externalising disorder conceptual model was chosen because its simplicity and parsimony, in order to present how this FMM model and scoring methodology can be applied, and which new type of information could provide. Although more complex models of disorder structure exists but the objective of this paper is not to choose sides on conceptual models. Alternatively, more detailed conceptual models can be also applied like three factor models (Krueguer 1999, Vollebergh et al 2001) or more recent models like the 6 factor structure proposed by Wittchen et al. (2009). The modeling strategy would be the same for any other conceptual model, but we deemed the internalising/externalising model to be sufficiently simple yet descriptive to present the FMM methodology. Also, the FMM methodology could also be used with conceptual models based on symptom data, not from disorders, or even combining both strategies in a hierarchical model. The procedure would be essentially the same as long as the indicators are considered categorical.

Methods

Sample

The ESEMeD Project was a cross-sectional survey based on a stratified, multi-stage, clustered area probability sample. Individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population was the non-institutionalized adult population (aged 18 years or older) of Belgium, France, Germany, Italy, the Netherlands and Spain. The sampling frame and the number of sampling stages used to obtain the final sample differed across countries. A more detailed description of the methods and the participants of the ESEMeD project is provided elsewhere (Alonso et al., 2002; Alonso et al., 2004c). In total 21,425 respondents provided data for the project between January 2001 and August 2003. The overall response rate in the six countries studied was 61.2%, with the highest rates in Spain (78.6%) and Italy (71.3%), and lower rates in Germany (57.8%), the Netherlands (56.4%), Belgium (50.6%) and France (45.9%). A two-phase interview procedure was used. The first phase contained the diagnostic assessment of the most common mood and anxiety disorders, health related quality of life, health services utilization and main demographic characteristics. Interviewees who exceeded a predetermined number of symptoms of specific mood or anxiety disorders, and a random 25% of the rest, were asked for the second phase (part 2 respondents, N=8,796). The second phase included an in-depth interview about additional mental disorders (posttraumatic stress disorder and externalising disorders) and physical chronic conditions amongst other information. Mental disorders assessment was based on version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI 3.0) (Kessler et al., 2004), a fully structured lay administered diagnostic interview that generates diagnoses according to both the ICD-10 and DSM-IV criteria. Within each country, individuals were weighted to adjust for the differential probabilities within household and the differential probabilities of selection for the second phase. Additional post-stratification weights were applied to restore age and gender distribution of the population within each country and the relative dimension of the population across countries. Disorders' descriptive analysis of the ESEMeD data can be found in (Alonso et al., 2004b; Alonso et al., 2004a). Data for the analyses conducted in this research article consisted on the part-2 subsample (N=8,796).

The main indicator variables analysed in this article are binary, and they describe whether a mental disorder was present in the previous 12 months to the interview (i.e disoreder diagnostic in the last year). Disorder diagnostics were

established by applying DSM-IV criteria to responses to the CIDI 3.0. The diagnoses under analysis included are: major depression episode (mde), dysthymia (dys), general anxiety disorder (gad), posttraumatic stress disorder (ptsd), agoraphobia (ago), specific phobia (sp), social phobia (so), panic disorder (pds), alcohol disorders (alc) – including alcohol abuse or alcohol dependence – and behavioural disorders (conduct disorder (cd), oppositional defiant disorder (odd) and attention deficit disorder (add)). Disorder definitions did not include hierarchy rules. The behavioural disorders are considered as mainly childhood and adolescent disorders, and they were not asked to individuals older than 44 years old because of concerns about recall bias among older respondents (Kessler et al., 2007). Consequently, for the analysis of this article, it was assumed that individuals older than 44 years old had zero-probability to endorse these disorders during the previous 12 months. This assumption is warranted given the decreasing estimated prevalence of having any of these disorders as age increases (for age groups 18-24, 25-34 and 35-44, the 12-month prevalence of having any behavioural disorder were 1.8%, 1.1% and 0.6%, respectively).

Statistical Analysis

Confirmatory Factor Analysis (CFA) was used to construct the statistical models from the conceptual internalising/externalising disorder models. CFA groups variables in previously defined factor or dimensions, where the observed variables are indicators of the unobserved factors. Because of the categorical nature of our data (binary data: having or not the disorder) a *probit* link was used to relate the continuous latent factor with the binary observed variables, leading to an IRT model: 2-parameter normal-ogive model (De Boeck, 2004; Lord et al., 1968). The measurement parameters are the intercepts and factor loadings.

First, the internalising factor was explored, beginning with the simplest model: a single factor model fitted to the internalising disorders (mde, dys, ago, pds, gad, pts, so, sp). This is the baseline model.

On a second step, we conducted invariance analyses on the IRT fitted model, in order to determine if measurement parameter differences among subpopulations could exist. To do so, we used multigroup analyses, which consisted on comparing three different models for each grouping variable: a restricted (invariant) model and two additional unrestricted, non-invariant models. In the invariant model, the factor mean was fixed to zero in one group and freely estimated into the others; thus factor means and variances were free to vary across groups while measurement parameters held

invariant. The first non-invariant unrestricted model allowed the intercepts to differ between groups. The second non-invariant model, allowed both the intercepts and factor loadings to differ between groups. For both unrestricted models, factor means were fixed to zero in each group for identification purposes. Then, for each grouping variable, we assessed whether the unrestricted models significantly differed in model fit as compared to the restricted one (Lubke et al., 2003; Muthen et al., 2002). We also compared the restricted model to the baseline model (internalising single-factor) to assess whether the grouping variable could operate as a covariate for factor scores. Multigroup analysis was conducted according to the following socio-demographic grouping variables: gender, age-group, country, physical chronic condition, years of education, marital status, income, urbanicity and working-status. Due to the low prevalence of the externalising disorders, which led to estimation problems, the MI analyses were conducted only on the internalising factor – an MI analyses on the externalising factor, tested in a larger sample, can be found in Markon et al. (2005).

On a third step we developed a mixture CFA/IRT model (FMM), in order to summarize the different solutions obtained in the Multigroup approach in a few main classes, instead of having a large number of different solutions (one per group variable), and to explore alternative sources of heterogeneity beyond the observed grouping variables.

As in the multigroup analysis, we tested the FMM versions of the restricted (invariant) and unrestricted (non-invariant) models. Covariates predicting class membership were mainly selected according to those that seemed to have a significant effect in the multigroup analyses. Additionally, we also tested different covariates predicting different levels of severity within the ill class.

Once the factor model was established for internalising disorders, we included an externalising factor into the model, constructed from alc, cd, odd and add disorders. The existence of a single externalising factor is based on conceptual psychiatric information (Krueger, 1999; Krueger et al., 2005; Markon et al., 2005; Slade et al., 2006). We also probed for latent classes with different means in the externalising factor (invariant FMM), and covariates were included to predict class membership probabilities.

Finally, factor scores were estimated for each individual in the final model, which included the appropriate classes and significant covariates. Factor scores were

computed as the mean of the factor posterior distribution, along with their standard deviation (Vermunt et al., 2005). This scoring method provides a measure in a continuous scale for both the internalising and externalising health state levels. Disorder variables were coded in the model in a way so that mentally healthy individuals achieved higher factor scores and lower scores represented ill individuals. In this manner, the latent variable stands for an internalising/externalising mental health state factor, ranging from worse to better mental health.

Model comparison was mainly made using the Bayesian information criterion (BIC). We also examined other comparative fit indexes for decision-making: Akaike's information criterion (AIC and AIC3 - an AIC modification that heavily penalizes factor over-parameterization). Using these indexes it is possible to choose the best-fitting model among a set of nested or non-nested alternative models (Raftery, 1995). The likelihood ratio test for nested-model comparison was not used in the MI analyses, because the large sample size led to significance even with minor differences. Alternatively, model of fit was assessed using bivariate residuals (BVR). The BVR reflects any residual association among pairs of observed after model estimation. Given a model with satisfactory fit, it is expected that no substantial amount of association between every pair of variables is left (Vermunt et al., 2005).

Notice that the election of the internalising/externalising 2-factor model is just an example of this methodology. More complex models can be implemented and compared using this same approach.

In order to obtain unbiased estimates and standard errors, the complex sample design was taken into account in all analysis by using linearization variance estimator (Alonso et al., 2004c; Vermunt et al., 2005). All models were estimated via Maximum Likelihood, with 125 start values to avoid a local-optimum solution, using the software LatentGold version 4.5.

Results

Specific phobia and major depression were the most prevalent disorders, with percentages 5.8% and 4.1% respectively (Table 1). Internalising disorders were more frequent than externalising ones. It was estimated that 12.2% of the population have at least one 12-month disorder (Table 2). There existed some tendencies in the prevalence of the disorders. For example, internalising disorders appeared more frequently in females than in males, but externalising ones were more frequent in males. Moreover, the youngest individuals had larger prevalences than the oldest ones, and Italy and Spain presented lower disorder prevalences compared to northern countries (see Table 2).

Table 1. Sample weighted 12-month prevalences

Disorder	N	Prevalence (%)	95% CI
Dysthymia	283	1.23	1.03 - 1.47
Major Depression	905	4.09	3.72 - 4.49
Agoraphobia	110	0.69	0.50 - 0.93
Genear Anxiety Disorder	196	0.94	0.75 - 1.17
Panic disorder	174	0.80	0.65 - 0.98
Post-traumatic Stress	214	1.13	0.93 - 1.38
Social Phobia	228	1.62	1.31 - 2.00
Specific Phobia	679	5.77	5.10 - 6.51
Alcohol Disorders	93	0.77	0.52 - 1.13
Conduct disorder	11	0.07	0.03 - 0.14
Oppositional Defiant Disorder	21	0.17	0.09 - 0.30
Attention Deficit Disorder	59	0.39	0.24 - 0.63

Measurement Invariance

Table 3 displays goodness of fit indices for the internalising factor models testing MI. The baseline model was compared against the invariant (restricted) ones from the multigroup analyses (baseline model was just the one factor internalising), and the invariant and non-invariant models against one another. In all cases, the invariant (restricted) model was to be preferred based on the BIC. According to the AIC and AIC3, for some of the grouping variables the free-intercept non-invariant model should

Table 2. Prevalences of 12month type of disorders by sociodemographic variables. Weighted percentages.

	Any Internalising		Any Externalising		Any Disorder		No Disorder		TOTAL	
	N	%	N	%	N	%	N	%	N	%
Gender										
Male	519	7.3	97	1.8	567	8.5	3122	91.5	3689	48.2
Female	1288	15.3	66	0.7	1310	15.6	3797	84.4	5107	51.8
Age										
18-24	173	15.4	32	3.8	185	17.4	479	82.6	664	11.4
25-34	339	10.8	55	2.4	362	12.4	1237	87.6	1599	18.3
35-49	583	12.8	59	1.0	609	13.4	2060	86.6	2669	27.8
20-64	450	11.6	17	0.4	459	11.9	1738	88.1	2197	21.8
+65	262	7.9	0	0.0	262	7.9	1405	92.1	1667	20.7
Country										
Belgium	219	12.6	29	2.0	231	13.2	812	86.8	1043	3.8
France	387	17.7	36	1.9	404	18.9	1032	81.1	1436	20.5
Germany	257	10.0	26	1.5	269	11.0	1054	89.0	1323	31.5
Italy	279	8.7	10	0.3	282	8.8	1497	91.2	1779	22.4
Netherlands	261	12.4	43	2.6	279	13.7	815	86.3	1094	6.1
Spain	404	9.3	19	0.5	412	9.7	1709	90.3	2121	15.6
Chronic Condition										
Yes	720	14.0	44	0.7	733	14.3	2184	85.7	2917	30.4
No	1087	10.3	119	1.5	1144	11.3	4735	88.7	5879	69.6
Education										
up to 12years	656	11.9	77	1.4	690	12.8	2591	87.2	3281	34.6
more than 12years	1151	11.2	86	1.1	1187	11.9	4328	88.1	5515	65.4
Work Status										
Working	960	11.1	111	1.3	1013	11.9	3850	88.1	4863	56.5
Not Working	847	11.8	52	1.2	864	12.6	3069	87.4	3933	43.5
Urbanicity										
Less than 10,000 inhab.	488	10.8	36	0.9	504	11.3	2021	88.7	2525	33.2
10,000 to 100,000 inhab.	767	11.5	77	1.1	805	12.3	3035	87.7	3840	38.7
More than 100,000 inhab.	552	12.0	50	1.8	568	13.1	1863	86.9	2431	28.1
Income										
Low	365	13.9	32	2.5	377	15.6	1213	84.4	1590	19.0
Low average	566	11.1	53	1.0	588	11.5	2121	88.5	2709	32.1
High Average	591	10.5	54	0.9	614	11.2	2362	88.8	2976	33.2
High	285	11.1	24	0.8	298	11.7	1223	88.3	1521	15.7
Marital Status										
Married/cohabiting	1109	11.0	84	0.8	1155	11.6	4633	88.4	5788	66.8
Separated/widow/divorced	313	13.1	16	0.5	316	13.2	1011	86.8	1327	11.1
Never married	385	11.9	63	2.9	406	13.6	1275	86.4	1681	22.1
TOTAL	1807	11.4	163	1.2	1877	12.2	6919	87.8	8796	

be preferred over the invariant one, although their intercepts were not substantially different across groups (parameter estimates provided on request). Given these results, choosing the measurement invariant one is an acceptable election for the sake of parsimony. Regarding the comparisons between the restricted models with the baseline model, it can be seen that the covariates gender, chronic-condition, and country are clearly significant predictors of the internalising level.

Table 3. Goodness of Fit indices testing Measurement Invariance for the Internalising factor.

	LogL	BIC	AIC	AIC3	Npar
Baseline Internalising model	-5896,4	11938,0	11824,7	11840,7	16
Gender: Invariant	-5829,2	11821,9	11694,5	11712,5	18
Free-intercepts	-5817,8	11862,7	11685,7	11710,7	25
Free-intercepts & factor loadings	-5811,7	11914,1	11687,5	11719,5	32
Age: Invariant	-5872,7	11963,3	11793,3	11817,3	24
Free-intercepts	-5828,7	12129,7	11761,5	11813,5	52
Free-intercepts & factor loadings	-5811,0	12348,6	11782,0	11862,0	80
Country: Invariant	-5849,6	11935,4	11751,3	11777,3	26
Free-intercepts	-5812,5	12179,0	11747,0	11808,0	61
Free-intercepts & factor loadings	-5794,1	12460,0	11780,1	11876,1	96
ChronicCondition: Invariant	-5880,4	11924,3	11796,8	11814,8	18
Free-intercepts	-5870,9	11968,8	11791,8	11816,8	25
Free-intercepts & factor loadings	-5869,7	12030,0	11803,4	11835,4	32
Education: Invariant	-5895,1	11953,6	11826,1	11844,1	18
Free-intercepts	-5885,7	11998,5	11821,4	11846,4	25
Free-intercepts & factor loadings	-5882,3	12055,2	11828,6	11860,6	32
Income: Invariant	-5885,6	11971,0	11815,2	11837,2	22
Free-intercepts	-5873,1	12136,7	11832,2	11875,2	43
Free-intercepts & factor loadings	-5864,1	12309,5	11856,2	11920,2	64
Marital Status: Invariant	-5888,4	11958,4	11816,8	11836,8	20
Free-intercepts	-5863,4	12035,5	11794,7	11828,7	34
Free-intercepts & factor loadings	-5850,4	12136,8	11796,9	11844,9	48
Urbanicity: Invariant	-5894,3	11970,2	11828,5	11848,5	20
Free-intercepts	-5880,3	12069,3	11828,5	11862,5	34
Free-intercepts & factor loadings	-5873,8	12183,6	11843,7	11891,7	48
Work status: Invariant	-5891,6	11946,7	11819,2	11837,2	18
Free-intercepts	-5884,0	11995,1	11818,0	11843,0	25
Free-intercepts & factor loadings	-5879,3	12049,2	11822,6	11854,6	32

When a latent grouping variable was introduced into the model to construct the FMM models, the appropriate number of latent classes was studied first (Table 4). Models with 3 classes did not improve significantly their goodness of fit respect the 2-class models, both in the restricted and unrestricted cases. Fully restricted models (free intercepts and factor loadings) were discarded from subsequent FMM models, given

that they did not yield better fit than free-intercept models. The inclusion of class covariates to predict the probability of class membership widely improved the models fit. Although the 2-class model did not improve over the baseline (the internalising one-factor, without covariates), it can be seen in table 4 that the 2-class model with covariates (models 16 and 17) improved over the 1-class with covariates (model18). BIC values suggested that the measurement invariant model had better fit in FMM models with covariates. Nevertheless, the AIC and AIC3 suggest that the free-intercepts models had better goodness of fit; additionally, intercept parameters were significantly distant between classes (not shown here). Close examination of parameter estimates of the best fitting restricted and unrestricted models (models with 4 covariates: gender, age, country and chronic-condition), gave further evidence of class constitution. Firstly, the second class of the restricted model had a mean around 10.8 and close to zero variance. Secondly, class two of the unrestricted (free-intercepts) model had much larger intercepts than the first class and its variance was close zero. Thus, in both models, individuals in class two had low probabilities of endorsing any disorder. These results suggest that both the unrestricted (free intercept) and restricted 2-classes models revealed 'healthy' and 'ill' classes – which was one of the main goals of this paper. The unrestricted model was not better in terms of fit and the class interpretation was the same in both cases, thus the restricted model was chosen for subsequent models.

Since a variance of zero is a boundary solution, the variance of Class 2 was set to zero; furthermore, the class mean was set to 10. Class 2 represents a homogeneous group of healthy individuals, where *homogeneous* denotes no variability in their health status, and *healthy* denotes having a high factor score. This class is clearly different from the class of ill subjects (whose members are *heterogeneous*, i.e. they do exhibit variability). It follows that the final model combining these two classes is a CFA-type model for Class 1 (mentally ill subjects) whereas all members of Class 2 have been assigned the same high-value in the factor, which implies zero-probability of endorsing every disorder.

Covariates predicting different levels of severity within ill-class individuals were also tested and marital status covariate resulted significant.

Table 4. Goodness of Fit indices testing FMM models for the Internalising factor, and final model for Internalising and Externalising factors.

			LogL	BIC	AIC	AIC3	Npar
1	Baseline Internalising model		-5896,4	11938,0	11824,7	11840,7	16
2	2-Classes Invariant		-5893,8	11960,2	11825,6	11844,6	19
3	Free-intercepts		-5857,9	11952,0	11767,8	11793,8	26
4	Free-intercepts & factor loadings		-5854,1	12008,0	11774,3	11807,3	33
5	3-Classes Invariant		-5892,0	11983,8	11828,0	11850,0	22
6	Free-intercepts		-5851,2	12029,3	11774,4	11810,4	36
7	Free-intercepts & factor loadings		-5839,3	12132,7	11778,6	11828,6	50
	2-Classes	*Class membership Covariates*					
8	Invariant	gender	-5824,5	11830,7	11689,0	11709,0	20
9	Free-intercepts		-5803,4	11852,0	11660,8	11687,8	27
10	Invariant	gender + age	-5792,6	11803,1	11633,1	11657,1	24
11	Free-intercepts		-5768,1	11817,8	11598,3	11629,3	31
12	Invariant	gender + age + country	-5758,0	11779,5	11574,1	11603,1	29
13	Free-intercepts		-5728,8	11784,5	11529,5	11565,5	36
14	Invariant	gender + age + country + chronic	-5729,3	11731,1	11518,7	11548,7	30
15	Free-intercepts		-5705,2	11746,4	11484,3	11521,3	37
16	Invariant (Healthy-class restrictions *)	gender + age + country + chronic	-5729,3	11713,0	11514,7	11542,7	28
17		+ marital status (*severity covariate*)	-5720,5	11713,5	11501,0	11531,0	30
18	1-Class	gender + age + country + chronic	-5740,9	11726,9	11535,7	11562,7	27
	Internalising and externalising Model [1]	*Externalising class-covariates*					
19		–	-6419,9	13203,1	12919,8	12959,8	40
20		gender	-6400,5	13173,4	12883,0	12924,0	41
21		gender + age^2	-6358,6	13107,6	12803,1	12846,1	43
22	(Final model)	gender + age^2+ country	-6343,1	13122,2	12782,3	12830,3	48
23		gender + age^2+ country + chronic	-6343,1	13131,2	12784,2	12833,2	49

* Second class restrictions: Mean=10 & variance=0

[1] Internalising factor modelled as in model 17. 2-Class Externalising factor with (healthy) second class restrictions: Mean=10 & variance=0

[2] Coded in three categories (18-34, 35-49 and +50). Age covariante in the internalising factor had 5 categories (18-24, 25-34, 35-49, 50-64 and +65).

Final internalising-externalising model:

First we fitted a single externalising factor and we found that it properly explains the four externalising disorders in the ESEMeD data because all BVR's among them were very low. Then, the externalising factor was added to the later internalising model previously described (model 17 in table 4). Similarly, a new categorical latent variable was included to describe externalising healthy and non-healthy population simultaneously (with zero variance and mean 10 restrictions for the healthy class). Both class variables, for the internalising and externalising factors, led to a 4-class cross-classification. Covariance between internalising and externalising factors was

estimated only for those individuals belonging to both ill classes, otherwise was fixed to zero. Variables gender, age and country were found to be significant covariates for the externalising classes (see models 19 to 23 in Table 4). BIC results for covariate country indicated not improvement in goodness of fit, but AIC and AIC3 supported the hypothesis of better fit. In addition, country parameters were significantly different from zero. The covariate age on the externalising factor was recoded into three categories (18-34, 35-49 and more than 50 years old), instead of the five categories used in most of the ESEMeD data analyses, because of the very low prevalence of externalising disorders in older population.

The structure of the final model (model 22 in table 4) is shown in figure 1. Table 5 shows the parameter estimation of this model.

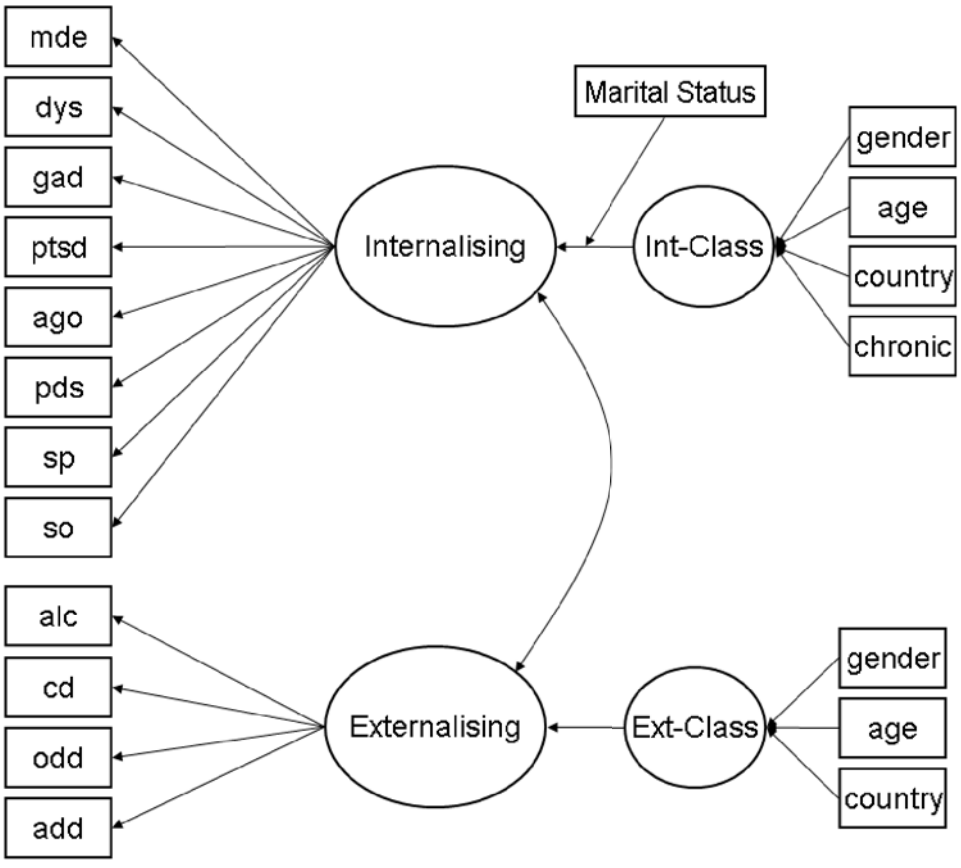


Figure 1. Final model-structure for the analysis of internalising and externalising mental-health states in general population.

Table 5. Final model parameter estimates. Standard error between brackets.

5.1 Measurement parameters:

		FactorLoading	Intercept
Internalising Factor	Dysthymia	1	2,48 (0,21)
	Major depression	1,41 (0,21)	1,94 (0,26)
	Agoraphobia	0,84 (0,22)	2,62 (0,33)
	General anxiety disorder	0,95 (0,20)	2,58 (0,27)
	Panic disorder	0,75 (0,18)	2,44 (0,20)
	Post-traumatic stress	0,51 (0,11)	2,03 (0,15)
	Social phobia	0,39 (0,12)	1,77 (0,14)
	Speciphic phobia	0,21 (0,08)	0,98 (0,10)
Externalising factor	Alcohol disorders	1	1,85 (0,26)
	Conduct disorder	1,09 (0,40)	3,01 (0,22)
	Oppositional defiant	2,90 (2,46)	4,21 (2,35)
	Attention deficit	2,03 (1,39)	2,81 (1,12)

5.2 Covariate parameters

		Internalising	Externalising
Class membership[1]	Intercept	0,47 (0,29)	2,14 (0,50)
	Gender: Male	0,60 (0,07)	-0,92 (0,17)
	Female	-0,60 (0,07)	0,92 (0,17)
	Age group: 18-24	-0,74 (0,26)	-1,68 (0,27)
	25-34	-0,12 (0,13)	
	35-49	-0,32 (0,12)	-0,04 (0,24)
	50-64	0,07 (0,14)	
	65+	1,11 (0,18)	1,71 (0,33)
	Country: Belgium	-0,24 (0,20)	-0,90 (0,44)
	France	-0,72 (0,13)	-0,32 (0,34)
	Germany	0,20 (0,14)	-0,32 (0,33)
	Italy	0,42 (0,11)	1,64 (0,45)
	Netherland	-0,03 (0,14)	-1,35 (0,38)
	Spain	0,35 (0,13)	1,25 (0,44)
	Chronic condition: Yes	-0,49 (0,09)	
	No	0,49 (0,09)	
Severity within ill class [2]	Marital Status		
	Married/Cohabiting	0,18 (0,06)	
	Previously married	-0,19 (0,09)	
	Never married	0,01 (0,08)	

[1] Logistic regression parameters: (Dependent) Class variable used Class 1 (ill) as reference; (Independent) Covariates used effect coding.
[2] Linear regression parameters: Internalising mean differences across covariate categories, within Class 1.

5.3 Factor mean and variances/covariances

Class*		Internalising-Factor		Externalising-Factor		Factor-Covariance
Intern.	Extern.	Mean	Variance	Mean	Variance	
1	1	0	1,02 (0,25)	0	0,47 (0,27)	0,60 (0,28)
1	2	0	1,02 (0,25)	10	0	0
2	1	10	0	0	0,11 (0,13)	0
2	2	10	0	10	0	0

* Class 1 refers the ill-class. Class 2 refers to the healthy class

Parameter covariates indicated that older people and southern countries (Spain and Italy) had lower probability of belonging to the ill class; males were more likely than females to belong to the externalising ill class, but less likely to belong to the internalising ill class. Having any physical chronic condition increase the probability of belonging to the internalising ill class (Table 5). The effect of gender, age, country and chronic-condition on the internalising/externalising dimensions was mediated by the latent classes, and they did not explained differences in the mental-health level within classes. Marital status had a significant effect on the severity of the internalising mental health among those who had internalising disorders: married (or cohabiting) individuals showed better internalising health, but previously married (separated, divorced or widowed) had a lower internalising level.

Both the externalising and internalising factor yielded two classes (healthy and ill); consequently, subjects may fall into any of four possible class-combinations. The estimated covariance factor in subjects belonging simultaneously to the classes "externalising-ill" and "internalising-ill" (i.e., comorbid individuals) was 0.60, leading to a factor-correlation of 0.87, whereas the externalising variance estimated for the combination of "externalising-ill" and "internalising-healthy" was very low (see Table 5.3). This result has two important implications: a) among mentally comorbid subjects, both dimensions are highly correlated and b) all subjects suffering of externalising disorders only (i.e. "externalising-ill" and "internalising-healthy") had very similar levels of mental health regarding the externalising dimension.

About the goodness of fit of this final model, most of the BVRs were low, so the model can reproduce the observed association between pairs of the disorder variables quite well. Only few of them indicated somewhat significant residual associations between certain pairs of anxiety disorders: specific phobia with agoraphobia (19.9), specific with social phobia (10.2) and social phobia with agoraphobia (12.8).

Factor scores:

Factor scores on the final model were estimated as posterior factor means, therefore taking also into account the posterior class membership probability (Vermunt et al., 2005). Table 6 shows the maximum and minimum probabilities of belonging to class 1 and factor scores, by disorder type. Recall that ill individuals formed class 1 (zero factor mean) whereas class 2 is formed by healthy individuals (factor mean 10 and zero variance). All individuals diagnosed with any internalising disorder were

assigned for sure (with probability one) to the internalising ill class – except the individuals with only specific phobia, who had a probability to belong to the ill class ranging from 0.9032 to 0.9998, and some of them had a factor score slightly over 0. Individuals with at least one externalising disorder were assigned with probability 1 to the externalising ill class, all of them with negative factor scores. Only two individuals without any internalising disorder (but with odd and add externalising disorders) scored -0.38 and 0.52 in the internalising factor, lower than the maximum score for individuals with any internalising disorder (1.16). A part from these specific two cases, individuals without disorders scored positively in both dimensions and their internalising (or externalising) scores were higher than those individuals with any internalising (or externalising) disorder.

Table 6. Minimum and maximum values of probability class membership and factor scores

	Internalising		**Externalising**	
	Prob. ill-class*	**Score**	**Prob. ill-class***	**Score**
Any Internalising disorder				
Yes	[0.90, 1.00]	[-2.96, 1.16]	[0.00, 1.00]	[-1.67, 10.0]
No	[0.03, 0.94]	[-0.38, 9.74]	[0.00, 1.00]	[-1.26, 9.98]
Any Externalising disorder				
Yes	[0.09, 1.00]	[-2.52, 9.09]	[1.00, 1.00]	[-1.67, -0.23]
No	[0.03, 1.00]	[-2.96, 9.74]	[0.00, 0.85]	[1.43, 10.0]

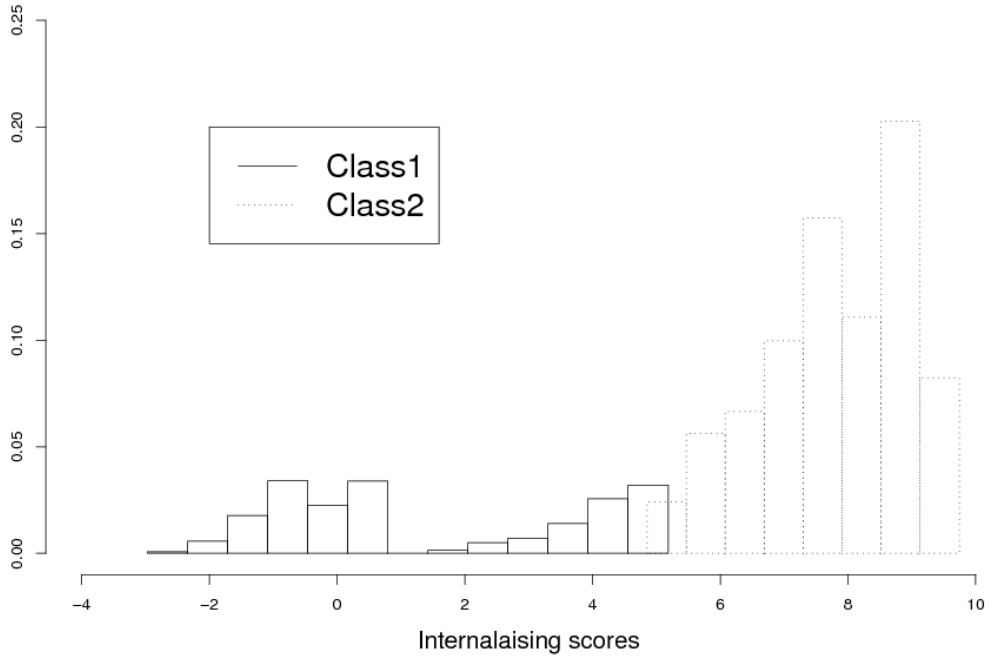
* Membership probability to belong to the ill class (Class 1).

There were cases of individuals without any disorder but with a high probability of belonging to class 1, up to 0.94 and 0.85 for internalising and externalising factor respectively (Table 6). Figure 2 shows the histogram of the score distribution by classes, once the individuals have been assigned to their highest probability class, for the internalising (2a) and externalising factor (2b).

It is possible to conclude from the score distributions that externalising disorders were much less prevalent than the internalising ones. The estimated latent class sizes were: for the internalising factor the class 1 included 34.7% of individuals and class 2 a 65.3%; and for the externalising factor the class 1 included 16.2% of the individuals and class 2 a 83.8%. According to the model, it is expected 21.6% of misclassification

in the internalising factor and 11.6% in the externalising factor when assigning the individuals to their most likely class.

a)



b)

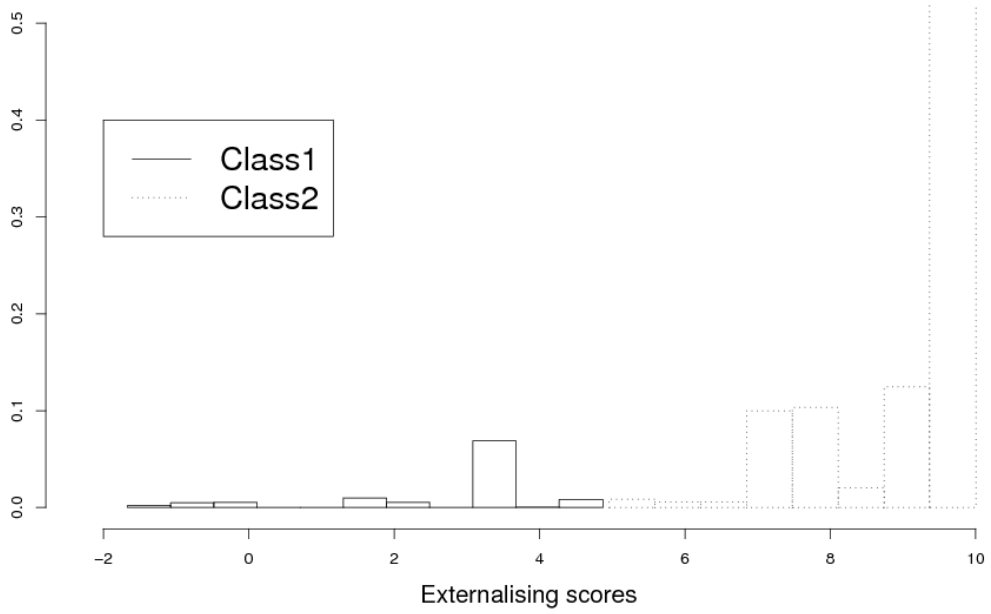


Figure 2. Histogram of the estimated scores from the internalising (a) and externalising (b) mental-health dimensions, stratified by class membership (individuals assigned to their highest probability class).

Figure 3 displays the bivariate plot of the factor scores. Dotted lines mark the maximum observed scores for those with any disorder. Average scores for age-group, country and gender categories have been marked in the graphic (see also Table 7). It can be seen in figure 3 the high correlation on the group of individuals having externalising and internalising disorders, and the low variability in the group with only externalising disorders.

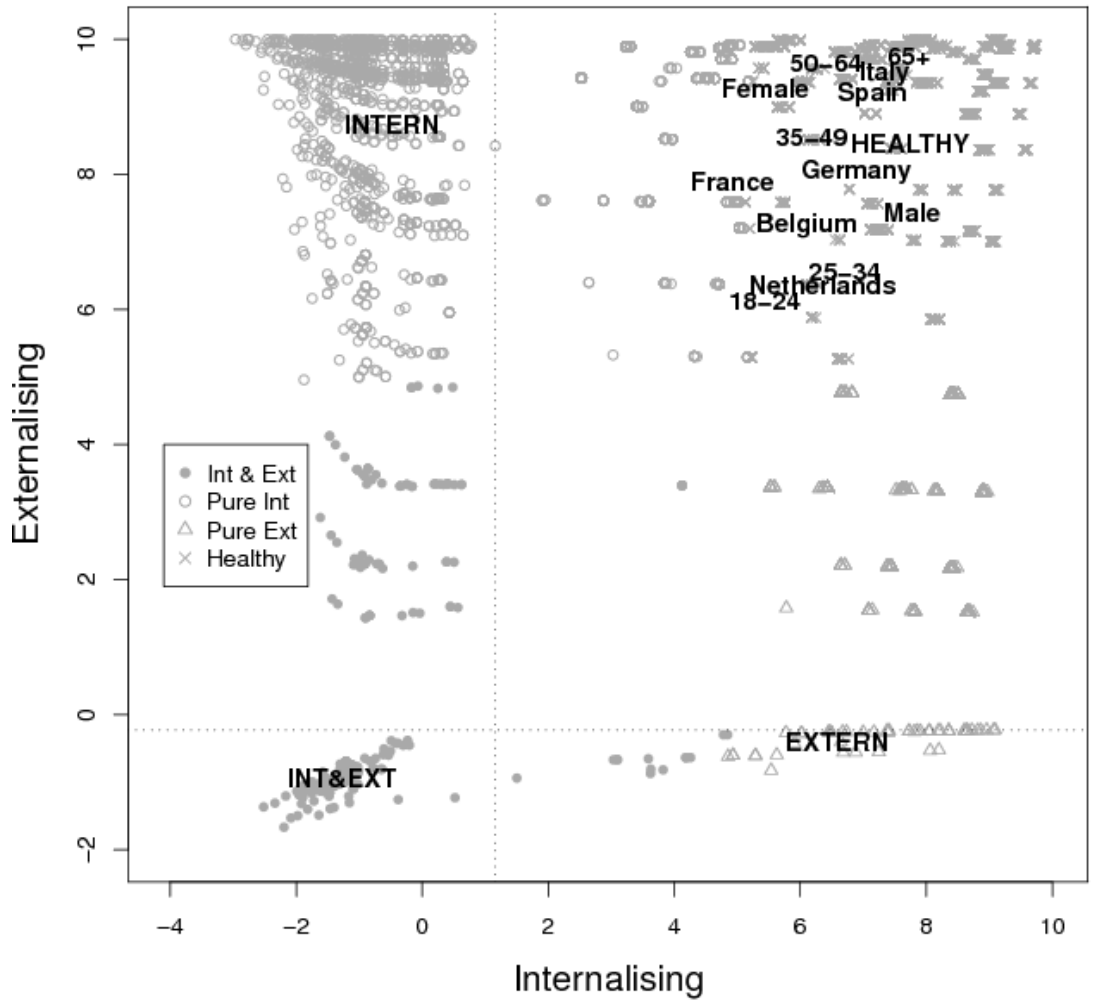


Figure 3. Bivariate scores grouped by latent classes

- Individuals assigned to their highest probability 4-class-combination.
- Labels allocate mean scores for covariates age(18-24, 25-34, 35-49, 50-64, 65+), Countries and Gender, and for those with pure internalising disorder (INTERN), pure externalising disorder (EXTERN), both types of disorders (INT&EXT) and no disorder (HEALTHY).
- Dotted lines mark the maximum observed scores for those with any disorder, for each dimension.

The graphic also makes evident a tendency for younger people to suffer from worse internalising/externalising mental health state, disorder differences by gender (males are more prevalent in externalising disorders and females in the internalising ones), and Southern countries showed better levels of internalising/externalising mental health. Socio-demographic mean scores were quite high because most of the population was classified as mentally healthy. Table 7 provides a more detailed summary of class membership and factor scores. Notice that factor means for the comorbid class were significantly lower than factor means in groups with just one disorder: internalising and externalising averages for the comorbid group were -1.28 and -0.95 respectively, while the internalising averages in the pure internalising group is -0.48 and -0.41 in the pure externalising. The lower average scores estimated for any-disorder respect pure-disorder can be explained by this negative interaction in the comorbid group. Differences in the externalising outcomes for chronic condition and marital status groups are explained by their relation with age (having any chronic condition and being previously married is associated with older ages).

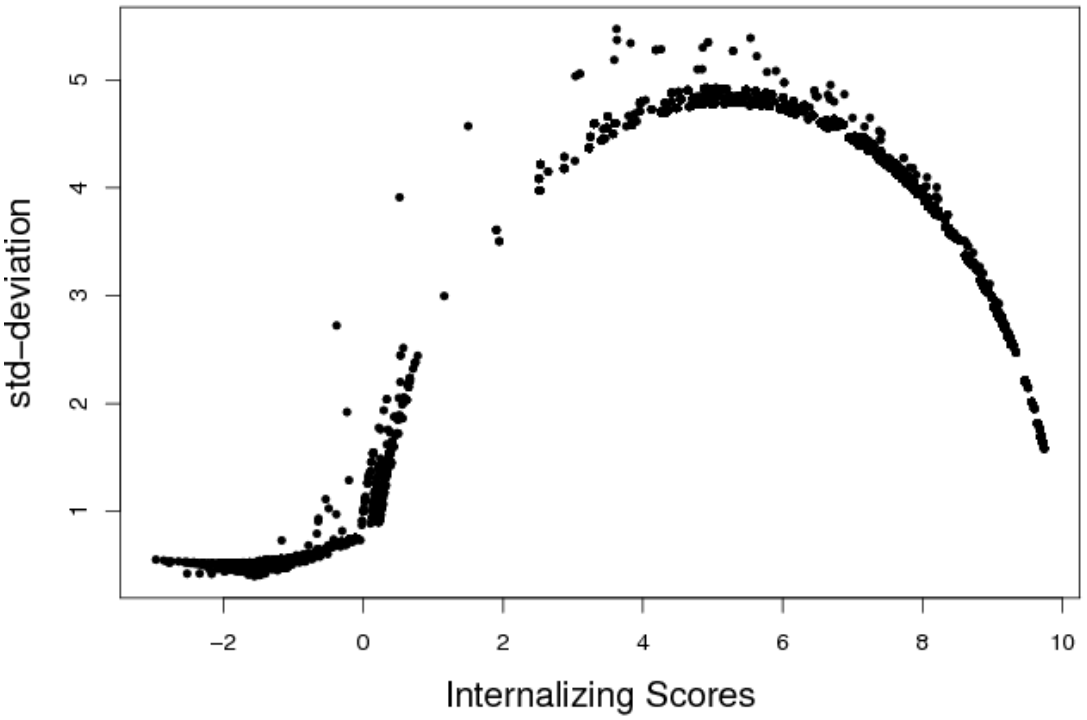
Score estimates for diagnosed individuals (i.e. low factor scores) were considerably accurate, as shown by their small standard deviations. Similarly, the very high scores (corresponding to healthy individuals) were estimated quite precisely. However, middle-score individuals had very large variability, so the model is expected to be imprecise when estimating middle-range scores for both factors (Figure 4).

Table 7. Mean of ill-class membership probability and factor scores

	Internalising		Externalising	
	Prob. ill-class*	**Mean**	**Prob. ill-class***	**Mean**
Overall sample	0.35	6.56	0.16	8.38
Any Disorder	0.95	-0.08	0.21	7.79
Pure Internalising disorder	0.99	-0.48	0.12	8.73
Any Internalising disorder	0.99	-0.52	0.16	8.33
Pure Externalising	0.32	6.59	1.00	-0.41
Any Externalising disorder	0.59	3.54	1.00	-0.62
Intern. and Extern. comorbid	1.00	-1.28	1.00	-0.95
No disorder	0.26	7.49	0.15	8.46
Gender				
Male	0.23	7.77	0.26	7.43
Female	0.46	5.44	0.07	9.26
Age group				
18-24	0.46	5.44	0.37	6.30
25-34	0.33	6.71	0.37	6.35
35-49	0.39	6.18	0.14	8.56
50-64	0.36	6.41	0.03	9.66
+65	0.23	7.72	0.03	9.75
Country				
Belgium	0.39	6.10	0.28	7.24
France	0.51	4.92	0.21	7.90
Germany	0.32	6.89	0.20	8.04
Italy	0.27	7.34	0.05	9.48
Netherlands	0.37	6.35	0.36	6.36
Spain	0.29	7.14	0.08	9.18
Chronic condition				
Yes	0.42	5.80	0.08	9.24
No	0.31	6.90	0.20	8.00
Marital Status				
Married/Cohabiting	0.35	6.60	0.13	8.69
Previously married	0.34	6.56	0.06	9.38
Never married	0.35	6.46	0.31	6.93

* Membership probability to belong to the ill class (Class 1).

a)



b)

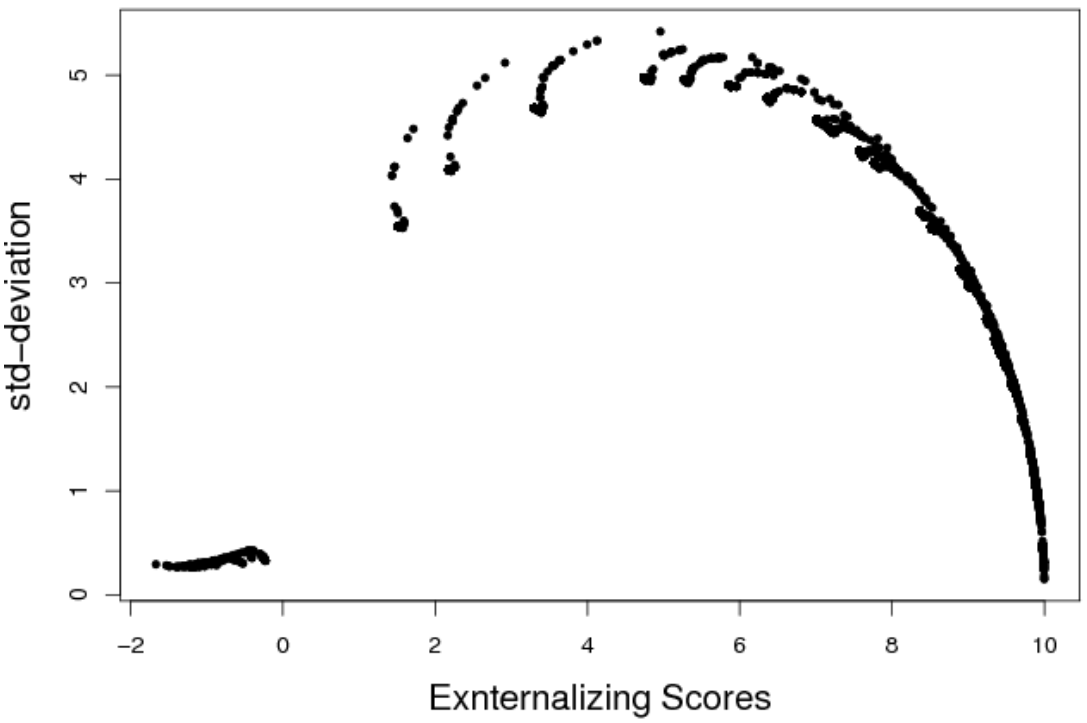


Figure 4. Precision of the internalising (a) and externalising (b) estimated scores.

Discussion

For quite a long time now, there has been a claim in psychiatry research for dimensional continuous measures of mental health states (Brown et al., 1998; Clark et al., 1991; Clark, 2005; Krueger, 1999; Krueger et al., 2001; Krueger et al., 2005; Mineka et al., 1998; Vollebergh et al., 2001; Watson et al., 1988; Watson, 2005). In spite of the existence of dimensional conceptual models, they had been scarcely used to score and classify the individuals given their comorbidity pattern. In this study, we developed a statistical model for the analysis of population mental health regarding internalising/externalising disorders that yielded such measures. This model summarized 12 dichotomous disorders into two continuous variables measuring severity, while the latent class part of the model retained the ability to describe categorical properties of certain subpopulations. Analyses support the usefulness of latent variable models to estimate scores of non-observable internalising/externalising mental health states directly from the conceptual models. Thus, dimensional measures with categorical description embedded in the final scores could be attained with relative ease.

To our knowledge, this is the first time that mentally healthy and ill subpopulation have been jointly analysed and explicitly modelled. From a methodological point of view, joint modelling is compulsory when analysing general population, not only because of the improvements in goodness of fit, but also because in so doing, the models approach closer to reality. Our 2-class model arose without imposing previous constraints, so it turns out to be a most trustworthy approximation to model the data. One advantage of the FMM model is that it allows the simultaneous classification of variables (in factors) and individuals (in classes).

While univariate and bivariate analysis of mental disorders are appropriate for detailed variable descriptions, multivariate finite mixture models based on conceptual psychiatric knowledge make available comprehensive depictions of mental health states. In addition, and contrary to the dichotomous diagnostics of disorders, latent variables provide continuous and dimensional measures of mental health state. Moreover, factor scores capture the simultaneous effects of a number of observed disorders on the individuals. In this fashion, these models are able to seize interactions and the differential impact of disorders on mental factors. Given the correlation between internalising and externalising factors, when no internalising disorders were observed a relatively low internalising score was estimated if externalising disorders

were present (and the other way round). This methodology models the comorbidity directly.

Another advantage of FMM models is that they make available a direct method for interpreting results (i.e. scores) across sample characteristics. A graphical representation of dimensional scores and the allocation of average values of covariates can be used as simple procedure to detect the existing mental health (most relevant) tendencies. For instance, in our model it was straightforward to detect differences in the type of disorders depending on gender, age and country of origin. Perhaps more interestingly, it was easy to see that the presence of internalising-externalising comorbidity had greater impact on the overall mental health state than pure disorders' type, and it can be measured quantitatively and directly in terms of level of mental-health state.

Other important benefit of this statistical model is that it measures the effect of the covariates over the common disorders' information, more parsimonious and easily interpretable than having an effect over each one of the disorders. The model also gives an interpretation about how socio-demographic variables influence the internalising/externalising dimensions. In this study, we found that the differential mental-health status between gender, age, country and chronic-condition socio-demographic groups was just due to differences in the proportion of healthy and ill individuals, but there were not found differences in the illness severity across groups. Conversely, marital status did not show influence in the proportion of healthy and ill individuals, but it had a significant effect on the severity of internalising 'ill' individuals, in which previously married had lower internalising level and married (or cohabiting) individuals had better internalising mental health. This double covariate-effect interpretation (on population proportions and severity) is only possible within FMM framework.

Moreover, greater score precision could be achieved using additional disorder information, other than diagnostic data, such as ordinal information of disorder severity, to increase the reliability of the scores within mild to moderate range of mental health states. Notice that one important advantage of latent model-based scores resides in that the score precision is a function of the score itself and not an instrument's property in a certain sample (Hambleton and Rogers 1991; De Boeck 2004). While diagnostic data can only provide information about the most severe mental health states (i.e. those that have been already diagnosed), latent methods allow to add further precision

in certain score levels just by taking into account any other dimensional information (for instance, symptoms or questionnaire data) at any measurement level into the model.

The dimensional modeling in a measurement invariant FMM is done exclusively through continuous latent factors. In our methodology, latent classes only serve to determine the factor mean scores. In this way, latent classes are not sensitive to inclusion or exclusions of disorders, as they are being used to model sample characteristics and not latent score structures.

This model also allows for the assessment of measurement invariance. MI is a crucial property for any measurement instrument that researchers overlook very often. Model stability of the model has seldom been tested in the literature of conceptual mental health models. To our knowledge only Chorpita (2002) conducted measurement invariance analyses in a tripatite model based on symptom's information and Markon et al. (2005) on the externalising factor. There is motive of concern: when MI is not present, the model cannot ensure its applicability over heterogeneous samples. Only a measure-invariant model is capable to summarize simultaneously all variable information into factor scores. As a result, applied researchers can compare sample characteristics via average scores. The MI property even warranties that the interpretation of the observed data (for example the Table 2 results) is not influenced by unknown confounder effects.

Model limitations

A first limitation is due to the participation rate, which was over 61%. This might limit external validity of our data. Nevertheless, internal validity is assured by the instruments, measurement and control methods used. And therefore we are totally confident on the validity and relevance of the associations described in this paper.

Another limitation concerning data gathering is that information based on disorders could be acceptable in clinical samples, but it is not good enough over general population when the main purpose it to score mental health states in any kind of disorders. In our example, we found that internalising/externalising scores' estimation had unacceptable high variance on the middle-level health states. Krueger et al. (2001) and Markon et al. (2005) found similar results using disorder information. In their studies, factor score precision was only acceptable for ill-range scores, but estimates were more unstable within the healthy range. In our study, the inclusion of latent classes for the healthy and non-healthy subpopulations improved precision of the

highest scores, but middle-ranged scores were still inaccurate. Our model was able to discriminate the clear cases of ill and healthy individuals but it was less precise on the intermediate scores, which could represent subthreshold or mild phases of the disorders. This lack of precision produces a 21.6% classification error when assigning individuals to their estimated higher probability internalising class. Simply put, the model had not enough power to distinguish states in the mild to healthy range. On the other side, those who fulfilled the criteria for at least one disorder were assigned to the ill class, together with those with a mild health state or subthreshold (not so sever to fulfil some disorder criteria). Consequently, the model ill-class refers to a wide range of mental health states. This is a direct consequence of the nature of disorder-level data, in which having the disorder implies the fulfilment of several (strict) criteria, but not having the disorder applies to a wide range of possibilities: from individuals who meet all the criteria except one, to very healthy individuals.

In the overall, the FMM model performed well in both the internalising and the externalising dimension. However, in both dimensions there were a group of individuals with middle score values that were most likely to belong to class 1. This points to the feasibility of a model with three classes: diagnosed (scores around zero or less), mild (scores approximately from 2 to 5) and healthy (scores over 5). On this instance, ill classes would include actual disorders as well as subthreshold or mild mental disorders. We opted for a two-class model because the inclusion of a third class did not substantially improve the BIC and AIC indexes. So, according to the results, a 3-class model might explain better the population mental health state, but such a model is not easy to estimate with only disorder information. Yet, the possibility of expanding the number of classes remains open for future research. Future investigations should search for additional variables measuring mild (and positive) health states to model a sensitive 3-class model. This strategy will be undoubtedly fruitful to increase the precision of score estimates all along the scoring continuum.

The internalising factor captures most of the information provided by the internalising disorders. Nevertheless, a few significant bivariate residuals between some anxiety disorders remained. The pattern disorder consisting on having specific phobia and not having any other disorder didn't result in 100% probability of belonging to internalising class 1, as expected from every individual with at least one internalising disorder. Nonetheless, the estimated probability was quite close to one (at least 0.9). This is a caveat for model interpretation, as the effect of some anxiety disorders on the internalising score could be slightly underestimated. There are previous results in the

literature indicating that anxiety disorders are no totally well explained by a single internalising factor (Fergusson et al., 2006; Almansa et al., submitted). Other models can be proposed to overcome this limitation. A two-factor model, splitting internalising disorders into Distress (mde, dys, gad, pts) and Fear (pds, sp, so, ago) captured better all the disorder associations (Krueger, 1999; Slade et al., 2006; Vollebergh et al., 2001; Almansa et al., submitted). Still, a single factor construct is useful as a measure of mental health in large population epidemiological research, because it yielded small measurement error and do not invalidate its use for epidemiological purposes given its parsimony.

Conclusion

This paper provides a methodology to assess the internalising and externalising psychiatric dimensions. This methodology is suitable for epidemiologic studies, and offers easily interpretable results. Once established a nosology model, a set of factors obtained, by means of a latent variable model, summarize the population health state. The model gathers the observed binary information to provide a continuous score estimate for each mental health factor. Whenever the purpose is the population mental-health state assessment, this methodology offers more and clearer information than univariate and bivariate disorders' descriptives. Latent variable models can account for mental comorbidity: the estimated factor scores take into consideration the number of disorders and their weight in mental-health state. A major contribution of our model is that it permits to describe healthy and ill subpopulations, estimated simultaneously with factor measurement parameters.

Beyond plausibility assumption that a completely healthy psychiatric subpopulation exists, the inclusion of a latent class variable for different levels of severity improved the epidemiological description and increased the score precision on the mental health factor continuum. As recent proposals extend the factor structure of disorders in various ways, FMM provides a method to open a promising line of on these models which would allow establishing individual scores, contrasting model adequacy and results from both clinical and epidemiologic approaches.

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Article 3

Mental-heatlh assessment using discrete factor models.

Mental-health assessment using discrete factor models

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Abstract

Factor analyses and IRT are widely used statistical models. They assume an underlying continuous latent variable that explains the association among a set of observed variables. Discrete-ordinal factor models has been already developed in the past, but they have not been used as widely as the continuous factor models, and have not been deeply explored yet. Discrete factors have a shapeless distribution assumption that allows a very flexible estimation of the underlying distribution, but it has the disadvantage of requiring larger number of parameters compared to the normal latent distribution. This article shows in detail how to construct discrete factor models and how to fit complex structures like multigroup and factor mixture analyses. Discrete factors can be used as an approximation to a continuous latent distribution when the normality assumption is doubtful. Additionaly, discrete factor models could be beneficial in order to achieve an easier interpretability of the underlying distribution, classifying all possible lantent values in a small number of "typical" ones. An application on European mental health data showed that the discrete factor models can be successfully used for the same purpose as the common FA or IRT analysis, with the advantage of gaining in computational cost and also, in this case, in the goodness of fit. A discrete factor mixture model was used to score mental-health states in the previous 12 month, in an European representative sample. The discrete factor models are a valid alternative to model the mental-health dimensionality.

Keywords: Mental disorders, psychiatric epidemiology, ordinal factors, internalising disorders, IRT, confirmatory factor analysis, measuement invariance.

1 INTRODUCCION

Factor Analysis (FA) and Item Response Theory (IRT) are techniques that model the underlying structure of a set of observed outcomes, in which outcomes are considered to be explained buy a small number of latent factors. A very general formulation of a continuous factor model could be expressed as follows:

$$g\left(Y|\Theta\right) = \alpha + \Lambda \cdot \Theta + \Psi \tag{1}$$

where Y is the vector of outcomes, $g\left(\cdot\right)$ is the link function that relates linearly the latent factors with a function of the observed outcomes, α is a vector of intercepts and Λ the factor loading matrix. The factors Θ are considered to be continuous and normal distributed unobserved variables. The residuals Ψ retain the item's information that is not explained by the common factors Θ. For continuous normal distributed outcomes $g\left(\cdot\right)$ is the identity function, leading to the common FA model. Categorical outcomes lead to the IRT family models.

Although the FA and IRT with continuous factor models are well known and widely used, their assumptions can be too strict for some specific applications. Recent studies have enlightened the appropriateness of discrete-ordinal factors, instead of continuous, in some contexts. For example, Vermunt and Magidson (2005a) emphasised that the advantages of discrete factors are: first, it does not require the normality factor distribution assumption, and second, the estimation procedure is computationally much less demanding because it does not use numerical integration. Additionally, previous research showed that discrete ordinal distributions can approximate quite well the underlying continuous one (Heinen, 1996), and Clogg (1988) demonstrated that if a continuous factor model is local independent, then its discretized factor model is local independent too.

Discrete-ordinal factor models are the appropriate method when the un-

derlying phenomena is supposed to be discrete. Moreover, it may be also suitable to approximate the continuous underlying latent distribution in two cases: first, when the latent normality assumption is questionable and, second, to achieve an easier interpretability of the underlying factors. Medical researchers and clinicians easily understand categorical descriptors (e.g. "mild", "sever") better than a continuous structure, tending to classify individuals in a small number of "typical" groups.

This article describes IRT models in which the factors Θ are discrete-ordinal latent variables, instead of the usual normal continuous ones. It is shown how to model complex factor structures (like multidimensionality, addition of covariates or multigroup analysis) and to test measurement invariance, through an application on European mental health assessment.

2 Discrete Factor Model

2.1 Basic model

A generic way to construct a discrete factor is through two related latent variables. First, a continuous latent variable regressed on a categorical latent variable in order to vary the means of the continuous latent variable according to the distribution of the categorical one. Second, the continuous latent variable is restricted to have zero variance to force it to be degenerated on a few possible ordinal values - as many as number of categories in the categorical latent variable. This formulation allows the estimation of the category allocations as well as their probability mass simultaneously.

Without any loss of generality, all the formulas and applications in this article consider binary or ordered categorical outcomes Y, where $g(\cdot)$ is the

probit link function, leading to a 2-parameter normal ogive model (Boeck and Wilson, 2004).

Let Y_{ij} be a binary or ordered categorical observed variable j, measured on individual i:

$$probit\left(P\left[Y_{ij}=1|\theta\right]\right)=\alpha_j+\lambda_j\cdot\theta_i+\psi_{ij} \tag{2a}$$

$$\theta_i=\mu+\sum_{k=1}^{K-1}\beta_k\cdot C_{ik} \tag{2b}$$

$$logit\left(\hat{P}\left[C_k\right]\right)=\tau_k \tag{2c}$$

The factor θ can take up to K different values, as many as categories are in the categorical variable C. Note that (2b) does not have error term, because the latent factor has been forced to zero variance. All possible values of θ will be denoted as $\theta(k)$, for $k=\{1,...,K\}$. The categorical variable C is expressed in (2b) by means of $K-1$ coding variables, using the last category as the reference one, but it could be easily expressed with a different categorical coding. An individual i belonging to category k has $C_{ik}=1$ (with $C_{ik'}=0$, $\forall k'\neq k$) and $\theta_i=\theta(k)$. Factor scores are computed as $\theta(k)=\mu+\beta_k$, for $k=\{1,...,K-1\}$, and $\theta(K)=\mu$. Thus, each category in C variable is linked with one factor score value.

The individuals' factor scores are not observed, but its probability distribution can be estimated. The parameters τ_k determine the mass probability of the factor categories.

One great advantage of the discrete factor model is that the probability distribution of the unobserved variable has not a fixed shape. In contrast to the usual normal latent distribution, the freely estimation of allocations and mass probabilities leads to a very flexible (shape-free) distribution.

This kind of models are also known as Latent-Class Factor (LCF), because this model is equivalent to a Latent Class Analysis (LCA) model where the latent classes are ordered over a unique dimension, and each class corresponds to one factor category (Vermunt and Magidson, 2005a).

As in the common FA (1), some metric restrictions have to be applied in order to be identifiable. It is required one location restriction, which can be implemented fixing one of the factor categories or the factor mean (for example to zero). To determine the factor scale there are also two possibilities: one factor loading (λ_j) has to be fixed at 1 (as an anchor variable), or a second location point (another factor category) can be fixed to a certain value. In the subsequent models the anchor-variable method is going to be used, in order to keep similarity with the common FA model.

One way to fix the factor mean to zero is to set $\mu = 0$ and use effect coding for $\theta(k)$ categories. Note that this fix the mean across categories, but not the sample mean. The sample mean restriction requires a function of the estimated category allocations and their mass probabilities.

The measurement parameters relates the observed outcomes with the latent factor, and they are the intercepts α_j and the factor loadings λ_j. The structural parameters define the factor distribution, and they are the μ, β_k and τ_k.

2.2 General model

A more general discrete-factor model may include several factors (multidimensionality), multiple groups and covariates. The expression for a 2-factor model for a group g, and categorical covariates $\boldsymbol{z}$ and $\boldsymbol{x}$, could be as follows:

$$probit\left(P\left[Y_{ij}=1|\theta^1,\theta^2,G=g\right]\right)=\alpha_{j|g}+\lambda^1_{j|g}\cdot\theta^1_{i|g}+\lambda^2_{j|g}\cdot\theta^2_{i|g}+\psi_{ijg} \quad (3a)$$

$$\theta^1_{i|g}=\mu^1_g+\sum_k^{K^1_g-1}\beta^1_{k|g}\cdot C^1_{ik|g}+\boldsymbol{\gamma}^{1x}_{k|g}\cdot\boldsymbol{x}^1_i \quad (3b)$$

$$\theta^2_{i|g}=\mu^2_g+\sum_k^{K^2_g-1}\beta^2_{k|g}\cdot C^2_{ik|g}+\boldsymbol{\gamma}^{2x}_{k|g}\cdot\boldsymbol{x}^2_i \quad (3c)$$

$$logit\left(\hat{P}\left[C^1_{k|g}\right]\right)=\tau^1_{k|g}+\boldsymbol{\gamma}^{1z}_{k|g}\cdot\boldsymbol{z}^1 \quad (3d)$$

$$logit\left(\hat{P}\left[C^2_{k|g}\right]\right)=\tau^2_{k|g}+\boldsymbol{\gamma}^{2z}_{k|g}\cdot\boldsymbol{z}^2 \quad (3e)$$

Factor covariates affect (differently) the two discrete distribution parameters: allocations (3b-3c) and mass probabilities (3d-3e). Covariates in (3b-3c) allocate differently the discrete factor points for all possible values of $\boldsymbol{x}$ variables, and covariates in (3d-3e) provide a different discrete factor probability mass for all possible values of $\boldsymbol{z}$ variables. Covariates can affect both allocations and probabilities (i.e. $z=x$) or just in one of them.

When using more than one discrete factor in a model, each of them can have their own number of discrete points ($K^1_g\neq K^2_g$) and even they could differ across groups. Diferences in structural parameters across groups allow for a different latent distribution-shape in each group.

Correlation across pairs of discrete factors is modelled through the joint mass probability of the combined factor categories:

$$logit\left(\hat{P}\left[C^1_k,C^2_{k'}\right]\right)=logit\left(\hat{P}\left[C^1_k\right]\right)+logit\left(\hat{P}\left[C^2_{k'}\right]\right)+\gamma^{12}\cdot\theta^1(k)\cdot\theta^2(k') \quad (4)$$

The parameter γ^{12} mearues their association, linearly related to the product of both factor scores.

The required identifiability restrictions for the discrete factor multigroup analyses are equivalent to the ones for the common FA. First, in the unrestricted model (in which the measurement parameters can vary across

groups), one allocation parameter needs to be fixed for all groups (the factor mean or one discrete factor allocation). Second, the factor scale needs to be fixed within each group (e.g. one factor loading equal to 1). In the restricted model (in which measurement parameters hold invariant), the allocation restriction require to be fixed only for one group and can be free estimated for the others.

Measurement invariance (MI) is achieved when all measurement parameters holds equal for all groups, that is: $\alpha_{j|g} = \alpha_j$ and $\lambda_{j|g} = \lambda_j$, $\forall g$. Only under MI the discrete factor distribution is meaningful comparable across groups, and factor scores are sufficient to compare all individuals (Mellenbergh, 1989).

The grouping variable can be observed or latent. A latent grouping (class) variable leads to a discrete factor mixture model (FMM). The discrete FMM formulation adds to equation (2.2) the class-size estimation as

$$logit\left(\hat{P}[G=g]\right) = \delta_g + \boldsymbol{\gamma}^w \cdot \boldsymbol{w} \tag{5}$$

where covariates $\boldsymbol{w}$ predict class membership probability. These class covariates could be equal or different to the factor covariates in (3b–3e). Factor covariates, then, determine systematic factor score differeces within classes, while class covariates determine differences in the class membership probability.

2.3 Factor score estimation

Individual factor scores can be estimated as Expected A Posteriori (EAP):

$$E\left(\theta_i|Y_{ij}, \boldsymbol{w}_i\right) = \sum_{k=1}^{K} \theta(k) \cdot P\left[\theta_i = \theta(k)|Y_{ij}, \boldsymbol{w}_i\right] \tag{6}$$

where $\theta(k)$ is the score value of the k-th factor category and $P\left[\theta_i = \theta(k)|Y_{ij}, \boldsymbol{w}_i\right]$ is the posterior class membership probability given the observed variables Y_j and (class) covariates $\boldsymbol{w}$ (Vermunt and Magidson, 2005b)(Lubke et al., 2003).

3 Application in Mental health Assessment

Next application shows the analysis of the internalising mental-health disorders using discrete factor models. Main data consist on 8 binary observed variables measuring the presence or absence of 8 internalising disorders within the last 12 months. This disorders are: major depression episode (mde), dysthymia (dys), general anxiety disorder (gad), posttraumatic stress disorder (ptsd), agoraphobia (ago), specific phobia (sp), social phobia (so) and panic disorder (pd). Data come form a representative European sample of 8,976 individuals, recruited for the ESEMeD project between years 2001 and 2003 (Alonso et al., 2004). Disorder assessment was done by means of the CIDI 3.0 instrument (Haro et al., 2006). The conceptual internalising disorders structure has been well described previously. The following analyses are based on the internalising two-factor model (Krueger, 1999; Watson, 2005; Vollebergh et al., 2001), which assumes that the internalising disorders can be modelled in two correlated factors: Distress (includes mde, dys, gad and ptsd disorders) and Fear (ago, pds, sp, so).

We assumed that disorders are continuous (underlying) variables measuring graded mental health states, but the manifest disorder variables only inform about if they exceed a certain threshold. Thus, the observed binary data used a probit link to relate each observed disorder with its latent variable (Agresti, 2002).

All statistical models were estimated with the software LatentGold 4.5, taking into account the complex sample design, and using 125 sets of start

values to avoid local-optimum solution.

3.1 Determining number of discrete factor points

A priori, nothing is known about the number of values that each discrete factor could have. The usual way to decide the appropriate number of categories of the discrete latent factor is to sequentially increase it until achieving a saturation point in which the likelihood is maximized (Aitkin, 1999; Vermunt and van Dijk, 2001). Adding more points, the likelihood function do not improve, and usually the new added points have a zero mass-probability.

The number of discrete factor points was explored for both Fear and Distress dimensions. According to the BIC (Schwarz, 1978), the appropriate number of discrete points are two in both factors (Table 1). The distress factor achieved the saturation point with only two categories. In the fear factor the AIC (Akaike, 1974) suggested the 3-points distribution, but it was discarded because one of the categories had a mass probability extremely low (only 0,3% of the sample was allocated in that point). So, further on, both factors are considered as 2-category discrete factors.

[— Insert Table 1 by here —]

3.2 Measurement Invariance Test

The measurement invariance of these two factors were assessed, each factor separately, by the following grouping variables: Gender (male; female), Age (18-24; 25-34; 35-49; 50-64; 65+), Country (Belgium; France; Germany; Italy; Netherland; Spain), Chronic condition (having any physical chronic condition in ther last 12 months; or not), Marital Status (married or cohabiting; previously married; never married) and Working Status (working; not working). Restricted model assumed equality on measurement parameters.

Two unrestricted models were fitted, the first one estimated freely the intercepts across groups and loadings held invariant, while in the second model both intercepts and loadings were freely estimated. Mean was fixed to zero for all groups in the unrestricted models and only for the first group in the restricted. For both types of models the structural parameters were freely estimated across groups.

Restricted and unrestricted models were compared with the BIC, AIC and AIC3 indices. According to the BIC index, the invariant models were always preferred over the invariant ones (Tables 2 and 3). Most of the AIC and AIC3 values also led to the invariant model. Given these results, the invariant assumption is acceptable.

[— Insert Tables 2 and 3 by here —]

3.3 Factor Mixture Models and covariates

A special factor mixture structure (invariant) was imposed. Given that not all the population suffers from mental health disorders, it was considered the existence of mentally ill and healthy subpopulations within each dimension, in which the ill subpopulation (class 1) followed a factor model, while healthy subpopulation (class 2) was homogeneously allocated in a (arbitrary) high value in which the probability of endorsing every disorder is negligible. This factor structure has already been successfully tested in the context of continuos factor models (Almansa et al., (Submitted)).

Then, in our discrete factor context, the ill subpopulation (class 1) followed the two-category discrete factor distribution, and the healthy (class 2) was allocated in a unique high value in which the probability of endorsing every disorder is negligible. This class structure was parameterized as follows: the μ parameter has been fixed to zero for the ill class and fixed to 10 for the healthy class, and the β parameters were free estimated in the

ill class, but they were fixed to zero for the healthy class (a unique factor score equal to 10 was allowed for the healthy class). Class covariates, predicting the class (ill/healthy) membership probability, increased largely the goodness of fit (see Tables 2 and 3). The signifficant class-covariates for the distress factor were Gender, Age, Country, Chronic-condition, Marital-Status and Work-status. Gender, Age, Country and Chronic-condition were the Fear class-covariates. Once class covariates were selected, no significant factor covariate was found.

3.4 Two-factor final model

Finally, both Distress and Fear factors were modelled together. Based on their conceptual construct, both factors were correlated; Distress and Fear are two subdimensions of a more general internalising factor (Watson, 2005). The factor mixture models allows for two possible ways of class correlation. The first one correlates factor scores within each class (e.g. ill-distress scores correlate with ill-fear scores). The second one relates the class membership probabilities, so class membership is not independent across factors (e.g. belonging to the distress-ill class increase the fear-ill class membership probability). In our data, the best fitting model had score correlation within the individuals in both ill-classes, and also the class membership probability for both factor was modelled with dependency.

The formulation of the final model for distress (θ^D) and fear (θ^F) factors, with ill and healthy latent groups (G^D and G^F respectively) is as follows:

$$probit\left(\hat{P}\left(Y_{ij}=1|\theta^D,\theta^F,G^D,G^F\right)\right)=\alpha_j+\lambda_j^D\cdot\theta^D_{i|G^D}+\lambda_j^F\cdot\theta^F_{i|G^F} \tag{7a}$$

$$\theta^D_{i|G^D}=\left(0+\beta^D\cdot C_i^D\right)\cdot\mathbb{I}_{[G^D=1]}+10\cdot\mathbb{I}_{[G^D=2]} \tag{7b}$$

$$\theta^F_{i|G^F}=\left(0+\beta^F\cdot C_i^F\right)\cdot\mathbb{I}_{[G^F=1]}+10\cdot\mathbb{I}_{[G^F=2]} \tag{7c}$$

$$logit\left(\hat{P}\left[C^D,C^F|G^D,G^F\right]\right)=\tau^D\cdot\mathbb{I}_{[G^D=1]}+\tau^F\cdot\mathbb{I}_{[G^F=1]}+\tau^{DF}\cdot\mathbb{I}_{[G^D=1,G^F=1]} \tag{7d}$$

$$logit\left(\hat{P}\left[G^D,G^F\right]\right)=\delta^D+\boldsymbol{\gamma}^{Dw}\cdot\boldsymbol{w}^D+\delta^F+\boldsymbol{\gamma}^{Fw}\cdot\boldsymbol{w}^F+\delta^{DF} \tag{7e}$$

Figure 1 shows the final model structure.

[— Insert Figure 1 by here —]

The discrete factor mass probabilities estimated in (7d) only affect to classes 1 (ill), and the association parameter τ^{DF} was only estimated for the both ill-class combination. Due to software limitations, the discrete factor correlation had been computed as a nominal-type correlation (see 7d), like in a loglinear model for a non-independent contingency table – instead of the ordinal correlation shown in (4). Given that both discrete factors have two categories, only one parameter is required for the nominal-type association estimation δ^{DF}.

The estimated discrete factors distribution had two-points within the ill classes and one fix score for the healthy classes. Estimated factor scores for the ill-classes were: 1) for the distress factor were obtained scores -0.66 and 0.66 with a mass probability 0.86 and 0.14 respectively; 2) for the fear factor were obtained scores -1.02 and 1.02 with a mass probability 0.03 and 0.97 (Table 4). So each factor has two categories that we could label as "high-sever" and "sever". Most of the distress-ill sample are allocated in the "high-sever" category, while the fear-ill sample are majorly allocated in the "sever" category. The estimated ill-class membership probability for the distress factor was 0.13 and for the fear factor 0.34.

Parameters estimates (Table 4) showed that males and females are clearly differenciated in fear factor, being females more likely to suffer from that disorders - when keeping constant the rest of the variables. Regarding countries, France showed low mental health levels for both factors, in contrast to Italy, which showed higher probabilities to belong to both healthy classes. Germany had higher proportion of ill-class individuals in the fear factor and lower in the distress one, just the opposite pattern as the individuals from

The Netherlands. The oldest group was less likely than younger ones to belong to the ill classes, for both dimensions. Having a (physical) chronic condition also had a negative impact on both mental-health factors. Marital status only had a signifficant effect on the level of distress. Married (or co-habiting) showed lower probability to belong to the ill class and previously married showed it higher. Not working individuals were also more likely to belong to the ill class.

It was estimated a positive association in the factor scores across both ill-classes (class 1). Thus, individuals belonging to the lower distress category (-0.66) were more likely to belong to the lower fear category (-1.02). There was also a positive association in the class membership, so ill individuals tend to be in the ill class for both factors (and the other way round).

The Bivariate residuals (BVR) is a chi-square measure from a two-way table of the estimated and observed frequencies, and it can be interpreted as a measure of residual association between pairs of observed variables (Vermunt and Magidson, 2005b) – given the latent structure, the observed variables are expected to be independent. In this final model, the BVR values were all within an acceptable range; the highest BVR was found between ptsd and pds (with a value of 5.8). So, beyond the fitted model there is very few association among the observed variables that left unexplained.

3.5 Factor scores

Individual factor scores were estimated from this final model as EAP. Disorder variables were coded using the presence of the disorder as the reference category (the probit link modeled the probability of not having the disorder); this coding method led to a factor with higher scores for healthy individuals and lower scored for ill ones. Factor scoring assigns a value of distress and fear mental-health level to each individual.

Figures 2 show the histogram of estimated scores, grouped by their most likely class membership (modal assignment). In the Distress dimension clearly defined the healthy and ill subpopulations.

[— Insert Figures 2 by here —]

Distress scores ranged from 0.14 to 1.31 for those who had any distress disorder (Table 5), except for those with only ptsd, which included 8 individuals with scores over 1.31, and only two of them above 3.58 – the minimum score of the non-disorder subsample.

[— Insert Tables 5 and 6 by here —]

Fear scores ranged from 0.05 to 2.03 for those who had any fear disorder (Table 6). Within those who didn't endorse any fear disorder there was a small proportion overlapping the ill-range score: 141 out of 7,802 non-diagnosed individuals had score lower than 2.03. The fear factor cannot discriminate between diagnosed and non-diagnosed individuals as precise as the distress factor.

[— Insert Figure 3 by here —]

Score descriptives serve as a rough summary description of the sample. Figure 3 shows the mean-score allocation for the covariates that were found signifficant. It can be seen that female and younger individuals had lower internalising mental-health (in both factors) than males and the older group respectively. Italy and Spain had better mental health than the rest of the countries. Mean distress scores for Germany was similar to that of Italy, but Germany had lower level of fear, and The Netherlands had lower values mainly in the distress factor. France was the country with lower internalising mental health state (in both factors). Regarding marital status, they differed in the distress scores: the highest group is the married (or cohabiting), then

the never married and the lowest level corresponded to the previously married individuals (divorced or widowed). Having any physical chronic condition had also a negative impact on both internalising dimensions.

3.6 Continuous vs. Discrete factor model results

It was also fitted the continuous-factor counterpart model to compare with the the latter discrete two-factor model. In this specific case, the discrete factor model fitted the data slightly better than the continuous factor in terms of loglikelihood and AIC comparative indices, although according to the BIC index the continuous factor model was more parsimonious. The discrete factor model estimated 47 paramters and had a loglikelihood equal to -5657.9, BIC=11742.7 and AIC=11409.8. The continuous factor model required 43 parameters, and had a loglikelihood value of -5675.0, BIC=11740.5 and AIC=11435.9. The interpretation of the distress and fear factors based on the factor-loadings estimates was equivalent for both models.

The BVR were very similar between the continuous and discrete factor models, although in continuous model a few BVR values were slightly higher than in the discrete models. For example, the BVR value between sp and ago for the discrete model was 0.79, but for the continuous model was equal to 5.00.

The modal classification assigns each individual to their most (estimated) likely class. The expected ill/healhty modal misclasification behaved differently in both type of models. The continuous model distinguished better the ill/healhty individuals in the fear factor (in the continuous case the misclassification probability was 0.12, and in the discrete factor was 0.23), but the discrete model classified better the individuals in the distress factor (misclassification probability of 0.17 for the continuous and 0.07 for the discrete model). The fear-ill distribution had a shape close to the normality-

shape with mean 1.02, while the distress-ill estimated discrete distribution was somewhat right-skewed. So, the distress factor seems better describe with the discrete factor methodology. The interpretation of the mean-scores covariates (as Figure 3) was the same for both models.

A big advantage of the discrete factor model was the computational-time saving. The required time for the estimation of the discrete factor model was largely inferior that the time required for the continuous factor. As an example, the final two-factor model with class covariates was estimated in a computer with intel-core-duo-2 2.33GHz processor and 3.23GB Ram memory. The required computational time for a estimation with 125 different random start-values was aproximately 15 minutes for the discrete factor model and around 25 hours for the normal continuous one (using 20 quadrature nodes). The discrete factor estimation avoids the heavy numerical integration that it is required when using continuous latent variables with maximum likelihood estimation.

4 Additional discrete-factor properties

4.1 Multigroup latent distribution

The discrete factor can be very flexibly estimated, not only because of its shapeless assumption, but because it can be estimated different distribution shapes for different subpopulations. Subpopulations may be defined by known or unobserved (latent classes) groups.

The structural parameters determine the factor probability distribution. In the common FA, factor mean and variance are sufficient to define the factor normal distribution. In the discrete factor model the free-shape factor distribution is determined by the number of categories, their allocations and

mass probabilities. The parameter allocations ($\beta_{k|g}$ and $\boldsymbol{\gamma}^x_{k|g}$) and mass probabilities ($\tau_{k|g}$ and $\boldsymbol{\gamma}^z_{k|g}$) can differ in each factor category k across grpus g (see equation 2.2), leading to a completely different discrete distribution for each covariate value. For example, a latent distribution for males could be right-skewed and left-skewed for females. Even the number of discrete points (K_g) can differ across groups. In the continous-normal case, the latent distribution can only vary in the mean and variances across groups.

When the number of discrete points is constant across groups, the different probability distribution can be modelled just through a covariate, keeping constant the μ and β_k parameters for all groups, otherwise different μ_g and $\beta_{k|g}$ parameters needs to be estimated for each subpopulation group.

When x is a categorical covariate, modelling a different discrete allocations per x category, the global number of discrete points is increased keeping fix the number of the factor discrete points. For example, if a discrete factor has two categories and they can be differently allocated according to gender, in total the individuals can be allocated in 4 different points on the latent continuum. This can help to get a better fit while keeping the model parsimony, and it adapts flexibly the latent probability distribution to the data.

When there are indeed different allocation per group and this is not taken into account, that is, the model is restricted by $\mu_g = \mu$ and $\beta_{k|g} = \beta_k$ $\forall g$, the estimated probability distribution may be affected: the model will estimate higher probability mass on the closer common point to compensate its distance from the true specific group value. Because of this reason, tests over equal allocations should be conducted before than tests over equality in the mass probabilities, and the default formulation should consider the estimation of both different allocations and mass probabilities per group.

Considering the existence of two groups, each of them with different number of factor categories, a practical way to fit a multigroup discrete factor

consist on defining two different (independent) categorical latent variables – each of them with their specific number of categories K_1 and K_2–, regress the latent continuous factor on both latent categorical variables, and restrict to zero the location parameters (μ_g, $\beta_{k|g}$) that not corresponds to its categorical latent variable.

$$\theta_i = \left(\mu_1 + \sum_{k_1=1}^{K_1-1} \beta_{k|1} \cdot C^1_{ik|1}\right) \cdot \mathbb{I}_{[g=1]} + \left(\mu_2 + \sum_{k_2=1}^{K_2-1} \beta_{k|2} \cdot C^2_{ik|2}\right) \cdot \mathbb{I}_{[g=2]} \quad (8)$$

4.2 Measurement Invariance

In a general way, it can be demonstrated that if the measurement invariant (MI) assumption holds for a continuous latent variable θ, then a discretization θ^* is also MI. Consider that the θ support is divided into D disjoint intervals $[\theta_{d-1}, \theta_d)$, for $d = 1..D$, with the assigned score m_d:

$$\begin{aligned} f\left(y|\theta^* = m_d, g\right) = f\left(y|\theta \in [\theta_{d-1}, \theta_d), g\right) = \int_{[\theta_{d-1}, \theta_d)} f\left(y|\theta, g\right) d\theta = \\ = \int_{[\theta_{d-1}, \theta_d)} f\left(y|\theta\right) d\theta = f\left(y|\theta^* = m_d\right) \end{aligned} \quad (9)$$

Given that model for θ was assumed to be invariant, the integral in (9) do not differ by g [$f(y|\theta, g) = f(y|\theta), \forall g$].

Thus, MI tests could be conducted with discrete factors as an approximation of the "true" MI analyses when the MI test is not trustable due to a doubtful factor normality assumption (or even to get a fast approximated result when the computational cost is excessive).

4.3 Factor Mixtures

Given that the discrete factor models are indeed a latent class model, it could be argued the necessity to build a factor mixture model, which includes an additional latent class variable predicting the factor distribution. In fact,

when the number of discrete points is equal for every group ($K_g = K, \forall g$), and the factor model is MI, a discrete factor mixture model with G latent classes and different factor distribution per group, can be equivalent to a discrete factor model with $K \times G$ allocations.

The structural part of a factor mixture model with G classes and K factor categories per class could be explressed as follows:

$$\theta_{i|g} = \mu_g + \sum_{k}^{K-1} \beta_{k|g} \cdot C_{ik|g} \tag{10a}$$

$$logit\left(\hat{P}\left[C_{k|g}\right]\right) = \tau_{k|g} \tag{10b}$$

$$logit\left(\hat{P}\left[G_g\right]\right) = \delta_g \tag{10c}$$

And the structural part of a one-factor model with $K \times G$ factor categories:

$$\theta_i = \mu + \sum_{k}^{K \times G - 1} \beta_k \cdot C_{ik} \tag{11a}$$

$$logit\left(\hat{P}\left[C_k\right]\right) = \tau_k \tag{11b}$$

It can be seen that the factor mass probabilities are equivalent in both cases, having $\tau_k = \tau_{k|g} + \delta_g$, and the restriction on the allocation required for the model identifiability could be fixed in both kind of models in order to get the same allocations. Thus, the factor probability distribution is the same, but parametrized in two different ways.

The allocation restriction required to make both kind of models equivalent could be not trivial. In our mental-health model we had one score equal to 10 for healthy class, and two scores for the ill class with category-mean equal to 0. An equivalent factor model, in (11a), could be obtained with the restrictions $\mu = 10$ and $\beta_2 = -\beta_1 - 2\mu$. More complicated restrictions should be placed when covariates are included in the model in order to get equivalent models. In our case, the mixture model with a 2-points ill-class

and a 1-point healthy-class achived the same loglikelihood as a 3-point factor model, but with one parameter less to estimate (the 3-point factor model had one location restriction and the mixture had one restriction per class).

When different meaningful subpopulations (clases) really exists in the data, the mixture model can define precisely all the parameters regarding each class distribution. In case of factor scale (variance) unequality across classes, the mixture model can easily specify this classes' diference. Moreover, the mixture parametrization offers a more detailed (causal) description of the factor distribution, in which the variation in the factor scores are partly explained by different underlying classes. Covariates in the mixture model can affect the class membership as well as the factor scores distribution within classes, and they can be included only in the part of the model where they have a significant effect. This two types of covarites provide two different meaningful effects on the factor score that may not be specified wihtout mixtures.

In case of measurement non-invariance across classes there is no equivalence between a G-mixture model and a $(K \times G)$-factor model.

4.4 Discrete-factor limitations

One disadvantage of discrete factor model, compared to the continuous factor, is that the latent distribution requires more parameters, and the number of parameters increases with the number of factor categories. In the normal distribution case, mean and variance is enough to define the probability distribution, but the discrete factor with K ordinal categories needs $K-1$ parameters for the probability mass estimation and, additionally, up to $K-1$ parameter allocations. Thus, the discrete-factor distribution description is a bit more complex than the continous normal one. The increment in the number of parameters needed for a driscrete factor model could be an sta-

tistical disadvantage. If number of items is small, it is possible to get a non-identifiable model before achieving the saturation point as the number of factor categories increases. When the normality assumption is not violated, the continuos factors will fit the data more parsimoniously than a discrete factor model.

The discrete-ordinal factor models can be straightly used within confirmatoy framework, but its use in exploratory factor analyses is not trivial, because the discrete distribution (number and allocation of points per factor) and number of factors needs to be estimated simultaneously.

5 Discussion

In these article we have presented an example of how to analyse data using discrete factor models. Important psychyatric researchers clame for a dimensionality assesment of the mental disorders (Mineka et al., 1998; Vollebergh et al., 2001; Clark, 2005; Watson, 2005). This article has shown that the discrete factor models are an alternative to the normal-continuous factors to model the underlying the mental health dimensions. Given that latent variables are not observed, their probability distribution are inexorably unknown. The usual latent-normality assumption is not easily ascertainable. The discrete factors approximate the unknown continuous-factor distribution without any (continuous) parametric assumption, estimating a totally free-shape latent probability distribution. The MaximumLikelihood estimation (ML) in general linear models can be sensitive to the misspecification of a parametric form for the mixing distribution (Aitkin, 1999).

The second big advantage of the discrete factors is the big computanional time saving, and becomes bigger as the number of factors increases, because the discrete factor distribution estimation does not requires the numerical

integration used in ML for continuous factor models (Aitkin, 1999; Vermunt and Magidson, 2005a).

We have shown that the discrete factors can be used to build the same models that are usually fitted in continuos factor contex: multigroup and factor mixture analyses, test of invariaces, factor correlation, addition of covariates, etc. Thus, discrete factor analysis is a suitable technique to describe popultaion according to some known construct. This tecnique is adecquate as an aproximation of a continuous factor when the assumption of factor-normality is doubtful or the continuos factor model is computational excessively demanding. It could be also possible the combination of normal and ordinal factors, using the discrete-ordinal distribution only for those factors who are clearly not normally distribuited.

A part from the statistical advantages, the discrete factor methodology can be used to summarize a large range of possible underliying values into a few typical ones, clustering all the possible latent values into a small number of most representative cases. This strategy has practical benefits in medical environments, when aiming to get a summarized and easy interpretable description of the unobserved phenomenum, even if there is some loose in the goodnes of fit, for the sake of a parsimonious interpretation.

It has recently appeared the guidelines for a new classification of mental disorders (DSM-V). These guidelines emphasises a graded dimensional modelization, in stead of the binary measurement (presence or absence) of the disorders. Ordinal factor models could be a way to model this dimensional gradation from a set of simptoms.

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A Final model LatentGold syntax

This is the syntax used in LatentGold 4.5 for the estimation of the final model (7). The *option* statment is ommited.

```
variables
   caseid caseid;
   stratumid stratum;
   psuid nest_sec;
   samplingweight wt5part2 rescale;
   dependent dys12 probit coding=first, mde12 probit coding=first,
             gad12 probit coding=first, pts12 probit coding=first,
             ago12 probit coding=first, pds12 probit coding=first,
             so12  probit coding=first, sp12  probit coding=first;
   independent sex_main nominal, age_grp nominal, country nominal,
               chro_12m nominal, MaritalS nominal, work nominal;
   latent
      Fear continuous, DFactF nominal 2 coding=effect, FClass 2 nominal ,
      Distress continuous, DFactD nominal 2 coding=effect, DClass 2 nominal;

equations
   FClass <- 1 + sex_main + age_grp + country + chro_12m;
   DFactF <- 1 ;
   Fear <- (mF)1|FClass   + (dF)DFactF|FClass   ;
   (0) Fear ;

   pds12 <- 1 +  Fear ;
   ago12 <- 1 + (1) Fear ;
   so12  <- 1 +  Fear ;
   sp12  <- 1 +  Fear ;

   DClass <- 1 + sex_main + age_grp + country + chro_12m + MaritalS + work ;
   DFactD <- 1;
   Distress <- (mD)1|DClass + (dD)DFactD|DClass ;
   (0) Distress ;

   dys12 <- 1 + (1) Distress ;
   mde12 <- 1 + Distress ;
   gad12 <- 1 + Distress ;
   pts12 <- 1 + Distress ;

   (cov)DFactF <-> DFactD | DClass FClass;
   DClass <-> FClass;

    mF[1]=0;    dF[1]=+;
    mF[2]=10;   dF[2]=0;

    mD[1]=0;     dD[1]=+;
    mD[2]=10;    dD[2]=0;

   cov[2]=0; cov[3]=0; cov[4]=0;
```

B Tables and Graphics

Table 1: Selection of number of discrete points per factor

Factor	points	logLikelihood	BIC	AIC	AIC3	Npar
Fear	1	-3437.8	6939.1	6889.5	6896.5	7
	2	-3277.7	6637.2	6573.5	6582.5	9
	3	-3274.3	6648.5	6570.6	6581.6	11
	4	-3273.6	6665.3	6573.2	6586.2	13
Distress	1	-3097.3	6258.1	6208.6	6215.6	7
	2	-2764.6	5610.9	5547.2	5556.2	9
	3	-2764.5	5628.9	5551.0	5562.0	11
	4	-2764.5	5647.0	5555.0	5568.0	13

Table 2: Measurement Invariance and FMM. Fear Factor

		LogL	BIC	AIC	AIC3	Npar
Basic model		-3277.7	6637.2	6573.5	6582.5	9
Gender	Inv	-3223.2	6555.3	6470.3	6482.3	12
	Free Intrc.	-3221.5	6579.3	6473.1	6488.1	15
	Free Intrc.&load.	-3221.0	6605.5	6478.1	6496.1	18
Age	Inv.	-3244.2	6679.2	6530.4	6551.4	21
	Free Intrc.	-3231.1	6761.9	6528.1	6561.1	33
	Free Intrc.&load.	-3226.7	6862.0	6543.3	6588.3	45
Country	Inv.	-3245.1	6708.1	6538.1	6562.1	24
	Free Intrc.	-3238.3	6830.8	6554.6	6593.6	39
	Free Intrc.&load.	-3234.6	6959.6	6577.2	6631.2	54
Chronic Condition	Inv.	-3270.8	6650.6	6565.7	6577.7	12
	Free Intrc.	-3266.0	6668.1	6561.9	6576.9	15
	Free Intrc.&load.	-3264.6	6692.7	6565.2	6583.2	18
Marital Status	Inv.	-3274.1	6684.4	6578.2	6593.2	15
	Free Intrc.	-3262.9	6716.6	6567.9	6588.9	21
	Free Intrc.&load.	-3260.2	6765.7	6574.5	6601.5	27
Work status	Inv.	-3276.9	6662.7	6577.8	6589.8	12
	Free Intrc.	-3275.7	6687.6	6581.4	6596.4	15
	Free Intrc.&load.	-3273.7	6710.9	6583.4	6601.4	18
FMM	ill/healthy classes	-3273.6	6638.0	6567.2	6577.2	10
	+ class covariates[a]	-3145.2	6499.2	6336.4	6359.4	23

[a] Gender, Age, Country, Chronic condition

Table 3: Measurement Invariance and FMM. Distress Factor

		LogL	**BIC**	**AIC**	**AIC3**	**Npar**
Basic model		-2764.6	5610.9	5547.2	5556.2	9
Gender	Inv.	-2735.2	5579.4	5494.4	5506.4	12
	Free Intrc.	-2729.3	5594.8	5488.6	5503.6	15
	Free Intrc.&load.	-2725.1	5613.7	5486.3	5504.3	18
Age	Inv.	-2733.1	5656.8	5508.1	5529.1	21
	Free Intrc.	-2725.3	5750.2	5516.5	5549.5	33
	Free Intrc.&load.	-2720.2	5849.1	5530.4	5575.4	45
Country	Inv.	-2716.7	5651.3	5481.4	5505.4	24
	Free Intrc.	-2712.0	5778.1	5501.9	5540.9	39
	Free Intrc.&load.	-2708.0	5906.4	5524.0	5578.0	54
Chronic Condition	Inv.	-2746.3	5601.5	5516.6	5528.6	12
	Free Intrc.	-2744.6	5625.4	5519.2	5534.2	15
	Free Intrc.&load.	-2742.7	5648.9	5521.4	5539.4	18
Marital Status	Inv.	-2745.1	5626.5	5520.2	5535.2	15
	Free Intrc.	-2739.3	5669.3	5520.6	5541.6	21
	Free Intrc.&load.	-2734.9	5714.9	5523.7	5550.7	27
Work status	Inv.	-2757.7	5624.4	5539.4	5551.4	12
	Free Intrc.	-2754.2	5644.5	5538.3	5553.3	15
	Free Intrc.&load.	-2752.8	5669.0	5541.5	5559.5	18
FMM	ill/healthy classes	-2764.5	5619.8	5549.0	5559.6	10
	+ class covariates[a]	-2653.1	5524.2	5354.3	5378.3	24

[a] Gender, Age, Country, Chronic condition, Marital Status, Work.

Table 4: Final model estimated Parameters

	DISTRESS			FEAR	
Measurement Parameters					
	Intercepts	**Loadings**		**Intercepts**	**Loadings**
dys	1.31 (0.20)	1	ago	1.67 (0.23)	1
mde	0.25 (0.21)	1.16 (0.33)	pds	1.56 (0.16)	0.78 (0.15)
gad	1.47 (0.20)	0.94 (0.29)	so	1.24 (0.14)	0.60 (0.12)
pts	1.32 (0.08)	0.20 (0.04)	sp	0.51 (0.13)	0.54 (0.12)
Structural Parameters					
	Allocation	**Probability**		**Allocation**	**Probability**
Class1 point1	-0.66 (0.16)	0.86 (0.05)		-1.02 (0.16)	0.03 (0.01)
Class1 point2	0.66 (0.16)	0.14 (0.05)		1.02 (0.16)	0.97 (0.01)
Class2 point	10	1		10	1
Class1 Size	0.13 (0.02)			0.34 (0.08)	
Class2 Size	0.87 (0.02)			0.66 (0.08)	
Class Covariates[a]					
Intercept	-3.24 (0.49)			-1.05 (0.53)	
Gender					
Male	-0.13 (0.13)			-0.61 (0.12)	
Female	0.13 (0.13)			0.61 (0.12)	
Age					
18-24	0.04 (0.23)			0.88 (0.34)	
25-34	0.38 (0.15)			-0.09 (0.21)	
35-49	0.01 (0.16)			0.54 (0.18)	
50-64	0.15 (0.15)			-0.22 (0.22)	
+65	-0.58 (0.21)			-1.11 (0.28)	
Country					
Belgium	0.18 (0.22)			0.17 (0.37)	
France	0.40 (0.21)			0.52 (0.24)	
Germany	-0.73 (0.15)			0.43 (0.23)	
Italy	-0.30 (0.13)			-0.26 (0.19)	
Netherlands	0.49 (0.17)			-0.38 (0.21)	
Spain	-0.03 (0.17)			-0.48 (0.24)	
Chronic Condition					
Yes	0.26 (0.10)			0.37 (0.17)	
No	-0.26 (0.10)			-0.37 (0.17)	
Marital Status					
Married/Cohab	-0.32 (0.08)				
Prev.Married	0.31 (0.12)				
Never Married	0.02 (0.11)				
Work Status					
Working	0.23 (0.06)				
Not working	-0.23 (0.06)				
Correlation Parameters					
	Factor[b]	**Class**			
	2.78 (0.73)	2.74 (0.75)			

[a] Class coded as dummy with class 2 (healthy) as reference. Covariates used effect coding

[b] Within both ill classes

Table 5: Distress score descriptive by comorbidity pattern disorder

mde	dys	gad	pts	N	mean	min	max
Yes	Yes	Yes	Yes	10	1.31	1.30	1.31
Yes	Yes	Yes	No	27	1.31	1.30	1.31
Yes	Yes	No	Yes	23	1.29	1.22	1.31
Yes	Yes	No	No	138	1.24	1.11	1.31
Yes	No	Yes	Yes	12	1.29	1.20	1.31
Yes	No	Yes	No	78	1.23	1.09	1.31
Yes	No	No	Yes	50	0.85	0.53	1.31
Yes	No	No	No	567	0.72	0.36	1.31
No	Yes	Yes	Yes	1	1.27	1.27	1.27
No	Yes	Yes	No	4	1.20	1.15	1.31
No	Yes	No	Yes	3	0.87	0.75	0.88
No	Yes	No	No	77	0.74	0.46	1.30
No	No	Yes	Yes	8	1.09	0.76	1.27
No	No	Yes	No	56	0.82	0.39	1.31
No	No	No	Yes	107	0.67	0.14	4.94
No	No	No	No	7635	9.26	3.58	9.97

Table 6: Fear score descriptive by comorbidity pattern disorder

ago	pds	so	sp	N	mean	min	max
Yes	Yes	Yes	Yes	6	2.03	2.03	2.03
Yes	Yes	Yes	No	1	2.03	2.03	2.03
Yes	Yes	No	Yes	5	2.03	2.03	2.03
Yes	Yes	No	No	12	1.98	1.92	2.03
Yes	No	Yes	Yes	13	2.00	1.97	2.03
Yes	No	Yes	No	10	1.91	1.72	2.03
Yes	No	No	Yes	29	1.84	1.49	2.03
Yes	No	No	No	34	1.33	0.61	2.01
No	Yes	Yes	Yes	7	2.02	1.98	2.03
No	Yes	Yes	No	7	1.96	1.76	2.02
No	Yes	No	Yes	24	1.46	0.92	2.02
No	Yes	No	No	112	0.94	0.24	1.96
No	No	Yes	Yes	45	1.20	0.46	2.00
No	No	Yes	No	139	0.49	0.09	1.81
No	No	No	Yes	550	0.32	0.05	1.73
No	No	No	No	7802	6.99	0.27	9.77

Figure 1: Internalising Model

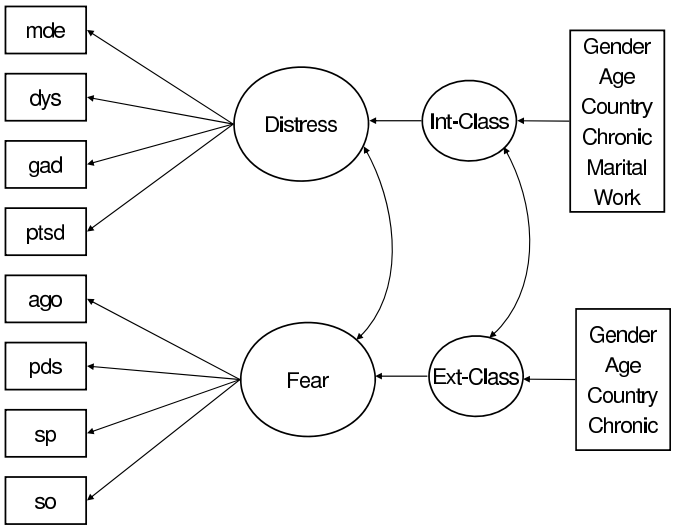


Figure 2: Factor scores histogram, by modal class membership

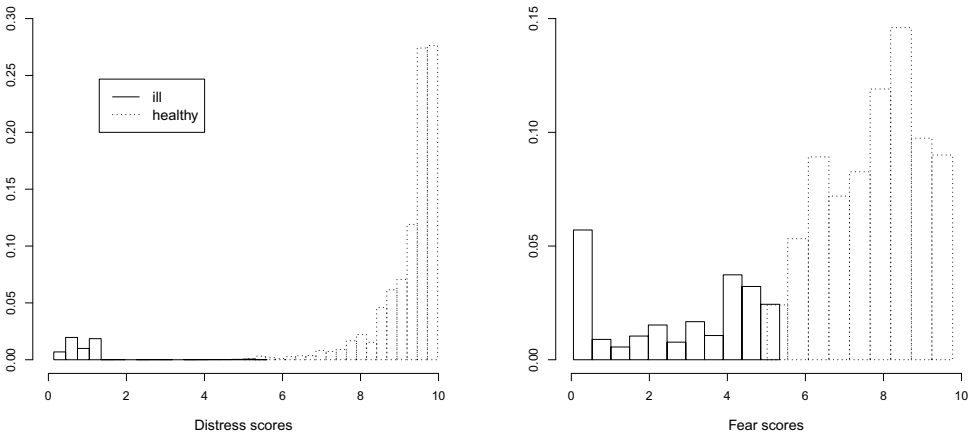
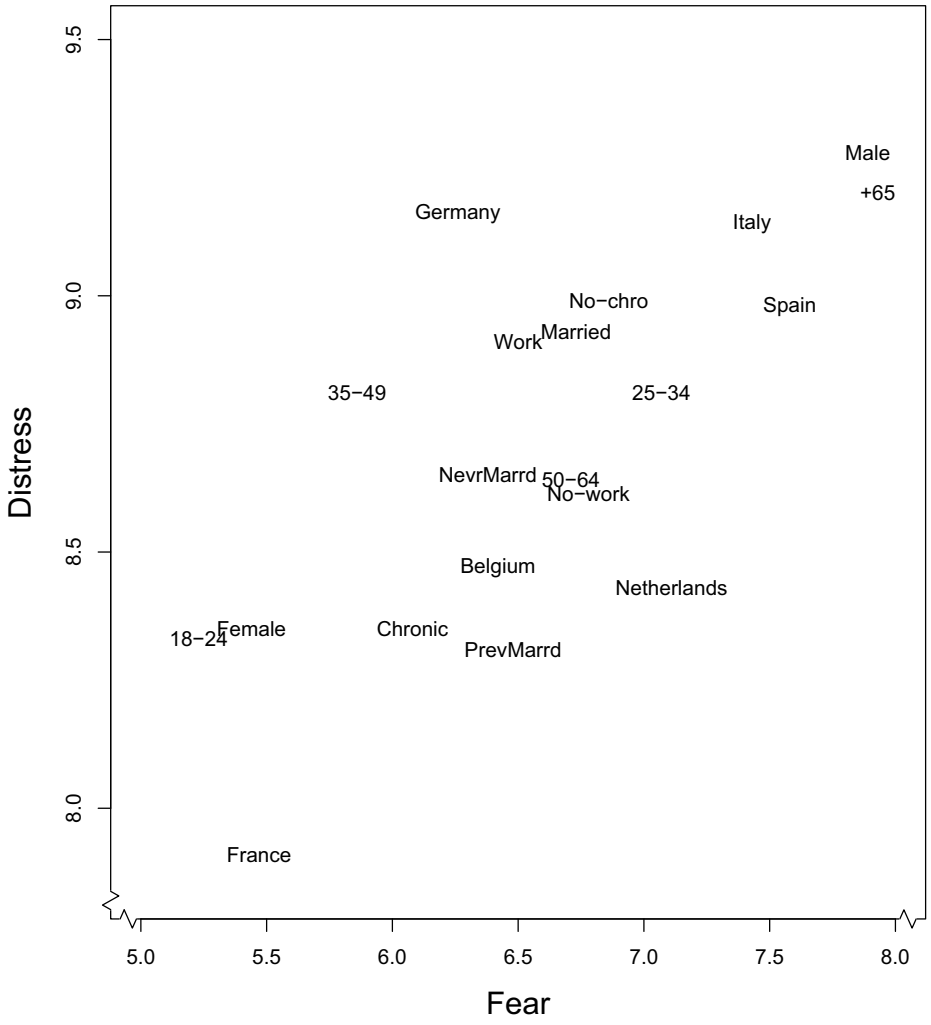


Figure 3: Fear *vs* Distress scores. Mean of covariates' categories.



Article 4

IRT models with censored binary indicators. Application to lifetime mental health comorbidity, assessed in the ESEMeD project.

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TITLE:

IRT models with censored binary indicators. Application to lifetime mental health comorbidity, assessed in the ESEMeD project.

ABSTRACT:

Cross-sectional mixed-age sample with current and retrospective information is the most widespread method for obtaining population representative psychiatric information. With such data gathering designs, lifetime prevalences of the disorders are often reported, but lifetime disorder data is intrinsically censored: individuals who did not report a disorder at the time of the interview are still at risk to suffer from it in the future. In this article we fit an IRT model using a data structure that takes into account censorship (censorship model). An IRT model has been successfully fitted with 12-months disorder. The main purpose is to extend it correctly to lifetime data. This model is compared with the same IRT model but ignoring data censorship (non-censorship model). The proposed censorship model yielded unbiased estimates of prevalences and comorbidities (under model assumptions), while the non-censorship model led to underestimation of prevalences and overestimation of (good) mental health states. Nevertheless, the censorship-model estimations could be biased when disorders show skewed age-of-onset distribution, with very different risk of onset disorder at different ages. An IRT censorship model was fitted with finite mixtures, distinguishing mentally healthy and ill subpopulations, on a representative European sample (ESEMeD), providing individual latent scores that can be interpreted as predisposition to disorders.

KEY WORDS:

Mental health epidemiology ; Psychiatric comorbidity; Internalising disorders ; Item response theory; disorder diathesis; missing data

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Background and aims

The prevalence of a disease in a population is defined as the percentage of diseased subjects who were diagnosed at any time during a certain time span. Due to the relapsing nature of mental disorders, a very informative prevalence measure in psychiatric epidemiology is the lifetime prevalence, which is defined as the proportion of individuals suffering form a disorder at any time during their lives. This measure encompasses very general information about the disorder: proportion of the population fulfilling diagnostic criteria, regardless of the age of onset, duration, severity an (unmeasured) environmental factors.

Prevalence information on psychiatric disorders is very often gathered from cross-sectional samples, like ESEMeD (Alonso et al. 2004c) or NCS-R (Kessler and Merikangas 2004). Sampling designs typically include representative individuals of all ages, and lifetime disorder information is collected retrospectively. Lifetime prevalences entail an important drawback: they are only perfectly measured when observed within the individuals' entire life span, which is unavailable. Cross-sectional designs have to serve as the basis to estimate lifetime prevalence. In this fashion, lifetime disorder information from cross-sectional samples is inevitably censored because no information on the appearance of mental disorders is available beyond the time of the interview.

Even though the data is clearly right-censored, most epidemiological studies about lifetime disorders have been conducted as if complete data were obtained. Lifetime estimation has been often done by assuming that the individual lifetime is equal to the age at the time of the interview (Alonso et al. 2004a;Herman et al. 2009;Khan et al. 2005;Kovess-Masfety et al. 2007;Wells et al. 2009). Such decision inevitably leads to biased prevalence estimates, as lifetime prevalence is underestimated. Recently, a specialized statistical model have been used to take into account data censorship: an actuarial survival method to project lifetime risk at a certain age (e.g. 75 years), which was considered the age limit for lifetime prevalence assessment (Bonnewyn et al. 2007;Karam et al. 2008;Kessler et al. 2005;Kessler et al. 2007;Lee et al. 2007;Medina-Mora et al. 2007;Merikangas et al. 2007;Stein et al. 2008). Even though they improved the prevalence estimation by accounting for data censorship, they fitted independent survival functions for each disorder, paying no attention to comorbidity issues (i.e. disorder co-occurrence on the same person).

In spite of the valuable contribution of works from a survival analysis perspective, the estimation of lifetime comorbidity is so important a part in psychiatry research that a method for accounting for disorder co-occurrence is a must. Lifetime comorbidity conditions are present whenever the same person has suffered from two or more disorders during his life, disregarding whether or not the disorders overlap in time. In this instance, cross-sectional implicit censorship produces even more biased comorbidity estimates biases if the prevalence estimations are biased (Kraemer et al. 2006).

A reasonable solution to this kind of estimation problems is implementing a model of disorder relationships. Conceptual models for psychiatric research generally assume that individuals have a non-observable psychic-state that determines their vulnerability to develop psychopathology in response to a sufficiently stressful environment. This vulnerability is known as diathesis (Clark 2005), which is rather chronic in nature (Clark and Watson 1991). The diathesis is intrinsic to the individual and has lifetime implication. For instance, an internalising mental health dimension is a consolidated construct in psychiatry research, which explains the presence and association among mood and anxiety disorders (Cerda et al. 2008). This factor structure has been tested on a variety of datasets (Cerda et al. 2008;Krueger and Finger 2001;McGlinchey and Zimmerman 2007; Almansa et al. submitted-a; Almansa et al. submitted-b) obtaining similar results (measurement parameters) in different target populations, irrespective of the time period considered (lifetime or 12-month disorders). This latent internalising factor serves as continuous estimator of the unobserved internalising-disorders' diathesis, which produces in the individuals the presence of internalising disorders at any time in their lives.

A potential caveat comes from the very essence of psychiatric disorder diagnoses. The object of study of psychiatric epidemiology compels that the model must rely on categorical information. In fact, this is not necessarily a problem, given that a family of methods dealing with categorical information to estimate continuous factors has been developing from Psychometrics since 40 years ago. Item Response Theory (IRT) models provide the statistical framework to relate binary observed indicators with unobserved continuous factor of interest (De Boeck 2004). By means of IRT models, it is possible to relate a continuous, dimensional unobservable trait (for instance internalising diathesis) with observable categorical outcomes (such as internalising disorders or symptoms). Moreover, using finite mixture models, the IRT framework permits incorporating qualitative distinctions within the population (Davier and Rost

2007). In this fashion, the statistical model can be adapted according to the theoretical considerations about the relationship between the latent trait and the disorders for each subpopulation. For instance, an internalising model might consider that there must be an important discontinuity in diathesis scores between individuals suffering from any disorder and others who do not. This is similar to the assumption that there is discontinuity between ill and healthy subpopulations. This assumption can be included into the IRT framework by allowing for the existence of two population classes, each showing a different variant of the model. A convenient advantage of such an approximation is that class sizes can be estimated. Notice that the model makes no assumption on the size of classes, but only states different forms of the model within each class, which in turn provides an estimate of the class size.

Thus, finite mixture IRT models make available a statistical framework to deal with comorbid prevalence estimation from a continuous diathesis/severity perspective of psychiatric disorders. Estimation is conducted on categorical data, which is frequently found in clinical or epidemiological applications. Censorship issues emerging from lifetime prevalence estimation with cross-sectional data can also be handled by imposing certain restrictions on the model and introducing the data in the appropriate way.

In this article we fit an IRT model in which the binary indicators of the latent dimension are censored. Our main purpose is to propose a statistical multivariate model (IRT-type) to accurately estimate lifetime prevalences and comorbidities, taking into account the censorship, and considering the dimensional internalising construct. That is, to extend the IRT model that has been successfully fitted on 12-month data, in order to be applicable to lifetime data. Two additional objectives are (1) incorporating a qualitative distinction between ill and healthy populations using latent classes and (2) quantitatively estimate levels of mental-health diathesis. Results from our models will be compared to an equivalent IRT model that does not account for the censorship in order to assess the model ability to produce correct estimates.

Statistical model description

Model

In this study, we used an IRT-type model (De Boeck 2004;Hambleton et al. 1991), in which the latent factor mean and variance differ according to latent class membership, resulting in a mixture IRT model (Davier and Rost 2007). Let y_{ij} be the observed realization of a disorder $j = 1,2,3,...,k$ for individual i, so that $y_{ij} = 1$ whenever the disorder is present and 0 otherwise. Let θ be the individual score on the latent variable and x the categorical variable indicating latent class membership. The probability of expression of a disorder, conditioned on a latent variable (in our case, disorder diathesis) and a latent class can be expressed as

$$\text{logit}\left(\hat{P}\left(y_{ij} = 1 \middle| \theta, x\right)\right) = \alpha_j + \lambda_j \theta_{i|x} \quad (1)$$

where α_j and λ_j parameters indicate disorder intercept and factor loadings, respectively. Notice that eq. (1) is the expression of the IRT 2-parameter logistic model. It is further assumed that the conditional distribution of the latent variable on latent classes is

$$\theta | x \sim N(\mu_x + \boldsymbol{\beta}_x \mathbf{z}^F, \sigma_x) \quad (2)$$

In so doing, the mean and the variance of the latent variable depend on class membership. Additionally, factor mean depends on a vector of factor covariates $\mathbf{z}^F$ indicating differences in θ across socio-demographic groups. Covariates $\mathbf{z}^F$ are weighted by regression parameters $\boldsymbol{\beta}_x$, estimated from the regression of θ on $\mathbf{z}^F$ within each class.

Latent class distribution is modelled using

$$\text{logit}\left(\hat{P}\left(x = 1\right)\right) = \tau + \boldsymbol{\gamma} \mathbf{z}^C \quad (3)$$

which is estimated from class covariates $\mathbf{z}^C$ and $\tau, \boldsymbol{\gamma}$ are regression intercept and slope parameters.

Latent variable models generally assume local independence among disorders, that is, disorders are independent when conditioned on the latent variables and classes. Thus, the probability that a disorder pattern $\mathbf{Y}$ takes the values $\mathbf{y}$ is given by

$$P\left(\mathbf{Y}=\mathbf{y}\middle|\theta,x\right)=\prod_{j=1}^{k}P\left(Y_j=y_j\middle|\theta,x\right) \quad (4)$$

In our implementation, the latent classes defined "ill" and "healthy" subpopulations and thus $x=\left\{1,2\right\}$. The existence of healthy and non-healthy subpopulations is a credible assumption because mental disorders do not affect the entire population (Almansa et al. submitted-b). The model was parameterized in a way that high scores imply healthy mental health levels. Thus, (2) was $N(0,1)$ for Class 1 (ill) while Class 2 (healthy) was distributed $N(10,0)$, so that class 2 denoted a homogeneous group of healthy individuals (where homogeneous denotes no variability in their health status, and healthy denotes having a high factor score). This parameterization allows this class to be clearly different from the class of ill subjects, whose members are heterogeneous, (i.e. they do exhibit variability).

It follows that the final model combining the two-class model is an IRT-type model for Class 1 (mentally ill subjects) whereas for individuals assigned to Class 2 the factor implies a near-zero probability of endorsing any disorder. Note that class membership is estimated: latent class is an unobserved categorical variable. Such a model structure has been successfully applied to model comorbidity in 12-month disorder data (Almansa et al. submitted-b).

For class 1 (ill) the factor mean can vary according to factor covariates $\mathbf{z}^F$, indicating differences in mental health diathesis across socio-demographic groups. For class 2 factor mean was always 10 (no effect covariate was considered). Class covariates $\mathbf{z}^C$ predict differences in the ill/healthy class membership probability.

Equation (1) models observed variables conditioned on latent variables: $Y\left|\theta,x\right.$. Consequently, factor scores conditioned on latent class $\theta\left|Y,x\right.$ – or, perhaps more interestingly, marginally with respect to latent classes $\theta\left|Y\right.$ – can be computed from the factor posterior distribution, for example, through the Expected A Posteriori (EAP) method (Vermunt and Magidson 2005).

Data structure

As abovementioned, lifetime disorders are binary variables, indicating whether the individual suffered from the disorder any time in his/her life, regardless of the age of onset or severity. This involves further modelling complications when the model is applied on a cross-sectional sample with retrospective disorder information, because individuals might or might not meet the criteria up to the time of the interview. There is no concern about individuals having met a disorder at the time of the interview: once the criteria are met, it is of no importance whether the disorder would reappear in the future. But the only information about individuals who did not report of a disorder is that they did not experience the disorder until the age of interview. These individuals are still at risk to suffer disorders in their remaining life. Data gathering design determine the available information: disorder data is dichotomous but, non-disorder information is right-censored and therefore incomplete. Thus, it is necessary to introduce the data in a way that considers the actual amount of sample exposure for the observed events.

To account for censorship, all the available disorder information can be introduced into the model as a binomial-type data, indicating the number of “trials” and “events”. Whenever a disorder was observed in an individual, the number of “events” and “trials” were both coded with the value 1. In the case of individuals without a disorder, all available information is the time of exposure during which they have not experienced the disorder. In such cases, the number of “events” is zero and number of “trials” can be imputed with a value representing the proportion of lifetime during which the disorder has not been observed. It is necessary to set an age-limit value, for example the maximum age of onset disorder found within the sample. Each disorder, then, has its own age-limit. This age-limit selection has the advantage of adjusting the exposure period to a reasonable time, in which the disorder may appear if the individuals have a level of diathesis enough towards the disorders. Disorder exposure (“trials”) for individuals without an observed specific disorder and older than the corresponding age-limit, will be coded with a value of 1, implying that once individuals cross the age-limit without been observed a disorder, they will not endorse the disorder for sure: they are not censored as they have no diathesis towards this disorder. Table 5 shows the disorders’ age-limits. Thus, a 35 year person at the time of the interview who did not fulfil the criteria for major depression lifetime disorder had 0 “events” and 35/86 = 0.41 “trials” in the major depression variable.

Prevalence estimations

Apart from testing a conceptual psychiatric construct and computing mental health levels (factor scores), the model described in (1) to (3) can also be used to estimate lifetime prevalences.

The prevalences of lifetime disorders can be estimated as a marginal probability. Let be w_i the individuals' sample weight:

$$\hat{P}\left(y_j = 1\right) = N^{-1}\sum_{i=1}^{N} w_i \left\{ \begin{array}{r} \int \hat{P}\left(y_{ij} = 1 \middle| \theta, x = 1\right) f\left(\theta \middle| x = 1, \mathbf{z}_i^F\right) d\theta \cdot \hat{P}\left(x = 1 \middle| \mathbf{z}_i^C\right) + \\ + \hat{P}\left(y_{ij} = 1 \middle| \theta = 10, x = 2\right) \hat{P}\left(x = 2 \middle| \mathbf{z}_i^C\right) \end{array} \right\} \quad (5)$$

The latent class distribution (i.e. class sizes) is computed as follows:

$$\hat{P}\left(x\right) = N^{-1}\sum_{i=1}^{N} w_i \hat{P}\left(x \middle| \mathbf{z}_i^C\right) \quad (6)$$

And $\hat{P}\left(x \middle| z_i^C\right)$ is computed from $\tau, \boldsymbol{\gamma}$ parameters in equation (3). Standard error estimates can be computed using the delta method (Agresti 2002).

Other type of prevalences can be also estimated, for instance, prevalence conditional on class membership. In our two-class model, these prevalences would take the form:

$$\hat{P}\left(y_j = 1 \middle| x = 1\right) = \frac{N^{-1}\sum_{i=1}^{N} w_i \int \hat{P}\left(y_{ij} = 1 \middle| \theta, x = 1\right) f\left(\theta \middle| x = 1, \mathbf{z}_i^F\right) d\theta \cdot \hat{P}\left(x = 1 \middle| \mathbf{z}_i^C\right)}{\hat{P}\left(x = 1\right)} \quad (7)$$

for class 1, whereas prevalence in class 2 could be computed using

$$\hat{P}\left(y_j = 1 \middle| x = 2\right) = \frac{N^{-1}\sum_{i=1}^{N} w_i \hat{P}\left(y_{ij} = 1 \middle| \theta = 10, x = 2\right) \hat{P}\left(x = 2 \middle| \mathbf{z}_i^C\right)}{\hat{P}\left(x = 2\right)} \quad (8)$$

Comorbidity prevalences between pairs of disorders can also be computed using:

$$\hat{P}\left(y_j = 1, y_{j'} = 1\right) = N^{-1}\sum_{i=1}^{N} w_i \left\{ \begin{array}{r} \int \hat{P}\left(y_{ij} = 1, y_{ij'} = 1 \middle| \theta, x = 1\right) f\left(\theta \middle| x = 1, \mathbf{z}_i^F\right) d\theta \cdot \hat{P}\left(x = 1 \middle| \mathbf{z}_i^C\right) + \\ + \hat{P}\left(y_{ij} = 1, y_{ij'} = 1 \middle| \theta = 10, x = 2\right) \hat{P}\left(x = 2 \middle| \mathbf{z}_i^C\right) \end{array} \right\} \quad (9)$$

Notice that, under the assumption of local independence, the bivariate disorder distribution of a pair of disorders jj' can be expressed as products of their univariate distributions:

$$\hat{P}\left(y_j = 1, y_{j'} = 1 \middle| x, \theta\right) = \hat{P}\left(y_j = 1 \middle| x, \theta\right) \hat{P}\left(y_{j'} = 1 \middle| x, \theta\right) \tag{10}$$

Finally, the proportion of people suffering form at least one lifetime disorder can be computed as 1 minus the probability of having no disorder:

$$\begin{aligned} &\hat{P}\left(y_j = 0, \forall j\right) = \\ &1 - N^{-1} \sum_i w_i \left\{ \begin{array}{r} \int \prod_j \hat{P}\left(y_{ij} = 0 \middle| \theta, x = 1\right) f\left(\theta \middle| x = 1, \mathbf{z}_i^F\right) d\theta \cdot \hat{P}\left(x = 1 \middle| \mathbf{z}_i^C\right) + \\ + \prod_j \hat{P}\left(y_{ij} = 0 \middle| \theta = 10, x = 2\right) \hat{P}\left(x = 2 \middle| \mathbf{z}_i^C\right) \end{array} \right\} \end{aligned} \tag{11}$$

In order to see how prevalences and comorbidities are affected by ignoring data censorship, the sample can be divided in two subsets of complete and censored cases. The complete subset contains all individuals with an observed disorder and individuals without any observed disorder observed at the end of their lives. The incomplete cases are the remaining cases (those where no disorder had been present at the time of the interview). Prevalence of a disorder j can then be computed splitting the sample in those who had complete y_{ij}^C and incomplete y_{ij}^I disorder information, as follows

$$\begin{aligned} \hat{P}\left(y_j = 1\right) &= N^{-1} \sum_{i=1}^N w_i \sum_x \int \hat{P}\left(y_{ij} = 1 \middle| \theta, x\right) f\left(\theta \middle| x\right) d\theta \cdot \hat{P}\left(x\right) = \\ &= N^{-1} \left\{ \begin{array}{l} \sum_{i=1}^N w_i \sum_x \int \hat{P}\left(y_{ij}^C = 1 \middle| \theta, x\right) f\left(\theta \middle| x\right) d\theta \cdot \hat{P}\left(x\right) + \\ + \sum_{i=1}^N w_i \sum_x \int \hat{P}\left(y_{ij}^I = 1 \middle| \theta, x\right) f\left(\theta \middle| x\right) d\theta \cdot \hat{P}\left(x\right) \end{array} \right\} \end{aligned} \tag{12}$$

As a consequence, when ignoring censorship it is assumed that $\hat{P}\left(y_{ij}^I = 1 \middle| \theta, x\right) = 0$, so the second term of the equation (12) is cancelled, which in turn leads to underestimated prevalences. The amount of bias increases as number of incomplete cases increase (that is, young individuals without a disorder). To take into account censorship we have considered that the incomplete (censored) information follows the same probability distribution as the complete data, instead of a zero-probability, resulting in $\hat{P}\left(y_{ij}^I = 1 \middle| \theta, x\right) \geq 0$.

Similarly, equation (12) could also be modified to estimate comorbidities. Omitting censorship treatment in this case is even more misleading, because a comorbid pattern

probability becomes zero whenever the information of an involved disorder is incomplete.

It is worth noticing that using this data structure is analogous to treating incomplete information as *missing at random* data in full information maximum-likelihood estimation. As a consequence, if the sample is representative and the model is correctly specified, the model will obtain unbiased prevalences estimations (Enders and Bandalos 2001).

Model assumptions

Regarding model assumptions, the IRT model assumes the existence of a constant lifetime underlying diathesis of endorsing an internalising disorder. Moreover, each disorder comorbidity (and covariates) pattern has a unique score (regardless to disorders' age of onset and other unobserved factors). As a consequence, it is assumed that the disorders' age of onset is determined exclusively by environmental factors (non-measured in our data), and its existence depends only on the underlying level of diathesis. Notice that this assumption is nothing but the classical unidimensionality IRT assumption.

Also, it must be assumed that data censorship is non-informative: disorder appearance depends only on the diathesis factor, and the censorship process is not related to the realization of any specific disorder. A second assumption is that for those individuals not reaching the disorders' age-limit, their cause of death is not related to the probability of having a disorder. A final assumption is that the measurement of the mental diathesis is constant over individuals' age, and not affected by any possible period effect (measurement is invariant across time period and age-cohort). Moreover, invariance is assumed in a wider sense: α_j and λ_j parameters do not vary across subpopulations (Lubke et al. 2003;Meredith 1993;Muthen and Asparouhov 2002).

Two final assumptions concern the data gathering design. Firstly, regarding period effect, the model assumes that expected lifetime prevalences are constant over time when conditioning on latent variables and covariates. Finally, the truncation process that created non-eligible sample is not related with the probability of having a disorder. That is, some people that were born within the 100 previous years could not enter in

the sample because they died or were institutionalized before the interview time – but this truncation is not related with probability of disorders.

It is readily seen that while the application of the model require from certain assumptions, some of them are truly related with the model and data structure herein proposed, while the rest are inherent limitations of lifetime data as measured in a retrospective way, and do not depend on the statistical model.

Aplication

ESEMeD Data

The ESEMeD Project was a cross-sectional survey based on a stratified, multi-stage, clustered area probability sample. Individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population was the non-institutionalized adult population (aged 18 years or older) of Belgium, France, Germany, Italy, the Netherlands and Spain, providing data between January 2001 and August 2003. For the present analysis, a representative ESEMeD subsample was used (N=8,796). Mental disorders assessment was based on version 3.0 of the World Health Organization Composite International Diagnostic Interview (CIDI 3.0) (Kessler and Ustun 2004), a fully structured lay administered diagnostic interview that generates diagnoses according to the DSM-IV criteria (American Psychiatric Association 2000). Individuals were weighted to adjust for their population representativeness. A detailed description of the methods and the participants of the ESEMeD project is provided elsewhere (Alonso et al. 2004c). Disorder descriptive analysis of the ESEMeD data can be found in (Alonso et al. 2004b;Alonso et al. 2004a).

The main variables analysed in this article are binary, and they describe whether a mental disorder was present in any time previous to the interview, according to the DSM-IV criteria. The disorders included for this research are: major depression episode (mde), dysthymia (dys), general anxiety disorder (gad), posttraumatic stress disorder (ptsd), agoraphobia with or without panic (ago), specific phobia (sp), social phobia (so), panic disorder (pd).

Analysis

First of all, an independence model was estimated, to serve as basis from which quantify the gain of fit in subsequent models. The independence model assumes that disorders are not related among them.

The internalising factor model was fitted, forcing factor loadings λ_j to be negatively related with disorder probability. That is, high factor scores implying a low probability of endorsing the disorders (low diathesis and high levels of mental health), and low factor scores implying high probability of endorsing disorders. In this way, factor scores can be interpreted in terms of “health”.

As abovementioned, we added latent classes defining healthy and ill populations to the model. An ill class is defined by a zero factor mean (and variance equal to one), and healthy class is degenerated at factor score equal to 10. This two-class structure is known to show improved statistical fit and to describe more accurately the population reality when applied to 12-month disorder prevalence (Almansa et al. submitted-b).

Finally, class covariates were added to better predict the class membership probability, and factor covariates were also explored to determine if diathesis differences could exist within the ill class. Covariates were selected among those variables expected to be more stable across time, like gender, year of birth and country (nevertheless, we assumed that sampled individuals are representative of their current country population).

Once a final model had been chosen, EAP factor scores and their standard deviation were estimated for each individual (Vermunt and Magidson 2005). This scoring method provides a measure in a continuous scale of the internalising lifetime diathesis. Disorder lifetime prevalences and bivariate comorbidities were estimated as marginal probabilities.

Model comparison was mainly made using the Bayesian information criterion (BIC). We also examined other comparative fit indexes for decision-making: Akaike's information criterion (AIC and AIC3 - an AIC modification that uses a more conservative penalty factor). Using these indexes it is possible to choose the best-fitting model among a set of nested or non-nested alternative models (Raftery 1995). Alternatively, model of fit was assessed using bivariate residuals (BVR). The BVR reflects any residual association among pairs of observed variables after model estimation. Given a model with satisfactory fit, it is expected that no substantial amount of association between every pair of variables is left (Vermunt and Magidson 2005).

We also compared results from our final model with the results (factor scores and prevalences) from an equivalent model, in which disorder data were included without taking into account the no-disorder censorship (see eq (12)). Thus, the coding for the disorder variables was 1 in case of having the lifetime disorder and 0 when the disorder was not detected before the interview time. This comparison will highlight the effect of not considering the data censorship, as has been often done in epidemiological studies. It was also obtained for each disorder the projected lifetime risk as of age 75 years, estimated using the survival actuarial method implemented in SAS 9.1 software.

In order to obtain unbiased estimates and standard errors, the complex sample design was taken into account in all analysis by using linearization variance estimator (Alonso et al. 2004c;Vermunt and Magidson 2005). All IRT models were estimated via Maximum Likelihood, with 150 different start values to avoid a local-optimum solution, using the software LatentGold version 4.5.

RESULTS

The internalising factor model fitted much better the data than the model in which disorders were independent (Table 1), supporting the adequacy of the dimensional internalising structure. The addition of a latent class variable defining healthy and ill subpopulations led to a large goodness-of-fit improvement (better BIC and AIC values as well as lower BVR). The socio-demographic covariates gender, country and birth-year were found to be predictors of class membership. They were also severity-diathesis predictors, that is, they had an effect on the factor mean within class ill class. Although these factor covariates did not decrease BIC value, they showed better fit according to the AIC indices and were deemed to improve model interpretation. Accordingly, the chosen final model (last model in Table 1) used an internalising factor and a latent class variable to define the ill and healthy subpopulations. Gender, country and birth-year were selected as class covariates, and also as mean-factor predictors within the ill class. Figure 1 shows the structure of the final model and Table 2 its parameter estimates.

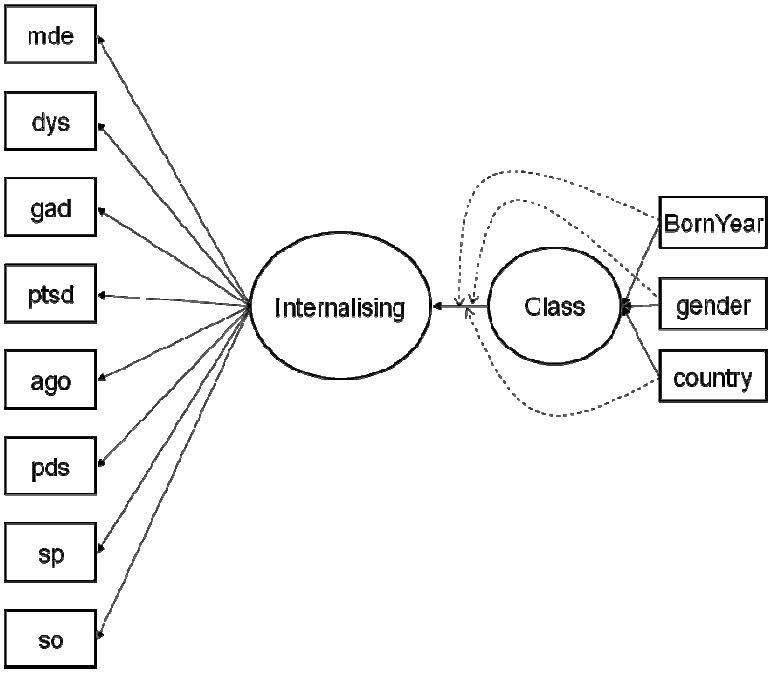

Figure 1. Final Model structure

Dotted lines indicate factor covariate effect within class 1 (ill).

Table 1. Goodness of fit indices of models with censored data.

Model		logL	BIC	AIC	AIC3	Npar
Independence		-10592.4	21257.5	21200.8	21208.8	8
1 Factor		-9616.9	19379.1	19265.8	19281.8	16
1 Factor with Classes		-9590.2	19334.8	19214.4	19231.4	17
Adding Covariates						
Class	*Factor*					
Gender		-9511.6	19186.6	19059.1	19077.1	18
Gender+country		-9393.1	18995.0	18832.2	18855.2	23
Gender+country+BirthYear		-9286.8	18809.8	18625.6	18651.6	26
Gender+country+BirthYear	Gender	-9282.2	18809.5	18618.3	18645.3	27
Gender+country+BirthYear	Country	-9267.6	18816.8	18597.3	18628.3	31
Gender+country+BirthYear	BornYear	-9276.5	18816.3	18610.9	18639.9	29
Gender+country+BirthYear	Gender+Country +BirthYear	-9255.4	18828.7	18580.8	18615.8	35

Males showed lower probability to belong to the ill class compared to females, and females had also higher diathesis within ill class. Italy and Spain had also significantly lower ill-class proportions, while France had higher ill-class proportion. The individuals' year of birth showed an increasing ill-class membership probability. Regarding the factor covariates, France and The Netherlands had the lowest internalising scores within ill class, while Germany and Spain showed the highest values on this class. An interesting age-cohort effect was found: scores decreased as the year of birth increase within ill individuals; the oldest group not only showed lower proportions of ill individuals, but also the lower levels of diathesis. Conversely, the youngest group had parameters indicating higher proportion of ill individuals, with higher diathesis levels.

According to the BVR indices the final model explained most of the disorder associations, although certain disorders were not totally explained (Table 3). Largest BVR's corresponds to *mde* with *dys* (80.8) and *sp* with *so* (20.7). However, these values are much smaller than the BVR's under the independence assumption – 774.6 and 279.2 respectively.

Most prevalent lifetime disorders from our final model were major depression and specific phobia. It was estimated that 20.4% of the population suffered from *mde* at some moment in their lives and 12.9% suffered from *sp* (Table 4). Nearly half of the sample (47%) belonged to the healthy class, in which for sure they do not endorse any disorder (Table 5). Within the ill class, 38.4% of them suffered from *mde*, and 24.3% from specific phobia. The estimated prevalence of any internalising lifetime disorder was 32.7% (computed using equation (11)).

Table 2. Parameter Estimates of the IRT final model. Standard errors in parenthesis.

Measurement Parameters

	Intercept	Factor Loading
Dysthymia	-2.18 (0.23)	-1.08 (0.20)
Major Depression	-0.60 (0.17)	-1.05 (0.16)
PostTraumatic Stress	-2.71 (0.21)	-1.04 (0.16)
General Anxiety Disorder	-3.14 (0.28)	-1.48 (0.19)
Agoraphobia	-4.79 (0.48)	-1.87 (0.29)
Panic disorder	-3.73 (0.22)	-1.38 (0.16)
Social Phobia	-3.25 (0.25)	-1.25 (0.19)
Specific Phobia	-1.24 (0.11)	-0.61 (0.09)

Covariate parameters

Class [1]		Factor [2]	
Intercept	0.16 (0.19)	Intercept	
		Class 1	0
		Class 2	10
Gender		Gender	
Male	-0.48 (0.10)	Male	0.13 (0.06)
Female	0.48 (0.10)	Female	-0.13 (0.06)
Country		Country	
Belgium	0.14 (0.24)	Belgium	0.03 (0.11)
France	0.72 (0.17)	France	-0.31 (0.08)
Germany	-0.04 (0.25)	Germany	0.26 (0.15)
Italy	-0.52 (0.16)	Italy	0.01 (0.11)
Netherlands	0.02 (0.18)	Netherlands	-0.23 (0.11)
Spain	-0.32 (0.17)	Spain	0.24 (0.10)
Birth Year		Birth Year	
→1934	-1.01 (0.23)	→1934	0.33 (0.16)
1935-64	0.04 (0.17)	1935-64	0.08 (0.08)
1965-74	0.00 (0.18)	1965-74	-0.22 (0.09)
1975→	0.97 (0.39)	1975→	-0.19 (0.16)

[1] Class 2 (healthy) as reference.

[2] Covariates modify factor mean within ill class (Class 1).

Table 3. Bivariate residuals from independence (upper triangular) and final model (lower triangular).

	dys	mde	ptsd	gad	ago	pds	so	sp
dys	.	774.6	170.2	252.9	72.6	57.9	40.0	58.9
mde	80.8	.	259.6	460.9	118.8	221.2	142.5	185.9
ptsd	3.6	6.4	.	114.3	28.6	52.4	82.0	112.4
gad	3.5	18.4	0.0	.	93.4	142.4	128.9	62.6
ago	1.1	0.9	3.1	2.3	.	443.4	252.7	242.8
pds	2.2	3.1	0.5	0.0	13.3	.	96.0	119.2
so	8.2	2.4	0.1	0.5	3.0	0.4	.	279.2
sp	6.4	3.5	1.3	3.5	17.7	1.6	20.7	.

dys: dysthymia, mde: major depression episode, gad: general anxiety disorder, ptsd: posttraumatic stress disorder, ago: agoraphobia with or without panic, pd: panic disorder, sp: specific phobia, so: social phobia.

Table 4. Observed, No-censoring model and Actuarial-survival estimated prevalences.

	Observed			No-censorship model		Actuarial survival*
	N	%	SE	%	SE	%
Dysthymia	958	4.4	0.21	4.4	0.21	7.6
Major Depression	2987	13.4	0.37	13.4	0.37	20.3
PostTraumatic Stress	442	2.6	0.20	2.6	0.19	4.1
Genear Anxiety Disorder	556	2.8	0.20	2.8	0.20	4.3
Agoraphobia	176	1.2	0.14	1.2	0.14	1.4
Panic disorder	388	1.8	0.13	1.8	0.13	2.5
Social Phobia	386	2.8	0.24	2.8	0.24	3.0
Specific Phobia	945	8.3	0.43	8.3	0.43	8.7

* Projected Lifetime Risk at Age 75 Years.

Table 5. Estimated prevalences in the IRT Final Model, by classes.

		Final model		Class 1 (53.0%)		Class 2 (47.0%)	
	Age-Limit	%	SE	%	SE	%	SE
Dysthymia	81	7.7	0.35	14.5	1.54	0.0	0.00
Major Depression	86	20.4	0.54	38.4	3.44	0.0	0.00
PostTraumatic Stress	89	5.0	0.37	9.5	1.08	0.0	0.00
Genear Anxiety Disorder	79	4.8	0.35	9.1	1.07	0.0	0.00
Agoraphobia	75	2.0	0.24	3.7	0.55	0.0	0.00
Panic disorder	70	2.8	0.21	5.3	0.62	0.0	0.00
Social Phobia	56[a]	3.8[b]	0.31	7.1	0.90	0.0	0.00
Specific Phobia	75[a]	12.9[b]	0.66	24.3	1.86	0.1	0.13

[a] Robust age-limit (age-of-onset 99th percentile): 43 for social phobia and 42 for specific phobia.
[b] Estimations with the robust age-limit (99th percentile): 3.3% for social phobia and 9.5% for specific phobia.

Estimated scores distribution show that a middle class could exist (Figure 2), although this hypothesis is shadowed by the low precision in this middle support scores (Figure 3). A 3-class model was discarded for the sake of parsimony, because it led to no important gain in the goodness of fit, two of the three classes had very close factor means, and it sometimes led to improper estimated (like infinite standard error). Anyway, this model uncertainty for middle diathesis-level led to a limited class-discrimination capacity: a 25.1% of miss-classification is expected when assigning each individual to their most likely class.

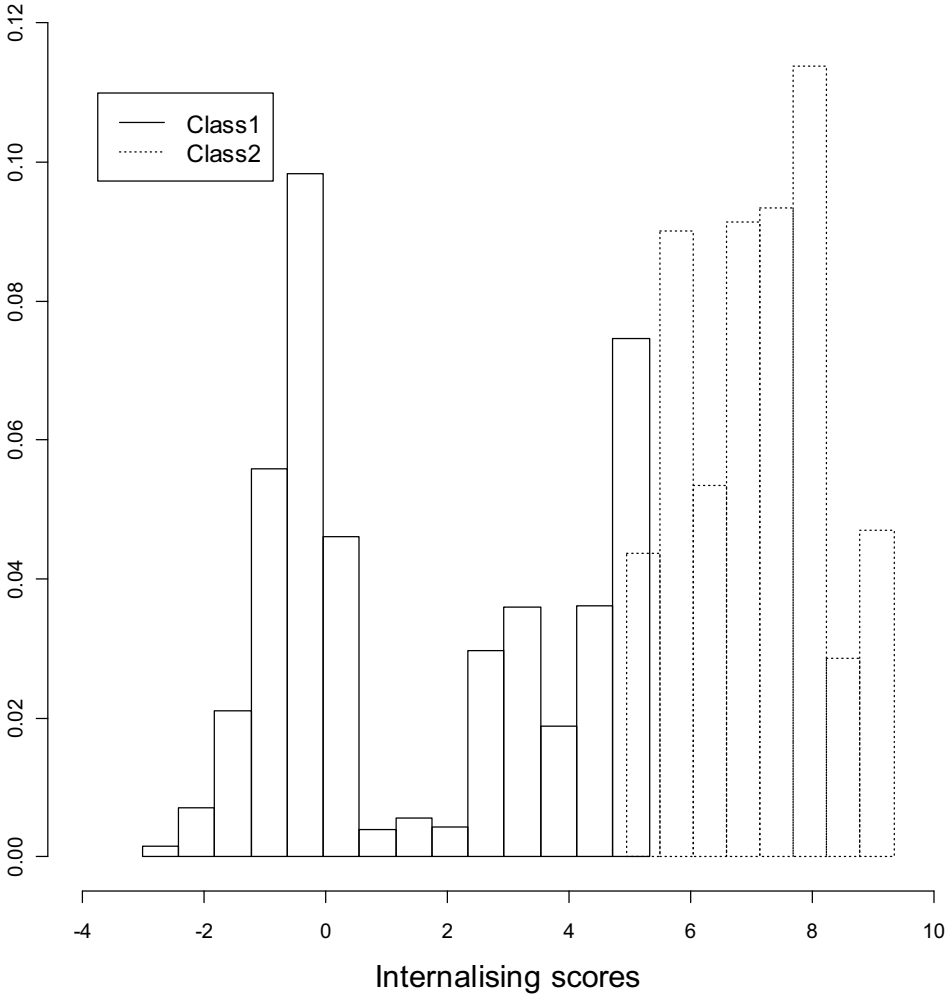

Figure 2. Histogram of estimated scores, stratified by class membership (modal assignment)

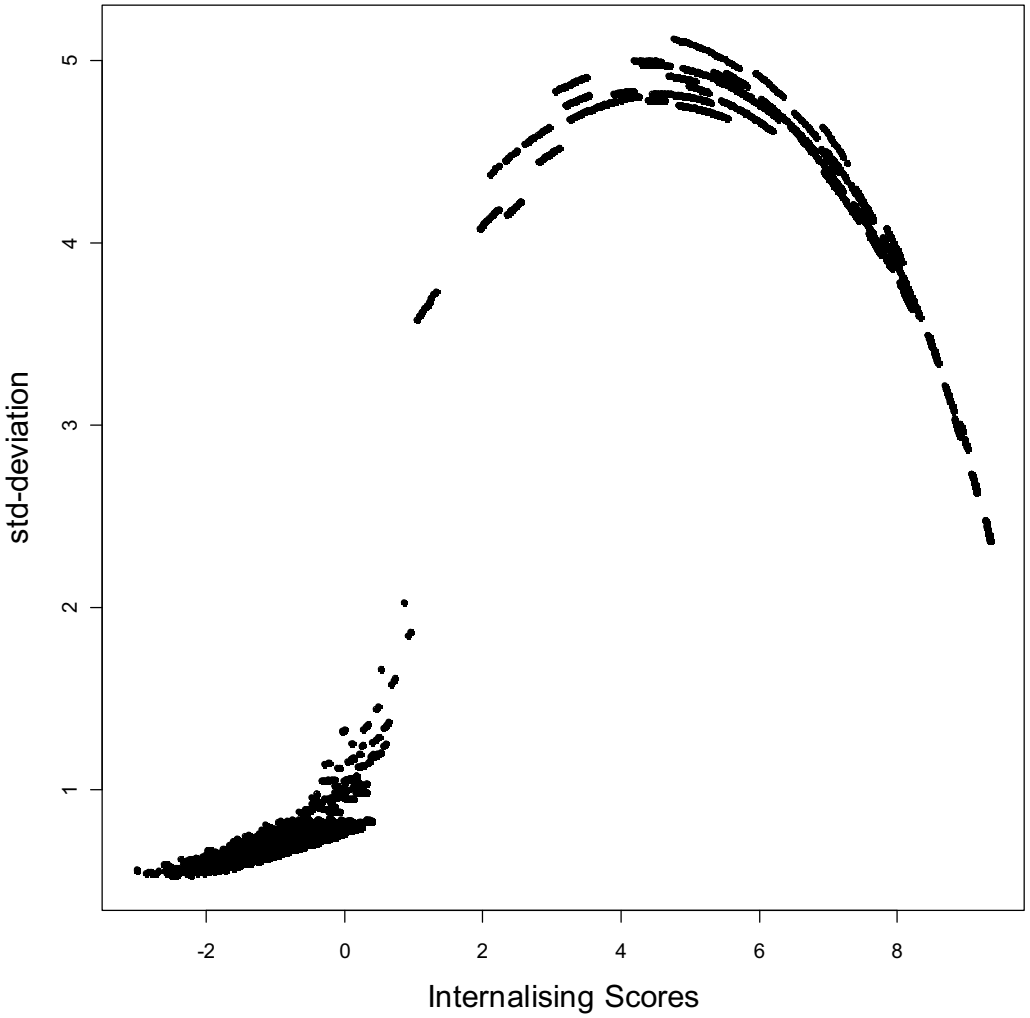

Figure 3. Precision of factor score (diathesis) estimation

A simple descriptive analysis on factor scores can be used as a rough measure of covariates impact on psychiatric diathesis (Table 6). As a very broad outline of a mental-health profile, it can be said that female, young and living in France cases showed the higher expected predisposition to endorse internalising disorders.

Table 6. Average factor scores and ill-class membership probability

	Mean	Probability ill-Class
Overall sample	4.69	0.53
Any disorder	-0.53	1.00
No disorder	6.21	0.39
Gender		
Male	5.78	0.43
Female	3.69	0.63
Birth Year		
→1934	6.80	0.33
1935-64	4.65	0.54
1965-74	4.56	0.53
1975→	2.63	0.73
Country		
Belgium	4.38	0.56
France	2.93	0.68
Germany	4.83	0.53
Italy	5.82	0.42
Netherlands	4.29	0.56
Spain	5.35	0.47

Comparison with no-censoring and actuarial-survival models

The final model was also fitted with observed binary data, but ignoring right-censorship in no-disorder cases. While the no-censorhip model reproduced accurately the observed disorder prevalences (Table 4), taking into account the no-disorder censorship approximately doubled the estimated prevalences. Moreover, the prevalence estimation of any lifetime internalising disorder was 23.1%, quite low compared to the prevalence estimated accounting for censorship (32.7%).

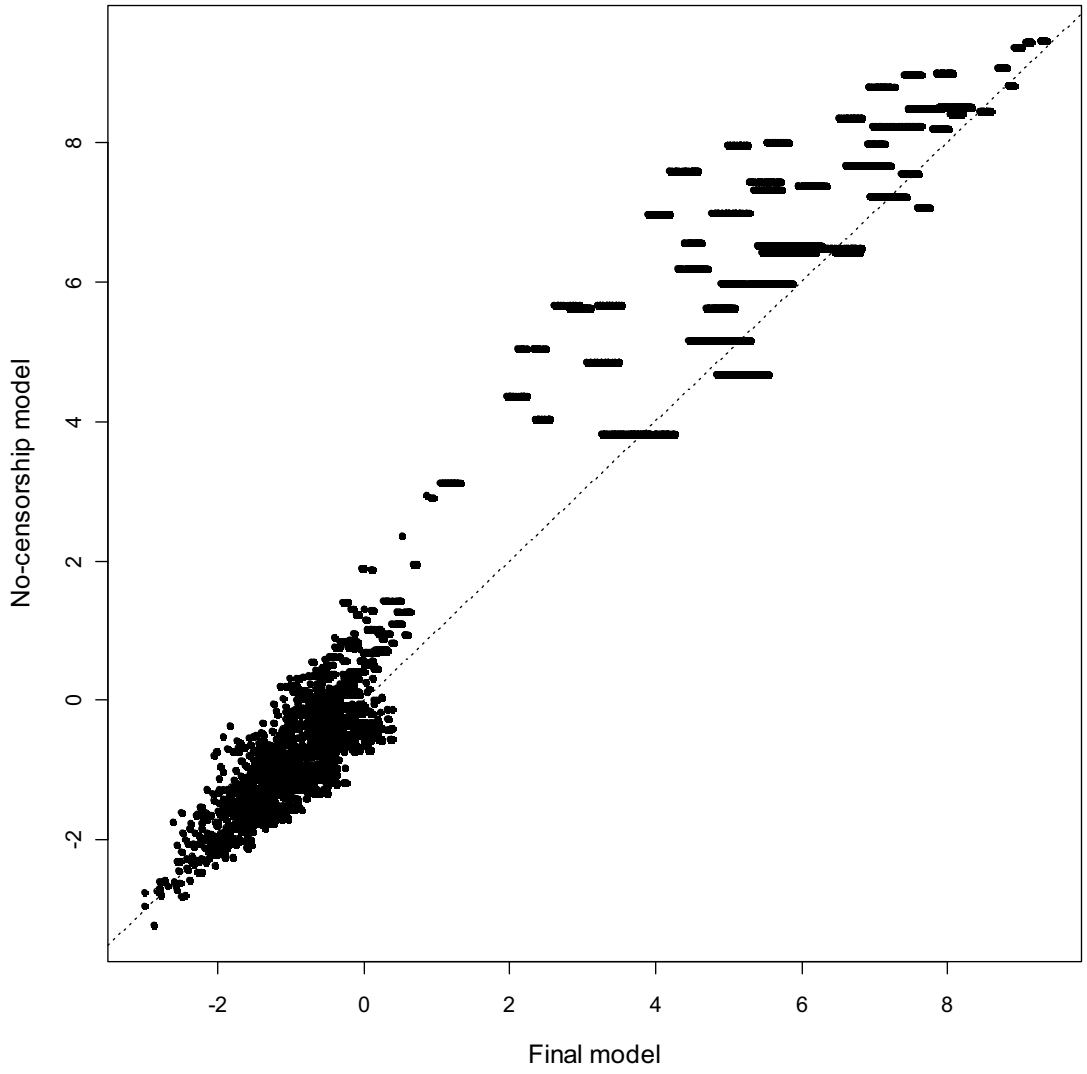

Figure 4. Comparison IRT scores: censorship (final model) *vs* non-censorship model

Regarding scores, no systematic difference was found in the low-range score, where individuals with disorders were assigned (Figure 4). Notice that the scores for individuals without disorders were higher when censorship was ignored. As a result, when omitting the no-disorder censorship, the model assumes that individuals without an observed disorder will never endorse the disorder. Thus, the model biases mental health-scores by considering that no-disorder cases have lower diathesis (i.e. they are mentally healthier) than they actually could have.

Scores from observed data patterns did not change with respect to the age of the individuals in the no-censorship model. The age at the interview time did not show any

effect on score estimation when no-disorder was observed. Conversely, scores from the censorship model took into consideration the number of years that individuals were observed, a peculiarity that can be observed in the horizontal point-lines in Figure 4.
Bivariate comorbidity estimates with the censorship model were much larger than the observed ones (Table 7), but the divergences showed no evident systematic pattern. For example, the bivariate estimated comorbidity for *so-sp* (1.41%) was relatively closed to the observed one (1.08%), while the estimated comorbidity for *ago-dys* (0.80%) was 3 times larger than the observed value (0.27%). These differences between the observed and expected values are a consequence of the model: they spring from taking into account (a) the amount of censorship existing in both disorders and (b) the strength of their relationship as measured by their correlation via the factor.

Table 7. Observed bivariate comorbidity prevalences (upper triangular) and final (censorship) model expected lifetime bivariate comorbidity prevalences (lower triangular). Percentages on the overall sample.

	dys	**mde**	**gad**	**ptsd**	**ago**	**pds**	**so**	**sp**
dys	**.**	3.10	0.76	0.63	0.27	0.31	0.35	0.88
mde	4.37	**.**	1.90	1.43	0.64	1.04	1.14	2.64
gad	1.56	3.07	**.**	0.39	0.22	0.33	0.40	0.63
ptsd	1.39	2.91	1.09	**.**	0.13	0.21	0.32	0.74
ago	0.80	1.41	0.71	0.58	**.**	0.36	0.33	0.63
pds	0.96	1.84	0.80	0.67	0.46	**.**	0.27	0.60
so	1.17	2.33	0.95	0.81	0.53	0.59	**.**	1.08
sp	2.63	6.21	1.85	1.76	0.86	1.11	1.41	**.**

dys: dysthymia, mde: major depression episode, gad: general anxiety disorder, ptsd: posttraumatic stress disorder, ago: agoraphobia with or without panic, pd: panic disorder, sp: specific phobia, so: social phobia.

The actuarial-survival approach, projecting the risk of disorder up to age 75, produced higher lifetime disorder prevalences than the no-censorship model, as a consequence of modelling censorship. Given that survival functions were fitted separately, no comorbidity information was provided. Moreover, the IRT estimations were still somewhat higher than the actuarial-survival approach.

DISCUSSION

In this research article we have successfully proposed and implemented a multivariate methodology to assess lifetime mental-health diathesis when using cross-sectional mixed-aged samples. This type of data is the most frequent in psychiatric epidemiology, in which lifetime disorder information is retrospectively obtained. We have shown that ignoring no-disorder censored information leads to underestimated lifetime disorder prevalences and comorbidities, and it produces overestimated mental-health states. So far, most of the lifetime disorder studies using observed data did not account for this particular type or censoring, leading to largely biased results. Recently, an actuarial-survival method was use to estimate lifetime disorder prevalences, projecting disorder risk at age 75, taking into account the data censorship. These estimations were higher than the observed lifetime prevalences. But they also seemed to be slightly underestimated, given that they did not consider the comorbid disorder association. When comparing the IRT and survival methods, the IRT method yield larger prevalence estimations; the IRT approach is heavily focused on multivariate modelling. The here proposed IRT model extended to lifetime disorders the IRT-internalising model that was applied for 12-month disorders, accounting for data censorship.

This IRT model achieved to create a scoring model that quantifies the individual diathesis to suffer any of the internalising disorders under consideration (Clark 2005). The model does not account for illness severity and duration, thus, it does not directly measure levels of mental health, but the vulnerability or diathesis of being mentally ill at sometime in the life of the individual. The model does not make any assumption on the origin of this diathesis, which might be due to biological, social or historical factors, and even to complex interaction between these factors (Eaton 2006). The statistical model just provides a score that measures the degree of diathesis as a dispositional trait, regardless its etiology. The diathesis scores summarize the common internalising-disorders' information, excluding the random comorbidity association, labeled by Kraemer et al. (Kraemer et al. 2006) as *pseudocomorbidity*.

The main strength of this methodology resides in that just one fitted model can explain disorder associations, describe the population, estimate disorder prevalences and quantify the individual diathesis. All the epidemiological information usually provided in psychiatric epidemiologic studies, like prevalences, disorder association, risk factors,

socio-demographic descriptors, etc. can be estimated from a unique model. Moreover the model can be readily already adjusted by the significant covariates just by introducing them into a structural model. All type of prevalences and comorbidities corresponding to any data pattern can be computed. This is easily done for any pattern of disorders and within any subpopulation. Other typical epidemiological measures of association – for instance, odds ratios – can be computed from the estimated probabilities.

Model Limitations

Perhaps the greatest limitation of the proposed IRT models arises from the way that observed disorder information is considered. Data were introduced in the model implicitly assuming implicitly that the risk of developing a mental disorder remains approximately constant throughout all life (up to the disorder age-limit). On the contrary, in those survival models that take into consideration disorder censorship (Bonnewyn et al. 2007;Kessler et al. 2005), the risk of endorsing a mental disorder for the first time was age-dependent. Given that missing data is age-dependent, IRT estimations of lifetime prevalences could be misleading for disorders that show large changes on the risk of onset across age. For instance, Bonnewyn et. al (2007) showed that anxiety disorders had an early age-of-onset, that is, they showed a higher risk in the youth when compared to older ages, while for mood disorders the risk of onset disorder was quite constant over all ages. This is also true in our sample, where the functions of the number of specific phobia onset and censures on age followed opposite shapes (Figure 5) while major depression onset was not so age-skewed. A similar pattern was found for social phobia and specific phobia, which mostly appeared before the age of 18. Thus, the lifetime prevalences could be somewhat overestimated for social phobia and specific phobia disorders.

A possible solution could be setting robust age-limit values for disorders that display a very skewed age-of-onset distribution, as specific and social phobia do. For example, the 99^{th} percentile could be chosen as the age-limit value for the disorders with much skewed age-of-onset distribution, while keeping the maximum age-of-onset for the rest of disorders. The 99^{th} percentile for social phobia and specific phobia were 43 and 42 respectively (quite lower, compared to their maximum 56 and 75). This method of age-limit selection is robust in the sense that it is omitting not-representative cases when the distribution is right-skewed. The estimation of lifetime prevalences using this robust

age-limit yielded 3.3% prevalence for social phobia and 9.5% for specific phobia, while other disorder prevalences remained practically unchanged. A more general age-limit selection could be build upon criteria definitions for infrequent cases (Tukey 1977).

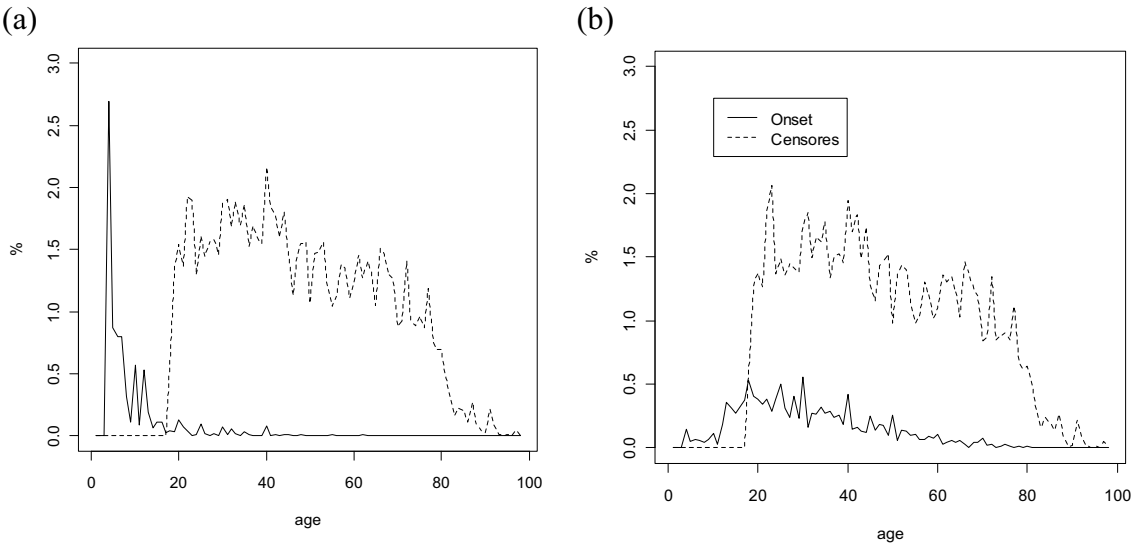

Figure 5. Age of onset (solid line) and censures (dotted line) distribution for specific phobia (a) and major depression (b). Overall percentage of cases by age.

As an IRT model, it was assumed that each disorder (item) response pattern is linked to a score in the latent dimensions, once conditioned on covariates – regardless to the individuals' age of onset of the observed disorders. This assumption is in accordance to (Clark 2005) and (Clark and Watson 1991). They assumed a constant person diathesis level, chronic in nature, as a vulnerability to develop psychopathology in response to a sufficiently stressful environment. Under this assumption, the environmental factors alone determine the disorders' age of onset; the environmental stress manifests the unobserved psychiatric diathesis. However, different assumptions about how diathesis and environmental factors interact to produce observed disorders could lead to different model specifications. For example, it could be assumed that the age of onset is also related to the unobserved diathesis. In that case, promising research will possibly allow to merge both survival and factor model perspectives, being conducted from the more general framework of structural equation models (Jung and Wickrama 2008;Muthen and Khoo 1998) or event history analysis (Vermunt 2009). The joint modelization of the diathesis and the disorders' onset would be reinforced with variables measuring the environmental stress.

However, the IRT model here proposed would fit perfectly data with random onset and length of the individuals' observed period, which the average risk of event is (approximately) constant across time, affected by time-independent covariates. The IRT model is likely to better reproduce the trend of those disorders whose appearance is not highly related with age.

Criticicisms to lifetime data

Lifetime disorder estimates have been reasonably criticised by psychiatric researchers. Streiner (Streiner et al. 2009) has recently highlighted the limitations in the lifetime prevalences estimation. These limitations are deeply rooted on the very logic of retrospective data recruitment methods. Examples of limitations that are related with cross-sectional retrospective methods are for instance, recall bias (Giuffra and Risch 1994), informative truncation (depression's association with a higher mortality (Wulsin et al. 1999) or affective disorders with suicidality (Bostwick and Pankratz 2000)), and reframing (reassessment of past experiences according to current circumstances (Bonnewyn et al. 2007;Hasin and Link 1988)). This could be the reasons of consistently finding lower lifetime disorders prevalences in older age-cohorts (Bonnewyn et al. 2007;Kessler et al. 2003;Kessler et al. 2005;Lee et al. 2007;Medina-Mora et al. 2007;Stein et al. 2008). Our results are consistent with this lifetime measure limitations, in which older individuals showed healthier mental health scores. Although this is consistent with the presence of a recall bias, it does not demonstrate its existence and other hypothesis are available,

Despite criticisms and limitations, we believe that lifetime prevalence is a useful measure that can complement other psychiatric epidemiological measures. These lifetime data limitations affect any model based on the same type of disorder information. The advantage of the proposed model is that, under the same assumptions that lifetime disorders have been generally analysed, our model offers more realistic prevalence and comorbidity estimations, moreover explains the nature of their associations.

Possible future developments

The modelling strategy herein presented opens a door for further research in lifetime mental disorders. This method can be improved in a number of ways, such as

extending the model to conduct wide-range mental health assessment. The internalising disorder dimension could be split into *fear* and *distress* factors or an externalising disorder factor could be added (Krueger 1999;Markon and Krueger 2005;Slade and Watson 2006;Vollebergh et al. 2001). Another interesting extension involves the development of a model that includes censored covariates. For instance, (physic) chronic conditions are related to lower levels of mental health (Almansa et al. submitted-b): a predisposition to some physical illness not yet manifested might increase the probability of endorsing lifetime disorders. The model could also include time-varying factors or covariates to measure personal or social environmental stress. All these research lines would help to understand how disorders develop and which environmental factors interact with the individual diathesis – for instance, is well known that marital status and mental health status are related (Almansa et al. submitted-b; Alonso et al. 2004a).

Although this specific censored data structure is hardly found in other areas than lifetime mental health assessment, the proposed methodology could be also suitable in other applications focused on event occurrence rather than time of onset. For example, profiling costumers and predicting product or service acquisition within a time span, when individuals are observed before the end of the specified period.

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B. Autoria dels articles publicats

El doctorand Josué Almansa Ortiz ha liderat el desenvolupament de les idees i reptes metodològics que inclou aquesta tesi. Ha treballat en el desenvolupament dels models estadístics que s'han plasmat en aquestes publicacions científiques, ha realitzant les anàlisis estadístiques pertinents i ha escrit les primeres versions completes dels articles, sent considerat, doncs, com a primer autor dels articles que conformen aquesta tesi doctoral.

La resta d'autors inclosos han col·laborat activament en l'elaboració de les publicacions científiques:

- donant formació, suggeriments, suport estadístic i fent correccions en la recerca realitzada (Jeroen K. Vermunt, Jordi Alonso, Carlos G. Forero)
- revisant i editant els manuscrits, tant els aspectes formals com lingüístics (Carlos G. Forero, Jeroen K. Vermunt, Gemma Vilagut, Jordi Alonso, Ron De Graaf, Johan Ormel, Josep Maria Haro, Giovanni de Girolamo)
- formant part del grup de treball internacional que va liderar la realització del projecte ESEMeD, des del seu disseny fins a la recollida de dades (Jordi Alonso, Gemma Vilagut, Ron De Graaf, Johan Ormel, Josep Maria Haro, Giovanni de Girolamo)

Cap dels articles científics inclosos en aquesta tesi doctoral formen part d'una altre tesi doctoral o qualsevol tipus de treball acadèmic.

Signat pels directors de la Tesi:

Dr. Jordi Alonso

Dr. Jeroen K. Vermunt

C. Resum de les publicacions

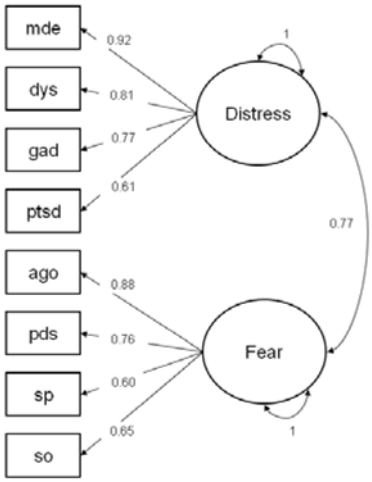
Article1: Exploring conceptual Comorbidity models as measurement instruments for Mental Health Epidemiology Research.

En el primer article presentat en aquesta tesi es fa una revisió de models conceptuals proposats per explicar les associacions entre mesures psiquiàtriques, ja siguin símptomes o trastorns, i els factors (no observables) que les causen. Posteriorment, es testen els models conceptuals basats en trastorns amb les dades ESEMeD, amb els trastorns estimats amb l'instrument CIDI. Aquests models conceptuals es comparen estadística i conceptualment, mitjançant el grau d'ajust de les dades en cada model i l'aportació psiquiàtrica rellevant de cadascun d'ells.

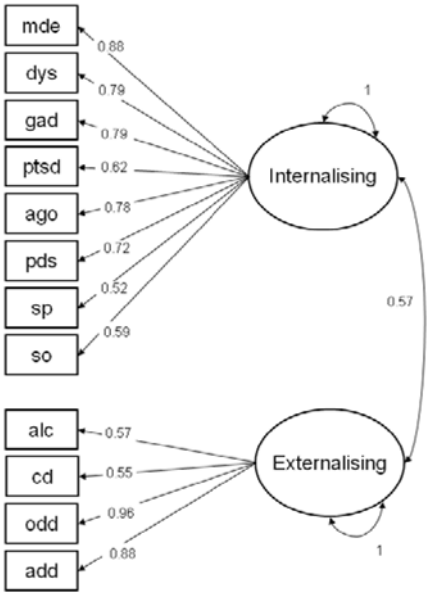
A pesar del gran nivell de recerca psiquiàtrica conceptual realitzada sobre estructures de comorbiditat mental, gaire bé mai s'han utilitzat aquests models com a instruments de mesura quantitativa de dimensions mentals no-observables. Les principals aportacions d'aquest article són: mostrar que es poden construir instruments de mesures de salut psiquiàtrica directament a partir dels models conceptuals, i proposar un model que pugui ser utilitzat de manera generalitzada com a instrument descriptor de la salut mental, tant en àmbit clínic (mesurant graus de severitat mental a nivell individual) com epidemiològic (a nivell poblacional) – basant-se en informació diagnòstica de trastorns mentals.

Els models conceptuals van ser testats estadísticament mitjançant models de tipus IRT, on factors latents continus expliquen un conjunt de variables binàries observades: presència o absència de trastorns mentals en el últims 12 mesos. Es van testar dos models per analitzar només trastorns *internalitzants* (són els que més habitualment es troben en estudis epidemiològics), i tres models que inclouen trastorns tan *internalitzants* com *externalitzants*. En la següent figura es mostren aquests models.

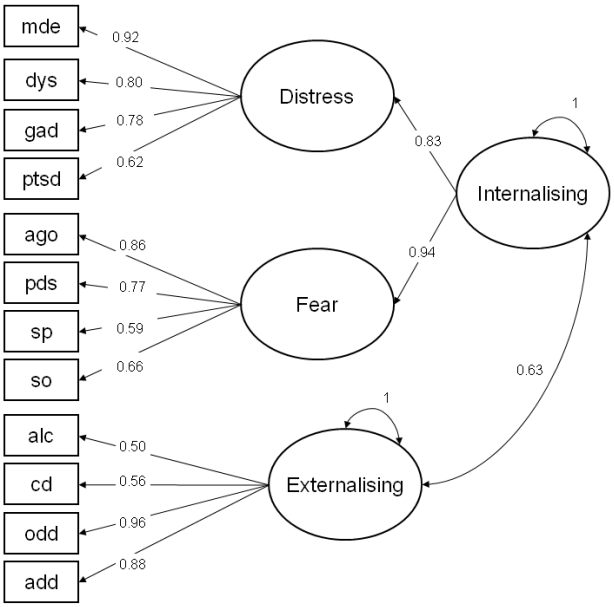
Model 1. Factor Internalitzant.



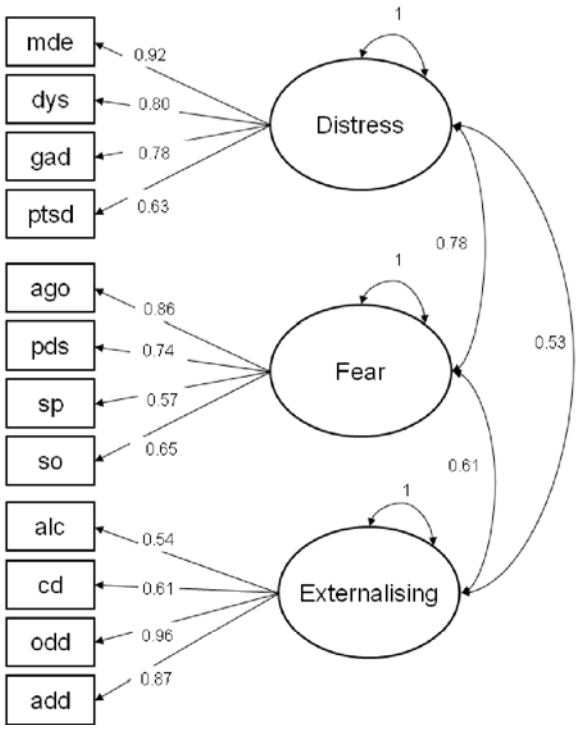
Model 2. Trastorns Internalitzants en 2 factors correlacionats.



Model 3. Internalitzant-Externalitzant.



Model 4. Factor Internalitzant jeràrquic.



Model 5. Tres factors correlacionats.

Els models conceptuals de trastorns mentals van resultar en un ajust estadístic acceptable en la mostra ESEMeD. Com a conclusió principal s'obté que un model amb un factor *internalitzant* (trastorns d'estat d'ànim i ansietat) correlacionat amb un factor *externalitzant* (trastorns del comportament i d'abús de substàncies) és adequat per a mesurar la salut mental (model 3). El factor *internalitzant* pot modelitzar-se una mica millor mitjançant dues subdimensions, referents a trastorns depressius (*distress*) i trastorns d'ansietat (*fear*), tot i que es perd en parsimònia. Els models 4 i 5 (factor internalitzant jeràrquic i model de tres factors correlacionats) són estadísticament equivalents i la preferència per un o altre vindrà donada en base a raons conceptuals.

Partint del model de 2 factors *internalitzant-externalitzant*, es mostren el tipus de puntuacions que s'obtenen i com es poden interpretar. Aquestes puntuacions inclouen tota la informació que defineix el model conceptual, per tant, té en compte el nombre i el tipus de trastorns observats (cada trastorn pot tenir un pes diferent en la construcció del factor latent). Per tant, modela directament la comorbiditat mental definida en un model psiquiàtric conceptual. Els patrons de trastorns mentals poden ser fàcilment comparats segons la seva gravetat per mitjà d'aquestes puntuacions latents estimades. Amb aquestes puntuacions es pot fer inferència sobre nivells de salut mental.

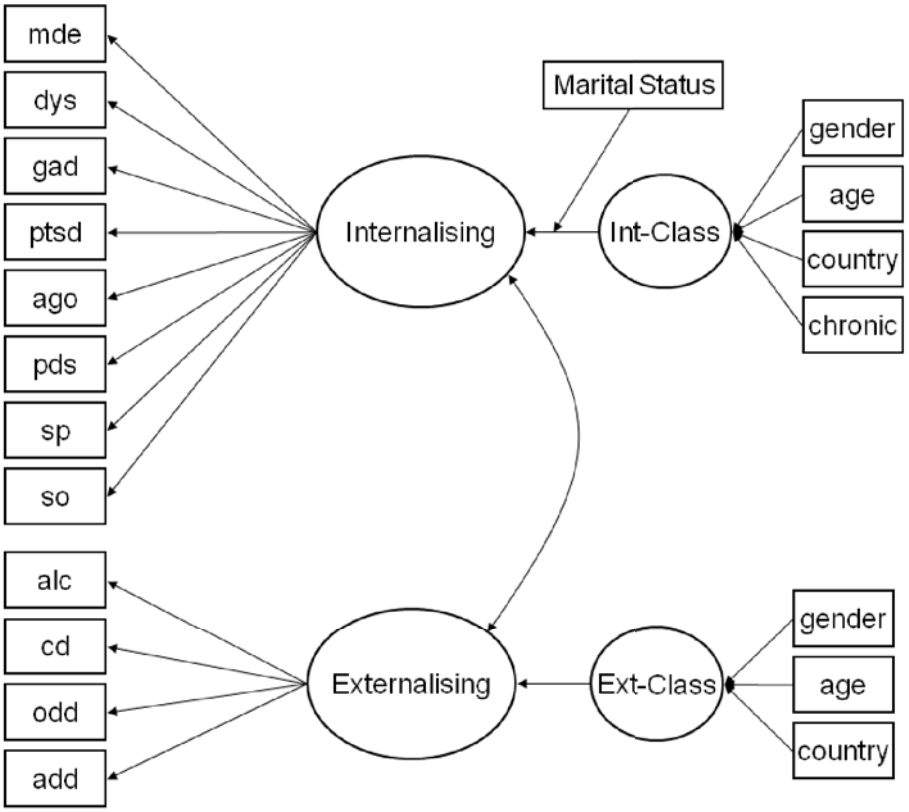
Article 2: Measurement and description of underlying dimensions of comorbid mental disorders using Factor Mixture Models: results on the ESEMeD project.

En el segon article es fa una descripció de l'estat de salut 'actual' de la població europea, partint d'un model psiquiàtric conceptual com a instrument de mesura de la salut mental. La gran majoria d'articles epidemiològics han basat els seus resultats en descripcions univariades i bivariades de les variables d'interès, sense considerar possibles estructures subjacents a aquestes variables, com si per la seva naturalesa fossin incorrelacionades. En el camp de la psiquiatria, aquesta metodologia és apropiada quan l'interès es centra en descriure uns trastorns específics, però no poden inferir un estat de salut mental en els individus. Així doncs, partint del model conceptual de dos factors *internalitzant-externalitzant*, s'avalua el nivell de salut poblacional segons aquests dos factors, a partir dels trastorns patits en els últims 12 mesos. Les puntuacions obtingudes en cada factor proporcionen una mesura quantitativa que té en compte la naturalesa intrínseca dels trastorns. Com ja s'ha mencionat en l'article anterior, aquestes puntuacions inclouen l'efecte de la comorbiditat mental i el diferent pes que cada trastorn té dins del seu factor.

En aquest article es fa una valoració estadística detallada d'aquest model. Per exemple, es va testar la propietat d'invariància. La invariància del model assegura que l'instrument de mesura funciona igual siguin quines siguin les característiques dels individus mesurats, és a dir, que els paràmetres que relacionen les variables observades amb les latents són invariants respecte de qualsevol subpoblació.

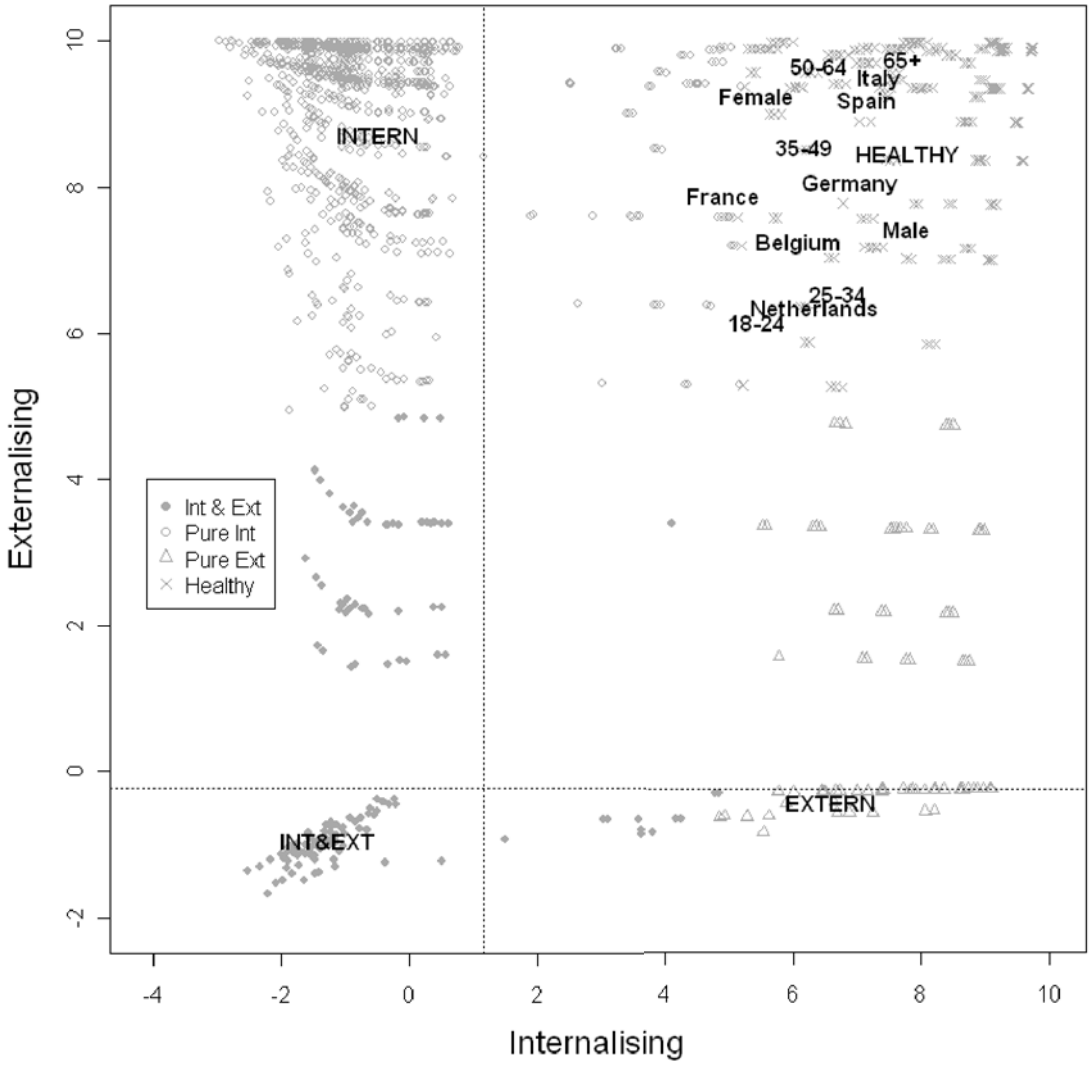
El model classifica la població en "sans" i "malalts" dins de cadascun dels factors, mitjançant una variable latent categòrica, millorant significativament tant l'ajust estadístic com la descripció epidemiològica. La combinació de factors i de classes latents donen lloc als Factor Mixture Models, on cada subpoblació segueix una distribució de probabilitat amb paràmetres diferents. Els classificats com a "sans" tenen una puntuació elevada en el factors, indicant bona salut mental – i resultant en una probabilitat pràcticament nul·la de patir trastorns mentals. Aquest model permet afegir dos tipus de covariables per explicar les diferències poblacionals de salut mental. Primer, aquestes diferències poden ser degudes a una diferent proporció de "sans" i "malalts" entre subpoblacions, i segon, dins de la classe "malalts" poden existir alguns individus que tendeixen a tenir un nivell de gravetat diferent segons les seves

característiques. En el nostre model hem trobat que el país, el gènere, l'edat i l'existència de malalties cròniques (físiques) tenen un efecte sobre la proporció de "sans" i "malalts", i que dintre de la classe "malalts" l'estat civil és un predictor del nivell de gravetat. La següent figura mostra el model final ajustat, amb el qual es



Trastorns internalitzans: depressió major (mde), distímia (dys), ansietat generalitzada (gad) estrès post-traumàtic (ptsd), agorafòbia (ago), trastorn de pànic (pds), fòbia social (so), fòbia específica (sp).
Trastorns externalitzants: trastorns d'abús i/o dependència d'alcohol (alc), trastorn de conducta (cd), trastorn negativista desafiant (odd), dèficit d'atenció i hiperactivitat (add)

Les puntuacions estimades per a cada factor poden ser utilitzades com a mesures resum del nivell de salut mental en cada dimensió. El següent gràfic descriu de manera general l'estat de la salut mental 'actual' en la població europea (ESEMeD), a partir de les puntuacions estimades de cada factor. Els punts representen las puntuacions de cada individu en ambdós factors, classificats segons assignació modal a cadascuna de les classes. També es mostren les mitjanes per categories de les variables socio-demogràfiques. Puntuacions elevades indiquen estats mentals saludables, mentre que puntuacions baixes fan referència a estats malaltissos.



- Puntuacions mitjanes per categoria d'edat (18-24, 25-34, 35-49, 50-64, 65+), país, gènere i tipus de trastorn observat: només internalitzant (INTERN), només externalitzant (EXTERN), ambdós (INT&EXT) i sense trastorn (HEALTHY).
- Les línies de punts indiquen la puntuació màxima observada per aquells que tenen algun trastorn.

Respecte de les variables socio-demogràfiques, es veu clarament que les dones tenen en mitjana millor salut mental de tipus externalitzant però pitjor d'internalitzant, en comparació amb els homes. Els grups d'edat més jove tenen pitjors nivells de salut mental que els més vells. Els països del sud d'Europa presenten millor nivells de salut mental en comparació amb el del centre-nort d'Europa.

Article 3: Mental-heatlh assessment using discrete factor models.

El tercer article aplica models de IRT on la variable latent és de tipus discreta-ordinal, en comptes de la distribució normal utilitzada habitualment. Així doncs, la distribució de la variable latent, $h(\boldsymbol{\theta})$ en l'equació (3), és una funció de probabilitat discreta (ordinal). Els models de variables latents discretes ja han estat desenvolupats en el passat (Laird, 1978; Aitkin, 1999), però, a pesar de les seves avantatges, és difícil trobar aplicacions on utilitzin factors discrets, en detriment del models amb factors continus. La distribució de probabilitat de la variable latent ordinal és molt flexible, ja que no té una determinada forma *a priori*, i és especialment adient quan l'assumpció de normalitat en la variable latent és dubtosa. També, el temps d'estimació és molt inferior en comparació als models amb variables latents contínues, ja que no requereix de integració numèrica.

Les variables latents ordinals també poden ser usades per a descriure les variables subjacents mitjançant un nombre petit de valors, estimant els de casos més "típics". De fet, en l'entorn de la investigació mèdica, en benefici d'una interpretació parsimoniosa de l'estructura latent, pot ser més adient classificar els individus segons un nombre petit d'estats representatius ordenats (per exemple: sa, malalt-lleu, malalt-greu), en comptes de tenir un conjunt infinit de possibles valors latents.

En aquest article es mostra com ajustar models amb factors ordinals, incloent-hi característiques habituals en models de factors continus com la realització de test d'invariància, modelització de més d'un factor (com correlacionar factors), anàlisis amb múltiples grups i inclusió de covariables. Tot això es mostra en una aplicació sobre els trastorns de tipus *internalitzant*, mitjançant un model de dos factors ordinals correlacionats: *distress* (trastorns d'estat d'ànim) i *fear* (trastorns d'ansietat). Cadascun d'ells incorpora una mixtura de 'sans' i malalts', i covariables per predir la pertinença a les classes. Aquestes anàlisis confirmen que les variables latents ordinals són una alternativa factible per a la modelització dimensional dels trastorns mentals.

Els resultats sobre les dades ESEMeD mostren que la distribució del factor *distress* dins la població malalta pot tenir una forma lleugerament asimètrica, amb major pes a l'esquerra de la distribució, mentre que la distribució del factor *fear* s'apropa més a una

distribució normal. Per tant, un factor *distress* ordinal sembla que podria modelitzar una mica millor l'estructura latent que una distribució normal. Comparant amb un model amb la mateixa estructura però de factors continus, ambdós models tenen una bondat d'ajust força semblant.

També s'exploren d'altres qualitats dels models de variables latents discretes. Per exemple, s'ha trobat que la realització de tests de invariància en la mesura (MI) d'un factor continu pot aproximar-se amb un test MI sobre una discretització del factor. La modelització mitjançant factors discrets permet molta flexibilitat a l'hora de definir una forma de la distribució de probabilitat discreta per a diferents subpoblacions. També es discuteixen avantatges de modelitzar mixtures en models amb factors discrets.

Article 4: IRT models with censored binary indicators. Application to lifetime mental health comorbidity, assessed in the ESEMeD project.

Per últim, en el quart article s'analitzen models de comorbiditat mental amb trastorns vida (*lifetime*). Aquest article proposa com ajustar models (multivariants) de tipus IRT quan les variables observades recullen informació incompleta. Com ja s'ha explicat en la introducció, les variables de trastorn vida en mostres transversals estan censurades, de manera que els individus en els quals no s'ha observat un trastorn encara estan a risc de patir-lo en el futur. En contrast, quan s'ha observat un trastorn la informació és completa. Els models IRT suposen que les variables observades estan relacionades degut a una causa comuna no observable, un factor latent continu. En el nostre cas, el model IRT utilitzat suposa l'existència d'una predisposició individual de patir trastorns de tipus *internalitzant* (estat d'ànim i ansietat). Aquesta predisposició és una característica individual constant de les persones que, sota un nivell suficient d'estrès ambiental, donen lloc a l'existència de trastorns mentals (Clark, 2005).

Molt sovint, estudis previs sobre prevalença vida han calculat la prevalences com a percentatge d'individus en els quals s'ha manifestat un trastorn mental en algun moment de la seva vida, és a dir, suposant que la informació sobre els trastorns és completa, assumint implícitament que la gent sense trastorn observat no el tindrà en el futur, donant lloc a estimacions esbiaixades.

L'objectiu d'aquest article no és res més que elaborar una extensió del model IRT que ja s'ha ajustat amb èxit sobre dades de trastorn 12-mesos, per tal de modelitzar correctament les dades de trastorns vida, tenint en compte la informació censurada. Per tant, és necessari incloure en el model la quantitat real de temps d'exposició de la mostra als trastorns mentals dins del quan s'ha donat els trastorns observats. Així doncs, aquest model IRT inclou tota la informació disponible observada en les dades, considerant que aquells individus sense trastorn observat fins el moment de l'entrevista tenen un pes el l'estimació del model relatiu a la seva edat, mentre que la informació dels individus amb trastorn és completa.

Per tenir en compte les censures, en lloc de considerar les variables resposta (trastorns) com a binàries, s'introdueixen com a dades de tipus binomial agregades, definides per "nombre d'intents" i "nombre d'esdeveniments". Quan un trastorn es dóna en un individu el seu nombre d'intents i d'esdeveniments prenen valor 1 per a aquest trastorn. En cas de no ser observat un trastorn, només sabem que aquest no s'ha donat fins a una determinada edat. En aquest cas el nombre d'esdeveniments és zero, i el "número d'intents" indicarà la proporció de temps de vida exposat (a risc). Per a calcular aquesta proporció es necessita una edat-límit dins de la qual les persones que no han patit encara un trastorn poden trobar-se a risc de patir-lo en el futur, és a dir, on sigui raonable observar els trastorns quan hi existeixi predisposició. Per exemple, s'ha escollit com a edat-límit l'edat màxima observada d'inici de trastorn. Cada trastorn tindrà, doncs, la seva pròpia edat-límit. Només tindrem dades censurades quan l'edat dels individus sense un trastorn observat sigui inferior a la seva edat-límit. Per als individus sense un trastorn i amb edat superior la edat-límit, el "nombre d'intents" es va codificar com 1 i el "nombre d'esdeveniments" com a zero; en aquest cas la probabilitat d'observar el trastorn en el futur és nul·la, i s'assumeix que no té predisposició suficient per patir aquest trastorn. Per als individus sense un trastorn observat, però amb edat inferior a l'edat-límit, es calcula el "nombre d'intents" (temps d'exposició) com a proporció de temps fins a l'edat-límit. Per exemple, l'edat-límit per depressió major és 86, i un individu de 35 anys sense depressió major vida tindrà "nombre d'esdeveniments" igual a zero i "nombre d'intents" igual a 35/86 = 0.41 en aquesta variable.

També s'ha plantejat una edat-límit més robusta (percentil 99) per aquells trastorn amb una distribució de l'edat d'inici de trastorn molt asimètrica, on la gran majoria de casos es donen per primer cop abans dels 20 anys.

Seguint la mateixa metodologia que en les anàlisi de trastorns 12-mesos, el model IRT proposat inclou la classificació de la població en "sans" i "malalts", i de dos tipus de covariables, on les característiques individuals poden ser predictores de la pertinença a cada classe o mesurar diversos nivells de predisposició dins de la classe de 'malats'.

La formulació d'aquest model és la següent. Considerem y_{ij} com la variable binària de trastorns observats ($j = 1,2,...,8$) per a un individu i, de manera que $y_{ij} = 1$ quan s'ha observat el trastorn en algun moment de la vida, i zero altrament. Sigui θ la puntuació latent de predisposició a trastorns mental (de tipus *internalitzant*) i x la variable

categòrica latent indicant la pertinença a les classes de "sans" o "malalts". La probabilitat d'observar un trastorn condicionat a les variables latents s'expressa com

$$\text{logit}\left(\hat{P}\left(y_{ij}=1\middle|\theta,x\right)\right)=\alpha_j+\lambda_j\theta_{i|x}$$

on la α_j i λ_j són els paràmetres del model IRT (*intercept* i *càrrega factorial*). La distribució de la predisposició latent varia per cada classe. La classe de "malalts" ($x=1$) té mitjana zero i variància 1, però depèn de covariables de gravetat ($\mathbf{z}^F$) que modifiquen la mitjana del factor en la classe de malalts segons característiques socio-demogràfiques: $\theta|x=1\sim N(0+\boldsymbol{\beta}\cdot\mathbf{z}^F,1)$. En canvi, la distribució latent per a la classe de "sans" ($x=2$) es troba degenerada en un valor latent elevat $\theta|x=2\sim N(10,0)$. Els paràmetres estructurals del model IRT (*intercepts* i *càrregues factorials*) són invariants respecte de les classes. La distribució de la classe latent també s'estima, incloent covariables ($\mathbf{z}^C$) que prediuen la probabilitat de pertinença a les classes: $\text{logit}\left(\hat{P}\left(x=1\right)\right)=\tau+\boldsymbol{\gamma}\cdot\mathbf{z}^C$.

Un cop estimat el model, es poden estimar les prevalences vida dels trastorns y_j per mitjà de les distribucions marginals respecte de les variables latents:

$$\hat{P}\left(y_j=1\right)=N^{-1}\sum\nolimits_{i=1}^{N}w_i\left\{\begin{array}{r}\int\hat{P}\left(y_{ij}=1\middle|\theta,x=1\right)f\left(\theta\middle|x=1,\mathbf{z}_i^F\right)d\theta\cdot\hat{P}\left(x=1\middle|\mathbf{z}_i^C\right)+\\+\hat{P}\left(y_{ij}=1\middle|\theta=10,x=2\right)\hat{P}\left(x=2\middle|\mathbf{z}_i^C\right)\end{array}\right\}$$

En comparació amb les anàlisi epidemiològiques clàssiques, aquest model de tipus IRT té la gran avantatge de què un sol model pot estimar simultàniament tots els indicadors epidemiològics d'interès, com poden ser les prevalences de trastorns vida, així com de comorbiditats i de qualsevol patró de trastorns, les puntuacions de la variable predisposició no-observable, quantificar factors de risc de patir algun trastorn mental, etc. on tots aquests indicadors ja es troben adequadament ajustats per les covariables significatives. A més a més, modela la comorbiditat mental.

Les prevalences calculades amb aquest model IRT per a dades binàries censurades són clarament superiors a les prevalences vida observades (sense tenir en compte les censures), i també lleugerament superiors a les calculades amb el mètode de supervivència-actuarial. Les dones mostren una major predisposició que el homes a patir trastorns de tipus *internalitzant*. Els països del sud d'Europa (Espanya i Itàlia) mostren els nivells de predisposició més baixos. També s'ha trobat un efecte significatiu respecte de l'edat, on els més joves tenen major predisposició a patir trastorns en comparació amb els de més edat. No obstant, aquest efecte és interpretat com 'artificial' per d'altres investigadors psiquiàtrics, com Strainer et al. (2009), degut al biaix de memòria i d'altres limitacions inherents a les dades retrospectives.

Aquest model IRT assumeix que cada patró de trastorns (i covariables) té associada una mateixa puntuació latent, independentment de quan s'hagi manifestat el trastorn. Aquesta assumpció es troba amb concordança amb la definició conceptual de Clark (2005), en la que l'aparició de trastorns depèn del nivell de predisposició latent i el moment concret (edat) depèn només de factors ambientals, com si ambdós factors fossin independents. No obstant, diferents assumpcions sobre el procés d'aparició de trastorns mentals en les persones poden donar lloc a diferents models estadístics. Per exemple, també és raonable pensar que les persones amb major predisposició patirà els trastorns en edats menors. En aquest cas la puntuació latent tenint tindrà en compte tant els trastorns observat com l'edat d'aparició del trastorn per primer cop. En el capítol de discussió d'aquesta tesi es mostra un model de supervivència multivariant amb variables latents, que donarà lloc a un nou article científic.