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A multi-cohort consortium for GEnder-Sensitive Analyses of mental health trajectories and implications for prevention (GESA) in the general population in Germany

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ABSTRACT

Introduction Mental health is marked by gender differences. We formed a multi-cohort consortium to perform GEnder-Sensitive Analyses of mental health trajectories and study their implications for prevention (GESA). GESA aims at (1) identifying gender differences regarding symptoms and trajectories of mental health over the lifespan; (2) determining gender differences regarding the prevalence, impact of risk and protective factors; and (3) determining effects of mental health on primary and secondary outcomes (eg, quality of life, healthcare behaviour and utilisation).

Methods and analysis We plan to perform secondary analyses on three major, ongoing, population-based, longitudinal cohorts (Gutenberg Health-Study (GHS), Study of Health in Pomerania (SHIP), Cooperative Health Research in the Augsburg Region (KORA)) with data on mental and somatic symptoms, medical assessments and diagnoses in north-east, middle and southern Germany (n>40 000). Meta-analytic techniques (using DataSHIELD framework) will be used to combine aggregated data from these cohorts. This process will inform about heterogeneity of effects. Longitudinal regression models will estimate sex-specific trajectories and effects of risk and protective factors and secondary outcomes.

Ethics and dissemination The cohorts were approved by the ethics committees of the Statutory Physician Board of Rhineland-Palatinate (837.020.07; GHS), the University of Greifswald (BB 39/08; SHIP) and the Bavarian Chamber of Physicians (06068; KORA). Together with stakeholders in medical care and medical training, findings will be translated and disseminated into gender-sensitive health promotion and prevention.

Strengths and limitations of this study

- The multi-cohort consortium (GESA) implements GEnder-Sensitive Analyses of mental health trajectories and elaborates on their implications for prevention.
- Over 40 000 participants from the German population contributed high-quality data on mental and somatic symptoms in multiple longitudinal cohorts.
- The combined samples originate from different German regions; their different socioeconomic characteristics will inform gender-sensitive analyses.
- Current waves lack strong gender measures; gender is instead estimated by socioeconomic proxies.
- The different measures, waves and age structures of the cohorts require substantial harmonisation and complicate interpretations.

BACKGROUND

Mental disorders have become a core challenge for healthcare in the 21st century.[1] With a 1 year prevalence of over 30%, mental disorders are highly prevalent and costly. Large cross-sectional population surveys have advanced our knowledge about different ways in which common mental disorders affect and burden men and women[1] (eg, quality of life, health behaviour, general health and gainful employment; for an overview see Kolip and Hurrelmann and Piccinelli and Wilkinson[2 3]): women are diagnosed more often with internalising disorders, especially depression,[4] anxiety, somatoform[1] and eating disorders.[5] They differ from men regarding incidence, course and symptom profiles. Men are diagnosed more often with externalising disorders, substance (eg, alcoholism) and behavioural (eg, pathological gambling) addictions[1 6] and conduct disorders.[7]

Differences between men and women are attributable to sex or gender differences. Sex as a biological construct is rooted in genetics, anatomy and physiology.[8] Gender subsumes psychosocial variables that differentiate men and women.[9] Sex and gender interact in the development of diseases.[10] Yet, the distinction

between sex and gender has been neglected in the health sciences, particularly in the area of mental health.[8 11 12] However, recommendations of public health agencies such as the US funding guidelines of the National Institutes of Health,[13] the Canadian Institute of Gender and Health and the Robert Koch Institute in Germany have provided new impetus for sex-sensitive and gender-sensitive health research.[14]

The following constructs are pivotal to operationalise gender[8 15]:

1. *Gender roles:* Refer to behavioural norms within a society. They form by observing men and women in different social roles. Perceivers observe role congruent behaviours (eg, caregiving women in a family) and develop corresponding expectations (eg, women are caring). Gender roles evolved from an interaction of physical sex differences and culture; gender roles influence behaviour by biosocial processes (hormonal, self-regulation and social regulation).[9]
2. *Gender identity:* Reflects how individuals see themselves as relatively female or male (or across a continuum). It determines feelings and behaviours.[8] Gender identity is measured on the two independent dimensions femininity/expressivity and masculinity/ instrumentality.[16–18]
3. *Gender relations:* Describe how individuals interact with or are treated by others based on their ascribed or displayed gender.
4. *Institutionalised gender:* Refers to the distribution of power between women, men and others in the institutions of a society (ie, social, political, educational etc). It shapes social norms defining and maintaining different expectations and opportunities for men and women.[8]

To overcome shortcomings in existing data recent research has developed gender measures that allow assessing gender in population-based studies that did not originally include measures of gender.[11 19] Pelletier and colleagues[11] have advocated to assess gender-related individual differences by characteristics that discriminate men and women. After conducting principal component factor analysis and logistic regression analysis (with sex as criterion) in a sample of patients with acute coronary syndrome (ACS), they identified seven variables associated with sex: primary earner status, personal income, weekly hours of housework, primary responsibility for housework, level of stress at home, masculinity scores, and femininity scores. Interestingly, a feminine gender score but not female sex was associated with traditional risk factors for ACS. A similar score was proposed by Smith and Koehoorn[19] that was based on work, childcaring and education. Both seem to measure a combination of gender roles and institutionalised gender.

The German Federal Ministry of Education and Research (BMBF) called for 'gender-sensitive studies in preventive and public health research' as part of the funding initiative life-long health, to promote the health of women and men. This paper presents the rationale and methodological approach of the project 'GEnder-Sensitive Analyses of mental health trajectories and implications for prevention: A multi-cohort consortium (GESA'.

Study aims

GESA performs gender-sensitive analyses combining three large-scale, prospective, representative cohorts with high-quality health data in order to fill the gaps of gender-related knowledge in mental health.[8 12] Each cohort includes multiple samples with two to four follow-ups. GESA seeks to (1) advance knowledge about vulnerable phases for the development of common mental disorders applying a developmental (lifespan) approach,[20 21] which will be complemented by gender-sensitive analyses. Here, we aim to identify gender-specific symptom patterns, which will allow to refine gender-sensitive assessment methods. (2) Following the vulnerability-stress model of mental disorders, *pathogenic* (risk factors and behaviours) and *salutogenic* factors (personal, biological and social protective factors) will be identified by comprehensive and large-scale assessments. We differentiate stable and variable protective (salutogenic) and stable and variable risk factors (pathogenic). *Stable* factors include personality, socioeconomic factors, physical environment (noise annoyance),[22] urbanity, reported adverse childhood experiences,[23] migration background[24] and the presence of chronic medical conditions. *Variable* factors, which are more accessible to preventive efforts, include social support,[25] loneliness,[26 27] perceived and work-related stress,[28] health behaviour (smoking, alcohol, physical activity) and healthcare utilisation. The relationship of baseline to follow-up conditions is further modified by intervening critical life events (including somatic diseases) or life cycle demands (eg, marriage, childbirth, or retirement). By exploring socioeconomic influences, we account for the diversity within groups of men and women and avoid creating an artificially homogeneous picture. (3) We will determine the effects of mental health on major outcome variables especially subjective health, healthcare behaviour and utilisation and quality of life. Women have higher rates of sick leaves[29] in addition to longer-lasting disabilities[1] and report a lower subjective quality of life.[30] We will relate the findings to local and regional, socioeconomic, environmental and healthcare conditions. Figure 1 gives an overview over the suggested relations and all measured variables with a special emphasis on differentiating between stable and variable risk and protective factors. Health promotion and prevention will be advanced by the increase of knowledge on sex and gender as determinants of mental health, health behaviour and mental health outcomes, while accounting for social, economic or environmental living conditions.

METHODS AND ANALYSIS

Study setting and participants

The overall project consists of three major, ongoing, longitudinal cohorts in middle, southern and north-east Germany: The Gutenberg Health Study (GHS), the Cooperative Health Research in the Augsburg Region

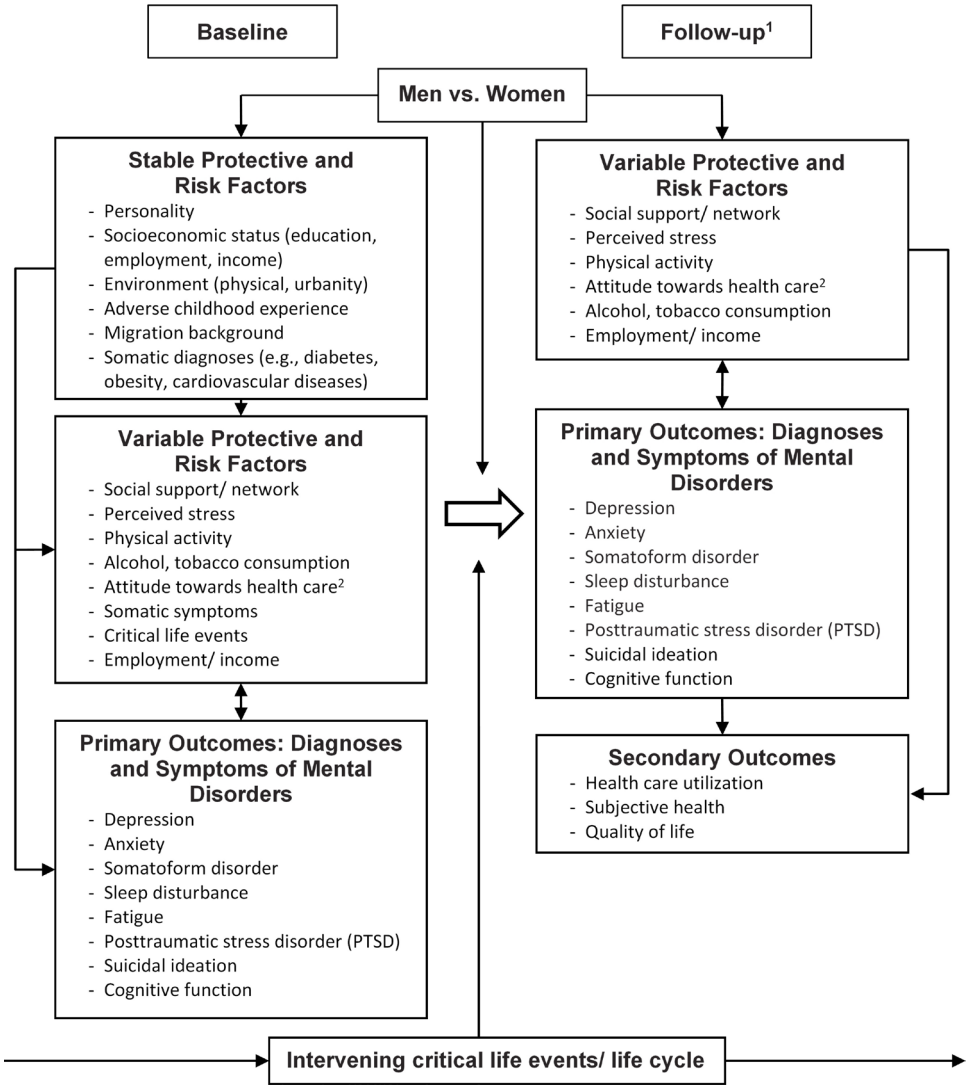

Figure 1 Relationships between common mental disorders, risk and protective factors and outcomes. [1]All studies are ongoing; up to three follow-ups conducted to date. [2]Only in SHIP.

(KORA) and the Study of Health in Pomerania (SHIP). Table 1 gives an overview over the specifics of the cohorts.

All cohorts are being recruited following comparable protocols based on stratified random selection of participants from the local registries. Registration is mandatory for any individual residing in Germany. Thus, representative samples of the general population are available based on comparative, stratified sampling (by sex, age and urban–rural residence) in different regions of Germany with comparable recruitment efficiency (GHS: 60%; KORA: 70%–80%; SHIP: 44%–69%). All studies contacted non-responders to estimate their effects on results. The longitudinal cohorts aimed at investigating the complex associations between risk factors, subclinical and clinical diseases; consecutive follow-ups were conducted in intervals of 2.5 years, respectively 5 (and up to 7 years). Each was powered for predicting the combined endpoint of primary myocardial infarction or cardiac death. All cohorts covered extensive anthropometric measurements, biobanking, laboratory and medical technical examinations (eg, spiroergometry, vascular function).[31–33] Data were acquired via thorough medical and psychological examinations (GHS 4–6 hours; KORA 3 hours; SHIP/SHIP-TREND up to 25 hours) in the cohort centres and additional telephone interviews. We focus on the extensive and overlapping sets of standardised and validated measures (self-report, interview, medical history and diagnoses) of mental health domains and related symptoms, as well as indices of distress, health behaviour, healthcare utilisation and subjective health.

Figure 2 illustrates the different samples of the cohorts and assessment years. The GHS recruited in the city of Mainz and the county of Mainz-Bingen in Midwest Germany since 2007. It started out with the largest sample with two completed follow-ups after 2.5 and 5 years (7.5 years and 10 years ongoing).[33]

The data were derived from three independent cross-sectional population-based WHO monitoring trends and determinants on cardiovascular diseases (MONICA) surveys conducted in the region of Augsburg (southern

Table 1 Overview of the participating cohorts

	GHS	MONICA/KORA	SHIP	Combined samples
Sampling area in Germany	City of Mainz and County of Mainz-Bingen, Midwest	City and county of Augsburg, south	Western Pomerania, north-east	
Age at baseline	35–74	25–74	20–79	20–79
Inclusion criteria	► Residency in the study area.	► Residency in the study area. ► German nationality.	► Residency in the study area. ► German nationality.	
Exclusion criteria	► Physical or mental inability to participate at the study centre. ► Insufficient knowledge of the German language.	None	None	
Stratification	Age, sex and city/county of residence			
Sample size baseline	S1: 15010	S1: 4022 S2: 4940 S3: 4856 S4: 4261 Total: 18079	S1: 4308 Trend: 8016 Total: 12324	45413
Participation rate	53%	70%–80%	69% SHIP 55% TREND	53%–80%
Years baseline examinations	S1 2007–2012	S1 1984–1985 S2 1989–1990 S3 1994–1995 S4 1999–2001	SHIP 1997 –2001 SHIP-Trend 2008–2012	Starting 1984 ongoing
Number of follow-ups	4	2–3	4	4
Follow-up intervals	2 ½ (CATI), 5 years	5–7 years	After 5 years	2.5–7 years
Non-responder	Structured questionnaires for non-responders including cardiovascular risk factor profile, concomitant diseases, sociodemography.	Depending on sample.	Information about non-responders includes age, gender and the reason for not taking part.	
Quality assurance	Computer-assisted structured interviews with hard and soft bounds for manual data entry. Tape-based backup (up to 6 months) for regular plausibility checks and quality control. Standard operating procedures for the conduction of interviews; regular (re-) training for interviewers. Semi-automatised plausibility checks.	Tapes serve as a backup for plausibility checks, and a random sample was used to control interviewer performance. During data collection all researchers participating KORA study are required to provide a written internal quality control report about the protocol elements for which they are responsible in 3-month intervals.	All interview data were checked semiannually for interviewer bias during data collection. Independent auditors regularly reviewed a sample of 10% of all interviews.	

CATI, computer-assisted telephone interview; GHS, Gutenberg Health Study; KORA, Cooperative Health Research in the Augsburg Region; MONICA, monitoring trends and determinants on cardiovascular diseases; SHIP, Study of Health in Pomerania.

Germany) with 13427 men and women (response rate 77%) aged 25–74 years in 1984/1985 (S1), 1989/1990 (S2) and 1994/1995 (S3). Each sample was reassessed up to four times and thus assuring a prospective follow-up within the framework of the KORA[31]

SHIP started following the German reunification, in 1996 in the east of Western Pomerania, northeast Germany. It includes two samples (SHIP and SHIP-TREND) with a maximum of four follow-ups. In addition to regular follow-ups, all participants from the baseline sample (SHIP) were invited to participate in SHIP-Life Events and Gene–Environment Interaction in Depression (SHIP-LEGEND).[32 34] SHIP-LEGEND comprised comprehensive psychological assessments. A total of 2400 subjects participated.

Outcomes

As figure 1 shows, the primary outcomes refer to common mental disorders such as depression, anxiety, somatoform disorders; symptoms such as fatigue, sleep disturbances, suicidal ideation; and cognitive functions. A plethora of validated and established measures was used to span the

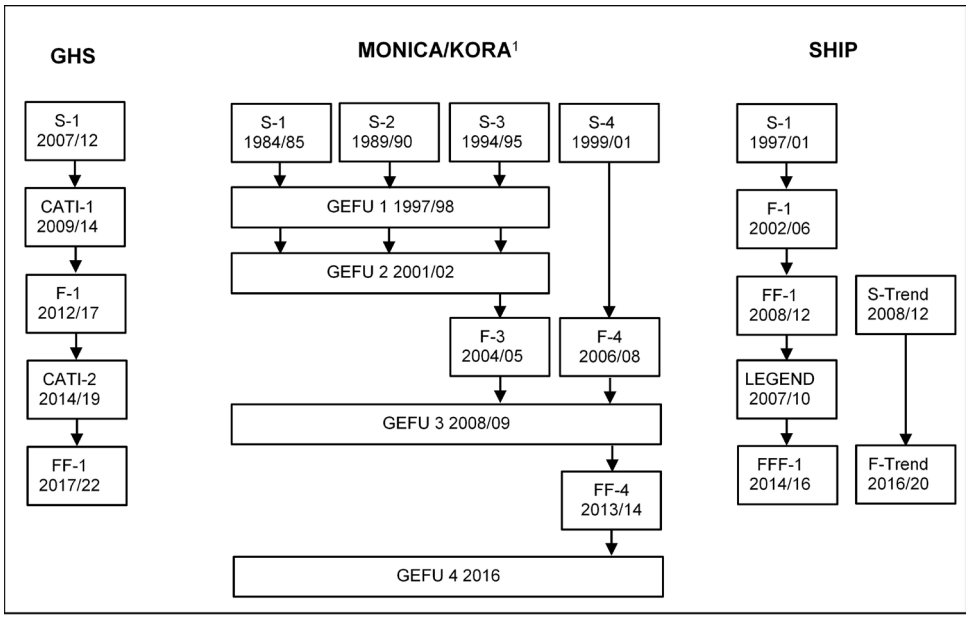

Figure 2 . Overview of cohort samples and assessment years. CATI, computer-assisted telephone interview; F, follow-up; FF, follow-up of the follow-up; FFF, follow-up of the follow-up of the follow-up, GEFU, postal general health follow-up; GHS, Gutenberg Health Study; KORA, Cooperative Health Research in the Augsburg Region; MONICA, monitoring trends and determinants on cardiovascular diseases; S, sample; SHIP, Study of Health in Pomerania. [1]Additionally, numerous smaller-scale examinations and surveys on special issues have taken place also older participants were examined within KORA age (includes participants ≥65 years from S1 to S4).

whole range of mental health-related symptoms. Except for cognitive functions all variables were assessed with self-report questionnaires that participants filled out on their own except for the computer-assisted telephone interviews (CATIs) assessments by the GHS. Additionally, SHIP-LEGEND assessed mental disorders in personal interviews using the Munich-Composite International Diagnostic Interview (M-CIDI)[35] by trained psychology students,[34] which diagnoses mental disorders according to the definitions of the Diagnostic Criteria for Research of ICD-10 and DSM-III-R. Secondary outcomes refer to healthcare behaviour and utilisation, subjective health status, quality of life and well-being. Again, measurements were taken as self-report or telephone interview. Table 2 gives an overview of the harmonised measures available in multiple cohorts. These shared measures will be complemented by measures available in single cohorts. The outcomes will be used for primary and secondary outcomes as depicted in figure 1.

While measures of sex are readily available in all cohorts, specific gender measures had not been previously implemented in them. To overcome this, we will create and validate a gender index similar to Smith and Koehoorn[19] and Pelletier and colleagues.[11] In the course of the harmonisation process, it became clear that the cohorts do not support using identical indexes. The GHS will derive a gender index by factor analysis from theoretically identified variables; especially, demographic variables (eg, education, contribution to household income) and indicators of quality and quantity of social relations to estimate the conformity with traditional feminine or masculine gender roles. Similar gender indexes will be established in each cohort. To cross-validate the indexes findings will be compared between cohorts.

To complement this gender index, which mainly measures gender roles and possibly institutionalised gender,[19] the new GHS wave (FF-1) added established measures of gender roles and identity. The German version of the Personal Attributes Questionnaire[20] was used to determine the sex-typing of personality. This self-report instrument consists of the two independent dimensions, 'expressivity' and 'instrumentality', corresponding to stereotypically feminine, respectively masculine traits. Earlier research has shown that people high on both scales show more positive health outcomes.[16 36] The German version of the Gender Role Orientation scale[37 38] was used to assess traditional normative expectations regarding men and women. Conformity to traditional masculine gender roles has been associated with negative mental health outcomes in men.[39]

Statistical analysis plan

We will perform secondary analyses on the three cohorts. Data will be analysed separately and jointly using aggregate statistics for evidence synthesis. Separate analyses will allow cross-validating findings from one cohort within the other, and we will test whether results generalise across samples and measures. Figure 3 gives an overview of the analytic procedures of GESA.

The data combination will rely on the DataSHIELD software infrastructure, which enables analyses that comply with data protection regulations by only sharing anonymous, aggregated data, while the individual data remain in the respective sites.[40 41] The data combination

Table 2 Harmonised variables per cohort

Constructed variables	Harmonisation process
Available for GHS, KORA and SHIP	
Depression	PHQ-9 scales or combination of PHQ-9 and BDI-2 recoded into binary variable
Suicidal ideation	Items from PHQ-9 and BDI-2, recoded into binary variable
Sleep problems	Question about falling asleep and PHQ-9 sleep item recoded into binary variable
Smoking status	Derived from several smoking variables including current and past habits, recoded into categories (regular/ irregular/ ex-smoker/ never smoked)
BMI	weight/height², continuous variable
Physical activity	Derived from variables of activities and doing sports, recoded into binary variable
Diabetes	Self-reported (diagnosed by doctor) and metabolic factors recoded into binary variable
Myocardial infarction	Self-reported (diagnosed by doctor), recoded into binary variable
Stroke	Self-reported (diagnosed by doctor), recoded into binary variable
Cancer	Self-reported, recoded into binary variable
Chronic disease	Any presence of diabetes, myocardial infarction, stroke and cancer, recoded into binary variable
Sex	Self-reported (male/ female)
Age (in years)	Self-reported or derived from birthday and study date
Education (in years)	Self-reported or derived from educational degree and work educational degree
Marital status	Recoded into categories married, not married/single, divorced, widowed
People per household	Self-reported participant and spouse, children etc., continuous variable
Living with partner	Similar questions in cohorts (yes/no)
Living alone	Derived from people per household (yes/ no)
Current employment	Derived from combination of employment variables, recoded into categories: no, fulltime, part-time, marginally employed
Household income	Ordinal variables with different categories per cohort, new metric variable constructed with mean value of income category per person
Available for KORA and SHIP	
Anxiety	Combination of GAD-7 and four CID items, recoded into binary variable (GAD-7≥9 as anxiety, any CID-S item score as anxiety)
PTSD	ICD-10 with four criteria: (A) traumatic event, (B) intrusion, (C) avoidance and (D) hyperarousal; fulfilment of A, B, C or D is coded as full PTSD, fulfilment of A and B, C or D is coded as partial PTSD, no fulfilment of A is coded as no PTSD
Alcohol consumption	Based on amounts and frequency of alcohol consumption, recoded into ordinal variable (categories: no, low, high)
Emotional abuse childhood	Combination of CTS item and CTQ item, similar answer categories, recoded into ordinal variable (five categories: not at all to very often)
Emotional neglect childhood Sexual abuse childhood Physical abuse childhood Physical neglect childhood	Combination of CTS and CTQ item, similar answer categories, recoded into one ordinal variable (five categories: not at all to very often)
Type 2 diabetes	Self-reported diabetes (diagnosed by doctor), metabolic factors and self-reported type of diabetes, recoded into ordinal variable (categories: no, yes, other type)
Parents with diabetes	Diabetes for mother and father each or combined, recoded into ordinal variable (no, father, mother, both)
History of myocardial infarction	Self-reported (diagnosed by doctor), recoded into binary variable
Hypertension	Blood pressure measures with same measurement units, recoded into continuous variable
Total cholesterol	Cholesterol measurement with different measurement units, recode measurement units and recoded into continuous variable

Continued

Table 2 Continued

Constructed variables	Harmonisation process
HDL-cholesterol	HDL-cholesterol measurement with different measurement units, recoded into continuous variable
Height (in cm)	Measured
Waist circumference (in cm)	Measured
Hip circumference (in cm)	Measured
Waist–height ratio	Waist circumference/height
Reason for retirement	Recoding categories and recoded into ordinal variable with three categories
Duration of unemployed (years and months)	Exact number or calculated from unemployment since certain date, recoded into continuous variable
Available for GHS and SHIP	
Pregnancy	Self-reported (yes/ no)
Lifetime unemployment	Recoded into binary variable
Children	Derived from having children and number of children, recoded into one continuous variable and one binary variable

BDI, beck depression inventory; BMI, body mass index; CID-S, composite international diagnostic screener; CTQ, Child Trauma Questionnaire; CTS, Childhood Trauma Screener; GAD, generalized anxiety disorder; GHS, Gutenberg Health Study; HDL, high-density lipoprotein; KORA, Cooperative Health Research in the Augsburg Region; PHQ-9, Patient Health Questionnaire; PTSD, post-traumatic stress disorder; SHIP, Study of Health in Pomerania.

use multivariate meta-analytic techniques[42] for data aggregation (eg, using covariance matrices). These techniques allow data combination without information loss (eg, regarding relative sample size) and are consistent with individual level analyses.

In a first step, univariate meta-analysis of regression estimates will be conducted. This will detect heterogeneity of effects (eg, assessed by I^2) between datasets as part of the meta-analytic approach. To limit heterogeneity, we will explore dataset exclusion and individual-level analyses to identify sources of heterogeneity. Remaining heterogeneity will be modelled using random effects. Differences in the availability of measurements between the cohorts in the course of time require extensive harmonisation prior to data combination. Thus, longitudinal regression models (that do not prescribe a fixed grid of times), with gender × time interactions, will be estimated at the three study centres as a basis for combination. Both analyses can uncover differences between different study and age cohorts. Further, the longitudinal regressions will yield joint sex-specific trajectories that describe the time course of common mental disorders (aim 1). We will also consider non-linear (ie, quadratic or exponential) terms, for example, for modelling mental disorder peaks in middle adulthood. These trends will be analysed for men and women potentially uncovering differences in peaks. Aggregate analyses of the sizeable cohorts enable us to perform differentiated analyses of subgroups (eg, minority populations such as migrants) within men and women.

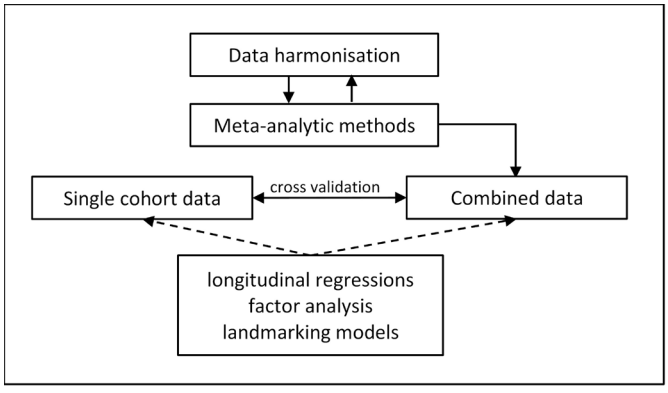

Figure 3 Overview of analysis plan GESA. GESA, GEnder-Sensitive Analyses of mental health trajectories and implications for prevention.

There is a considerable overlap regarding crucial concepts such as depression, which were assessed using both identical and different measures. For instance, each cohort included the Patient Health Questionnaire (PHQ-9)[43] as a measure of depression in at least two assessments. Additionally, the Depressed Mood/ Exhaustion scale,[44] the Geriatric Depression Scale (GDS-15),[45] the Hospital Anxiety and Depression Scale,[46] the CIDI[35] and the Composite International Diagnostic–Screener[47] were used. Data from multiple measures of the same concept will be converted into a common metric using Item Response Theory.[48] We plan to generate a gender-sensitive metric by separate analyses for male and female participants accounting for demographic and socioeconomic background.

The secondary objective (risks and protective factors; consequences of mental disorders) will also be addressed by longitudinal regression models, considering mental disorders, healthcare utilisation, quality of life and subjective health as outcomes (see table 2). Research teams will propose specific analyses to the steering committee for

approval. The analyses will test the effects of sex × time interactions with and without a gender index for the different outcomes. Different measurement times will be addressed by landmarking approaches, which can incorporate risk factors that have occurred up to a certain landmark lifetime.[49] Results from landmarking models, fitted at each centre, will be combined by multivariate meta-analysis. For factors that are absent for one of the cohorts, imputation approaches (based on relations obtained from the other cohorts) will be considered.

Data collection, management and oversight

Each cohort puts strong emphasises on data quality by frequently training interviewers, physicians and any personal interacting with participants. To complement training all current interviews are computer-assisted. All cohorts can build on a long history of research and field work. The implementation of standard operating procedures and the employment of qualified personnel lead to a high level of quality and efficiency in the realisation of studies. Data are managed at the single cohort centres following well established standards. Data aggregation is supervised by Prof Dr Binder at the University of Freiburg.

PATIENT AND PUBLIC INVOLVEMENT

The BMBF's call determined the overarching goal to conduct gender-sensitive analyses to improve disease prevention and promote lifelong health. The investigators, who are in continuous contact with key stakeholders, especially, German sickness funds, the German statutory pension insurance and patient advocacy groups, continue to specify the research questions.

Ethics and dissemination

Dissemination policy

Yearly in-person meetings supplement monthly telephone conferences between principle investigators and other researchers. The yearly meetings are supported by the scientific advisory board (Eric Brunner, Alexandra Kautzky-Willer, Eva Prescott and Monika Sieverding). Due to the duration of the data harmonisation process, mayor healthcare organisations and other stakeholders (eg, sickness funds, patient advocacy groups) are planned to join the in-person meetings in the last period of the project. The investigators will develop further strategies for dissemination, which will be adjusted to the regional demands. They will be coordinated and approved by the advisory board.

DISCUSSION

Population-based designs with register-based sampling of participants offer the highest external validity. The longitudinal data will provide evidence on the temporal course and potential causal relations between gender, risk and protective factors and mental disorders. A strength of the combined samples is that they originate from different German regions, with different socioeconomic or regional characteristics, such as economic parameters: Unemployment rates are highest, discretionary incomes, and life expectancy lowest in Greifswald (SHIP). Mainz (GHS) and Augsburg (KORA) are economically stronger regions with Mainz (GHS) showing slightly higher discretionary incomes. These regional differences allow us to compare effects of relative and absolute deprivation. For historical reasons the study regions show pronounced differences regarding full-time employment rates among mothers resulting in different gender pay gaps.[50] Further, life expectancy is highest in Mainz (GHS), while Greifswald (SHIP) shows the lowest life expectancy and the biggest gender gap.[51] Combining the three studies will allow a more complete representation of the German population (eg, former eastern and western regions) and a bigger set of measures, even though the data harmonisation process poses a considerable challenge. Separate analyses will allow cross-validation. The application of novel analytical methods (ie, network analyses across lifespan) may become a blueprint for other multi-cohort studies. The purpose of our cohort is to fill the gaps of gender-sensitive knowledge of mental health and to provide the basis for scientifically grounded strategies of gender-sensitive health promotion and prevention.

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Contributors All authors contributed to the development and refinement of the GESA consort. MB, EB, JB, HB, HG, JK, KL, GS and PW are grant holders. JB and MB drafted the first version of the GESA grant proposal, which was thoroughly revised by all authors. Based on this proposal JB, AT and MB drafted the first version of the study protocol, which was substantially revised by DO and subsequently refined and approved by all authors.

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Disclaimer The BMBF had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Competing interests HJG has received travel grants and speakers honoraria from Fresenius Medical Care, Neuraxpharm and Janssen Cilag. HJG has received research funding from the German Research Foundation (DFG), the German Ministry

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Patient consent for publication Not required.

Ethics approval The cohorts were approved by the ethics committees of the Statutory Physician Board of Rhineland-Palatinate (GHS: 837.020.07; original vote: 22.3.2007, latest update: 20.10), the University of Greifswald (SHIP: BB 39/08; original vote: 19.6.2008) and the Bavarian Chamber of Physicians (Bayerische Landesärztekammer; KORA: 06068). All participants have given written consent and have the right to withdraw their consent at any time. Local data protection officers supervise and monitor protection of participants' data.

Provenance and peer review Not commissioned; externally peer reviewed.

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