COMPLEMENTARY INFORMATION ON ASSESSEMENTS OF COLAUS|PSYCOLAUS

CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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I) Complementary information on the baseline evaluation

1. Somatic part

1.1. Screening instruments for cognitive disorders and psychopathology

Mini-Mental State Evaluation (MMSE) was administered to subjects older than 65 years of age. The MMSE(*1*) is comprised of two sections, the first using verbal responses to assess orientation, memory and attention, the second assessing the ability to name objects, to carry out a verbal or written instruction and to spontaneously write a sentence or reproduce a geometrical figure. The test is used to screen for cognitive deficiency, to evaluate its intensity and to measure changes in states of confusion and dementia in older subjects. The MMSE has shown satisfactory concurrent validity with the Wechsler Intelligence test and the French translation was validated by Hoff(*2*).

General Health Questionnaire (GHQ12) was applied in order to screen for the presence of non-psychotic psychiatric disorders. The GHQ12 is a short version of the GHQ developed by Goldberg(*3*). This screening instrument assesses psychopathological symptoms experienced over the previous weeks. Many epidemiological and medical studies have used this questionnaire as it allows for the assessment of severity of psychological suffering (dimensional approach) and distinguishes between subjects in terms of psychiatric caseness (categorical approach). In France, Pariente et al.(*4*) confirmed the validity of the GHQ-28 instrument in terms of its factor structure and screening qualities. The French version of the GHQ-12 instrument is a similar short version of this instrument.

1.2. Additional phenotypic investigations in 2 subsamples

AngioLaus (P.I.: D. Hayoz, completed 2007):

Including 400 hypertensive and 100 control subjects aged 55-75 years the following variables were measured:

a) Intima media thickness (IMT) and vascular plaques (carotid and femoral artery) by high resolution ultrasound
b) Arterial compliance and pulse wave velocity
c) Central arterial pressure (Sphygmacor®)
d) Endothelial function with reactive hyperemia

Hercule (P.I.: M. Burnier, completed 2009):

Including 400 randomly selected subjects aged 35-75 with the following assessment:

a) Ambulatory 24-hour blood pressure measurement (ABPM)
b) 24 hour urine collection in parallel to ABPM (separate day and night collections): Na, K, Ca, urate, creatinine excretions and clearances
c) Lithium clearance as a marker for proximal tubule sodium reabsorption.

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PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
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2. Psychiatric part

2.1. Interviews

Diagnostic Instrument for Genetic Studies (DIGS)

The Diagnostic Interview for Genetic Studies (DIGS)(*5*) was used to collect diagnostic information. Its goal was the more precise assessment of phenotypes through 1) a semi-structured design corresponding to a wide spectrum of DSM-IV Axis I criteria including mood, anxiety, psychotic and specific substance use disorders as well as suicidal behavior and 2) the collection of extensive information on the course and chronology of comorbid conditions. An updated version of the DIGS includes DSM-IV criteria (NIMH Molecular Genetics Initiative 1995).

The DIGS was translated into French in a collaborative effort from sites in France (INSERM, Paris) and Switzerland. Inter-rater and test-retest reliability of the French version were established in a clinical sample in Lausanne(*6*). Excellent inter-rater reliability was found for schizophrenia, bipolar disorder, major depression and unipolar schizoaffective disorder while fair inter-rater reliability was demonstrated for bipolar schizoaffective disorder (Table 1). Using a six-week test-retest interval, reliability for all diagnoses was found to be fair to good except for bipolar schizoaffective disorder. High kappa coefficients for inter-rater reliability and slightly lower kappas for test-retest reliability were also found for drug and alcohol as well as antisocial personality diagnoses (Table 2)(*7*). We also observed the age of onset of alcohol and drug disorders to be reliable as well as, to a lesser extent, the order of onset between depression and substance use disorders. Reliability was also established for subthreshold depressive (Yule's Y=0.91) and manic (Yule's Y=0.89) syndromes.

Table 1: Inter-rater and test-retest reliability for major mood and psychotic disorders(*6*)

	Inter-rater		Test-Retest	
Diagnosis	Kappa	95% C.I.	Kappa	95% C.I.
Psychosis	0.88	0.71-1.00	0.63	0.44-0.83
Schizoaffective bipolar	0.60	0.44-0.77	0.38	0.23-0.53
Schizoaffective unipolar	0.87	0.70-1.00	0.48	0.29-0.67
Bipolar I / Bipolar II	0.85	0.68-1.00	0.63	0.43-0.83
MDD / Dysthymia	0.93	0.78-1.00	0.62	0.42-0.81
No target diagnosis	1.00	0.83-1.00	0.65	0.45-0.84

Table 2: Inter-rater and test-retest reliability for substance use disorders(*7*)

Substance	Inter-rater			Test-Retest		
	Dependence or abuse	Dependence	Abuse	Dependence or abuse	Dependence	Abuse
Alcohol	0.98	0.79	0.65	0.72	0.73	0.19
Drug	1.00	1.00	1.00	0.93	0.77	0.52
Cannabis	0.94	1.00	0.88	0.80	0.64	0.63
Cocaine	1.00	1.00	1.00	0.59	0.48	0.80
Opiates	1.00	1.00	0.39	1.00	0.95	-
Sedatives	1.00	1.00	-	0.82	0.71	-
Hallucinogens	0.87	0.91	-	0.65	0.73	-
Inhalants	1.00	1.00	-	0.72	0.77	-

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1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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The DIGS also allows the establishment of the overall Global Assessment of Functioning (GAF) as well as a GAF score for each specific disorder. Modifications of the French version involved the following sections:

- Major Depression: 1) in addition to the questions on increased appetite and hypersomnia, complementary questions were included on leaden paralysis, long standing patterns of interpersonal rejection sensitivity as well as mood reactivity, in order to be able to assess atypical depression features; 2) a question asking about the maximal number of episodes within a 12-month period was integrated in order to be able to diagnose brief recurrent depression; 3) questions on the clinical characteristics of the first episode in life (in addition to the regularly investigated most recent and most severe episodes) were added in order to obtain a better picture of the course of the disorder.
- Anxiety disorders: 1) The GAD chapter was added using the questions from the Schedule for Affective Disorders and Schizophrenia - Lifetime Version (SADS-L)(*8*); 2) the brief phobia chapter of the DIGS was replaced by the corresponding more extensive chapters from the SADS-L.
- Nicotine use: The original DIGS section on nicotine consumption has been extended to elicit DSM-IV abuse and dependence criteria.

Moreover, a page on mood disorders in connection with a lifetime review designed to facilitate active memory search for lifetime episodes summarizes all mood episodes, their duration and major clinical features (threshold vs. subthreshold; manic vs. mixed vs. depressed; with vs. without psychotic features) in order to obtain a more accurate assessment of the course of disorders.

Diagnostic Interview for Headache Syndromes (DIHS)

Persons who endorsed either headache or migraine in the DIGS went on to complete the semi-structured DIHS(*9*). This interview was developed through inter-site collaboration centered at the Genetic Epidemiology Research Unit of Yale University School of Medicine for an observational study of chronic daily headache. Its inter-rater reliability for overall migraine was high (kappa = 0.83), while reliability for migraine subtypes was adequate (kappa =.60) (Kathleen Merikangas, personal communication). The DIHS was translated into French by our research group.

Short interview of F. Amiel-Lebigre

In order to assess life events, the short interview of F. Amiel-Lebigre was employed(*10*). This instrument elicits information on 53 types of life-events (including time of occurrence, duration and impact of the event). It was validated by its originators(*11, 12*).

Family History-Research Diagnostic Criteria (FH-RDC)

In order to obtain an estimate of the familial aggregation of the assessed mental disorders prior to the family study currently conducted, a translated modified version of the FH-RDC developed by Andreasen et al.(*13*) was administered. The instrument allowed for the collection of diagnostic data of the participants' first-degree relatives and partners. The modified FH-RDC version was developed for the Yale Family Study in order to obtain DSM-III and DSM-III-R diagnoses in adults and children, but DSM-IV and DSM-5 diagnoses can also be made. The family history instrument was recently validated against direct diagnostic interviews for diagnoses of mood(*14*), anxiety(*15*) and substance use disorders(*16*) as well as for diagnoses in children(*17*).

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Switzerland
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Fax: +41 21 314 84 69
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2.2. Self-rating scales

State-Trait Anxiety Inventory (STAI)

The STAI(*18*) is a widely used and validated instrument for the evaluation of both current (state) and lifetime (trait) anxiety. Each of the two scales is comprised of 20 questions. The correlation between the corresponding items of the two scales was between 0.59 and 0.75. The test-retest reliability of the French version(*19*) was 0.71-0.75 within 30 days and 0.65-0.68 within 60 days. The correlation between the STAI and the Neuroticism scale of the EPQ was 0.71.

Retrospective Self Report Childhood Inhibition (RSRCI)

Behavioral inhibition is considered as a temperamentally based predisposition of children to react consistently to unfamiliar events with initial restraint. Inhibited children in particular express fear in the presence of novel stimuli or sometimes even familiar ones. There is some evidence to suggest that it is a stable trait. A 31 item instrument to retrospectively assess childhood inhibition in parents (RSRCI) and current behavior inhibition in children (CRSRCI) was developed by Reznick et al.(*20*). The questionnaire has two subscales to evaluate a fear and a school dimension of behavioral inhibition. The overall score is reported to correlate with the State-Trait Anxiety Inventory and the Center for Epidemiology Studies Depression Scale(*20*). Our research group established a French version of this instrument and tested its validity. The postulated two factor structure could be replicated(*21*).

Dimensions of Temperament Survey (DOTS) / Dimensions of Temperament Survey – Revised version (DOTS-R)

The DOTS(*22*), a temperament scale of 34 dichotomous items developed for children and adults, was translated into French for use in our bipolar study. This instrument can be administered by self-report or interview (for children between 5 and 8 years). The 5 temperament dimensions: Activity level, Attention span/distractibility, Adaptability/approach withdrawal, Rhythmicity and Reactivity were obtained by maximum-likelihood exploratory factor analysis and promax rotation(*22*). The original English instrument was extensively tested in 1,386 subjects of 3 age groups (nursery school children with reports of mothers on children, 11-year old elementary school and 21 year old college students with self-reports). The 5 postulated factors could also be replicated using the French version.

Considering the psychometric problems of the DOTS, Windle and Lerner(*23*) developed an improved instrument, the DOTS-R. This scale contains 54 items (responses according to a 4-level likert scale) to elicit 9 temperament dimensions: Activity level - general, Activity level - sleep, Approach - withdrawal, Flexibility- rigidity, Mood, Rhythmicity - sleep, Rhythmicity - eating, Rhythmicity - daily habits, Task orientation, which were obtained by maximum-likelihood exploratory factor analysis. In adults, the task orientation factor splits into Distractibility and Persistence. The English DOTS-R was extensively tested in preschoolers, sixth-graders and undergraduate students. Our research group has established a translation of the DOTS-R. In the study on school children and their parents we could replicate the factor structure of the instrument. In order to maintain comparability to the baseline assessment and take advantage of the revised version both instruments are included in the follow-up battery. However, questions which were part of both DOTS versions are only asked once.

Eysenck Personality Questionnaire (EPQ)

The EPQ(*24*) is a 90-item self report personality inventory that has been widely used for personality assessment in psychiatry and other medical fields. The four factor analytically derived dimensions are Extraversion, Neuroticism, Psychoticism, and social desirability (Lie scale). A validated French version of the instrument is available(*25*). The factor analytic examination of the French version revealed four factors which corresponded closely to those originally

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CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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found in England(*25*). Reliability of the resulting scales, and correlations between factors, were also found to be similar to those of the English version.

The Bortner Scale (Type A Personality)

The Bortner Scale(*26*) is a self-rating questionnaire designed to evaluate the type A behavior as described by Friedman and Rosenman(*27*). Type A behavior was found to be associated with Cardiovascular Disease (CVD) and especially Coronary Heart Disease (CHD). The questionnaire includes 14 visual analogical scales (VAS) ranging from 1 to 24. Each of the scales is supposed to reflect one characteristic of Type A behavior. The French version was established by Pichot et al.(*28*) and widely used by the French-Belgian Collaborative Group (1977, 1982). It has a test-retest reliability of 0.71(*29*) and correlates with the Type A subscale of the Jenkins Activity Survey(*30*).

Euronet: Problem resolution strategies

The Euronet questionnaire developed by Grob et al.(*31*) covers 3 domains: 1) daily constraints, 2) problem resolution strategies, and 3) well-being of adolescents. We will only use the second part of the instrument which contains 17 items (4-level Likert scale) on possible reactions in problematic situations. This factor can be split into 2 subscales: Active problem resolution strategy (8 items) and Emotional problem resolution strategy (5 items). The instrument was tested by its originators in a population based sample of German- and French-speaking 12 to 18 year-old school children in Switzerland. The Cronbach alphas of the Active and the Emotional problem resolution strategy were 0.49 and 0.54, respectively(*32*). The French version of the instrument was also validated in adults using the data from PsyCoLaus and revealed a 3-factor solution including the dimensions of Emotion-focused coping (alpha=0.65), Help-seeking (alpha=0.69) and Problem-focused coping (alpha=0.44)(*33*).

Family Attitude Scale (FAS)

The FAS is a 30-item instrument which measures the emotional climate of families (Expressed Emotion)(*34*). Answers are coded on a 5-level likert scale. The FAS was tested in families of university undergraduates as well as in families of psychiatric patients(*34*). The instrument revealed very high internal consistency (Cronbach alpha between 0.95 and 0.97 in adolescents and their parents). It correlated in the expected direction with the hostility, high criticism and low warmth dimensions of the Camberwell Family Interview. This self-report was translated into French and validated in the PsyCoLaus adult data by our research group and revealed an excellent one-factor solution with an alpha coefficient of 0.96(*35*). The FAS scores of respondents were affected by their mood, anxiety and alcohol psychopathology, and showed a moderate reciprocity of attitudes and behaviors with those of their partners(*35*).

Parental Bonding Instrument (PBI-M, PBI-F)

The PBI(*36*) is a self-report measure of fundamental parental dimensions of care and protection which has been used to quantify any parental contribution to subsequent psychiatric disorders. This self-report is designed for completion by subjects at least 16 years of age who score each of their parents on 25 attitudinal and behavioral items (each with a 4-point scale) retrospectively for the first 16 years of life. The test-retest reliability for the English version of this instrument was high with correlation coefficients ranging from 0.79 to 0.96(*37*). The high stability of this instrument over a period of 34 weeks was demonstrated in a community sample(*38*). The validity of the PBI was examined by comparing subjects' PBI scores to their mothers' scores, yielding moderate levels of agreement, 0.44 for care and 0.55 for protection(*39*). This study showed that interviewers blind to PBI scores discriminated PBI-determined over-protective mothers as significantly more over-protective and dependency-inducing at interview than the others(*39*). The resistance of the instrument to contamination by symptoms or mood state was also demonstrated(*39*).

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Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
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Our group revealed the French version of the PBI to have comparable psychometric properties to the original version(*40*). Similar to recent findings(*41, 42*), our results support a three-factor rather than the two-factor structure of Care and Overprotection posited by Parker, with the further partitioning of the protection factor into a positive (Encouragement of behavioral freedom) and negative pole (Denial of psychological autonomy).

Family Adaptability and Cohesion Evaluation Scale (FACES III)

FACES III is the third version of the Family Adaptability and Cohesion Evaluation Scales developed by Olson et al.(*43*). The self-report scale was developed to assess two major dimensions of family functioning, namely Cohesion (10 items) and Adaptability (10 items), in a more adequate and systematic way. The concept of family Cohesion incorporates elements such as emotional bonding, supportiveness, family boundaries, time and friends, interest in recreation as well as the notion of autonomy(*44*). The concept of family Adaptability incorporates elements such as leadership, control, discipline, roles and rules(*44*). The instrument is applied to assess how each family member perceives their own family currently (real version) as well as how they would like it to be (ideal version). The discrepancy between perceived and ideal versions provides an indirect measure of family satisfaction. The ideal version provides information on the individual's direction and amount of desired change of the family system. Reliability, internal consistency and test-retest reliability are generally good. Internal reliability scores (Cronbach alpha) of 0.77 for Cohesion and 0.62 for Adaptability were obtained(*45*). Regarding construct validity, the correlation between Cohesion and Adaptability as well as the correlation between social desirability and Cohesion/Adaptability have been reduced to almost zero.

With respect to our French translation, the results of both adult and adolescent confirmatory factor analyses were compatible with a two-factor structure, similar to that proposed by the authors of the original instrument(*46*). Internal reliability estimates were 0.78 and 0.68 in adolescents and 0.82 and 0.65 in adults, for Cohesion and Adaptability respectively.

Dyadic Adjustment Scale (DAS)

The DAS(*47*), a widely used assessment for four dimensions of marital adjustment, will be administered to probands and their spouses. This 32 item scale was derived from a factor analytic study of all available instruments for measuring marital quality, distress, and/or adjustment. The four subscales are: Dyadic Satisfaction, Dyadic Cohesion, Dyadic Consensus and Affectional Expression. Spanier(*47*) presented substantial evidence for its reliability and construct validity. In developing the scale, the author attempted to provide a measure that examines the process of dyadic adjustment rather than a static phenomenon. The scale is easy to administer and can be completed in a few minutes.

A French version of the scale was established and its validity was tested by Baillargeon et al.(*48*). The Canadian study revealed similar characteristics to the original scale. The validity of the French version was further established by our group using confirmatory factor analysis. Our validation also revealed the French translation to possess similar characteristics to the original scale(*49*). Lower dyadic adjustment as measured by the DAS was shown in PsyCoLaus to be associated with more hostile attitudes of respondents towards their marital partners(*35*).

MOS-Sleep Module

The MOS-Sleep Module is a 12-item self-report to measure the quality of sleep during the past 4 weeks(*50*).

Sensitivity to Reward (STR)

Sensitivity to Reward (STR) will be assessed using a 30-item self-report scale derived from the Sensitivity to Reward Scale(*51*). Items are rated on a 6-level Likert scale. The instrument was designed to assess both appetitive and the

consummatory sensitivity to reward. Factor-analytic procedures identified 4 moderately correlated factors: Sensory Pleasure assesses the degree of pleasure derived from visual, auditory, olfactory, and tactile stimuli; Physical Activity assesses the hedonic reward experienced from physically active pursuits; Food and Comfort reflects the pleasure experienced from eating and relaxation; and Hedonic Motivation assesses the appetitive aspect of a range of rewarding stimuli. The internal consistency of the scale is good, and preliminary validation of the factors has been demonstrated by the authors with three separate samples.

II) Complementary information on the first follow-up (FU1) evaluation

1. Somatic part at FU1: added self-rating scales

Questionnaire alimentaire Bus Santé - food frequency questionnaire (FFQ)

The assessment of diet is done with the "Questionnaire alimentaire Bus Santé", a self administered semi quantitative food frequency questionnaire (FFQ). The FFQ covers the 4 weeks prior to the day of data collection. It was developed and validated in the general adult population of Geneva, Switzerland(*52, 53*) and is currently used for the Bus Santé follow-up. It comprises a list of about 80 food items and their serving sizes. Food intake data can be converted into daily energy and nutrient intakes.

Physical activity frequency questionnaire (PAFQ)

Physical activity is assessed with a self administered quantitative physical activity frequency questionnaire (PAFQ) developed in the Geneva general adult population and validated using a heart rate monitor(*54*). It is designed to measure respondent's total and activity specific energy expenditures. The questionnaire is completed for the last 7 days.

Epworth Sleepiness scale (ESS)

The Epworth Sleepiness scale (ESS), a self administered questionnaire, which provides a measurement of the subject's general level of daytime sleepiness(*55*). ESS scores distinguish normal subjects from patients in various diagnostic groups including those with obstructive sleep apnea syndrome, narcolepsy and idiopathic hypersomnia.

Ullanlinna Narcolepsy Scale (UNS)

This self administered screening questionnaire of eleven items was validated in narcoleptic patients by Hublin et al.(*56*). In this study, UNS had 98.8% specificity and 100% sensitivity in distinguishing narcoleptics from other diagnostic groups.

Berlin questionnaire

This questionnaire screens for risk of sleep apnea and was developed by Netzer et al.(*57*). Questions survey the presence and frequency of snoring, daytime sleepiness or fatigue and high blood pressure.

Circadian typology questionnaire

The questionnaire developed by Horne and Ostberg assesses circadian typology i.e. morningness and eveningness(*58*). It has been translated in French and validated by Taillard et al.(*59*).

Pittsburgh sleep quality index (PSQI)

The Pittsburgh sleep quality index, a self administered questionnaire, assesses sleep quality and disorders for the month preceding the evaluation(*60*). In particular subjective sleep quality, sleep duration, efficiency, use of hypnotics and poor daytime functioning are screened.

Restless Leg Syndrome (RLS) screening questionnaire

Presence of RLS is screened using a self administered questionnaire based on the 4 basic diagnostic criteria of RLS developed during and international NIH workshop and approved by the International Restless Legs Syndrome Study Group(*61*). In CoLaus, subjects with periodic limb movements during sleep measured during the polysomnography exam also had a higher proportion of restless legs syndromes according to the RLS questionnaire(*62*).

Munich Parasomnia Screening (MUPS)

This 21-item screening questionnaire assesses the lifetime prevalence and current frequency of parasomnias and unusual nocturnal behaviors in adults(*63*).

Persistent pain and the TnsSofres questionnaire

Persistent pain (>3 months) is screened with the self administered TnsSofres questionnaire assessing the presence of pain for more than 3 months and its localization. This instrument has been applied in a population based study(*64*).

The Center for Epidemiologic Studies Depression Scale (CES-D)

The CES-D(*65*), a 20 item self-report instrument developed for research in the general population is used to assess the severity of depressive symptoms over the past week on a 4-point scale. It was translated into French by Fuhrer and Rouillon(*66*). It has been used in other recent epidemiological studies assessing the link between depression and cardiovascular risk factors.

2. Psychiatric part at FU1

2.1. Added investigations: Screening of cognitive impairment (CognoLaus)

Screening of cognitive impairment in subjects aged from 65 to 80 years was introduced based on the Do 80 (Epreuve de dénomination orale d'images(*67*)), the Cognitive Complaint Questionnaire(*68*), the Grober and Buschke episodic memory test(*69*), the CERAD praxis items(*70*),the lexical and semantic fluency tasks(*71*) and the Stroop color test(*72*). Severity staging was based on the Clinical Dementia Rating (CDR(*73*)).

2.2. Added self-rating scales

Symptom Check List 90 Revised (SCL-90 R)

The SCL-90 R(*74*) is a list of symptoms in the form of 90 questions. A 10-factor structure was first found for the following domains: Somatization, Obsessions, Sensitivity, Depression, Anxiety, Hostility, Phobia, Paranoid traits, Psychotics traits, and other symptoms. Three of the original ten factors (Depression, Somatization and Panic-agoraphobia) were replicated in a subsequent study using a large French general psychiatric outpatient sample(*75*). Our group further conducted factor analysis on the French version of the SCL-90-R in a general population sample of parents of school-children and analyses revealed similar results to those of Pariente et al.(*76*).

The DS14 (Type D Personality)

The DS14 questionnaire was developed and validated by Denollet(*77*). The scale yielded two factors encompassing Negative Affectivity (NA) which covers dysphoria, worry and irritability, and Social Inhibition (SI) which covers discomfort in social interactions, reticence and lack of social poise. The NA and SI scales were internally consistent, stable over a 3-month period, not dependent on mood or health status and correlated positively with the Neuroticism and negatively with the Extraversion dimensions of the NEO-Five Factor Inventory(*77*). The scale was translated into French for the study and will subsequently be validated with the data from the study population.

Hypomania Checklist-32 first revised version (HCL-32-R1)

The HCL-32-R1(*78*) is a self-rating questionnaire developed to assess a lifetime history of hypomanic symptoms in normal subjects and out-patients as well as for screening patients with a diagnosis of depression (Major Depressive Disorder, Dysthymia, Minor Depression, Recurrent Brief Depression) for hypomanic symptoms. The 32 items of the checklist load on two separate factors, which were replicated in patient and general population samples and were labeled "active/elated" and "irritable/risk-taking"(*79*). In a study testing the transcultural robustness of the instrument in 2,606 patients from twelve countries, Angst et al.(*80*) found the frequency of the 32 items to show remarkable similarities across geographic areas. The scale was translated into French by Angst and colleagues(*78*) and validated in the PsyCoLaus data, where confirmatory factor analysis and item response theory models supported the postulated two-factor structure similar to the original version(*81*). Therefore, the screening properties of the HCL-32 for bipolar disorder remained good, while two previously proposed shorter versions of the scale were found to perform just as well(*81*).

Multidimensional Scale of Perceived Social Support (MSPSS)

The MSPSS was developed by Zimet et al.(*82*) to assess the degree of social support subjects may benefit from three sources (family, friends and a special person). This questionnaire showed satisfactory psychometric properties with alpha coefficients ranging from .90 for the family subscale to .94 for the friends subscale and .95 for the significant others subscale(*83*). The questionnaire was translated for the study and was found to be significantly associated with perceived quality of life(*84*).

Manchester Short Assessment of Quality of Life (MANSA)

The MANSA questionnaire was developed by Priebe et al.(*85*) to assess the degree of quality of life subjects may benefit from. Recently, quality of life as measured by the MANSA has not only been shown to be influenced by depressive symptoms during the course of schizophrenia(*86*), but also by symptoms in neurotic and mood disorders(*87*). This questionnaire was translated for the study.

NEO Five-Factor Inventory (NEO-FFI-R) - revised

The NEO-FFI-R(*88*), a personality inventory which was derived to improve the 5-factor NEO-FFI by replacing several problematic items, has been shown to have adequate construct validity and measures the five personality dimensions of Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness. It was translated into French by Jean-Pierre Rolland et Jean-Michel Petot and was validated in a study assessing its factor structure and reliability estimates in a French-speaking Swiss sample compared to a Spanish translation assessed in Spain. Indeed, three shorter versions of the original longer NEO-PI-R including the NEO-FFI-R revealed satisfactory psychometric properties in both samples(*89*). In PsyCoLaus, the NEO-FFI-R was shown to have lower response validity and

reliability in subjects with bipolar disorder, showing potential bias of these subjects in responding to personality questionnaires(*90*).

3. Additional investigations at FU1

3.1. HypnoLaus

(P.Is.: Dr R. Heinzer, Prof. M. Tafti)

This sub-study included the following assessments:

- Polysomnography, including
  - Nocturnal EEG (sleep structure)
  - Nocturnal ECG (nocturnal arrhythmia)
  - Oxygen saturation during sleep (nocturnal hypoventilation, sleep apnea)
  - Chest and abdominal bands (breathing patterns, sleep apnea)
  - Leg electrodes (periodic leg movements during sleep)
  - Body posture (positional sleep apnea)
- Self-rating questionnaires on subjective sleep quality, current medication and alcohol intake filled in by the subjects in the morning after the polysomnography.

The aim of the HypnoLaus was to analyze sleep characteristics in a large population-based sample (CoLaus Cohort) and to assess their associations with cardio-vascular risk factors and mental health. With more than 2100 subjects randomly selected from the CoLaus cohort at the FU1, HypnoLaus is the largest population based sleep cohort worldwide.

3.2. OsteoLaus

(P.Is.: Prof O. Lamy, Prof. D. Hans)

The evaluation included the following assessments:

- Spine and hip bone mineral density (Discovery A®, Hologic, USA)
- A blind processing of lumbar Trabecular Bone Score (TBS, iNsight v1.9, medimaps, France) based on a previously acquired spine densitometry
- Vertebral fracture assessment using the semiquantitative approach of HK. Genant (independent evaluation by 2 experts)
- Heel ultrasound (GE Healthcare Lunar Achilles, USA)
- FRAX® Swiss (10-year probability of hip and major osteoporotic fracture)
- Whole body composition (Discovery A®, Hologic, USA) in a subset of 800 women
- A questionnaire about clinical risk factors for fracture/osteoporosis

More than 1500 randomly selected women aged 50-80 years took part in this sub-study at FU1.

4. Psychiatric evaluation of offspring

For this nested project "Psychiatric evaluation of offspring younger than 18 years" (Prof. JM. Aubry) that is still ongoing, we could select 561 offspring who were younger than 18 years at the moment of recruitment. Among them, 69.0% have already undergone at least one follow-up evaluation.

4.1. Interviews

Kiddie-Schedule for Affective Disorders and Schizophrenia – Epidemiologic version (K-SADS-E)

The translated version of the K-SADS-E was used to gather diagnostic information. The interview is composed of sections that elicit information about the child's demographics, general medical and neuropsychiatric history, as well as a social adjustment section. The K-SADS-E has been found to be a reliable and valid instrument for obtaining lifetime diagnoses on pre-pubertal children(*91*), and older children as well(*92*). Inter-rater reliability analyses of video-taped interviews of hospitalized children using our French translation revealed high kappa coefficients for depression (.84), for separation anxiety disorder (.86) social phobia (1.0) and psychosis (1.0)(*93*).

Assessment of headache and migraine (see baseline description for details of the DIHS interview)

Junior High Life Experiences Survey (JHLES), lifetime version

This semi-structured interview is designed to gather information (age and frequency) on 35 types of life-events in adolescents(*94*). The interview was translated into French by M. Bolognini of the Child Psychiatric Department of Lausanne.

4.2. Self-rating scales

State-Trait Anxiety Inventory for children (STAIC)

A version of the STAI (see baseline assessments) for children and adolescents (STAIC) is available in English(*18, 19*) and was translated into French by Vera and Nollet in France. In our study of school children and their parents, we have obtained normative data for the French part of Switzerland.

Eysenck Personality Questionnaire - Junior (EPQ-Jr)

Similar to the EPQ (see baseline assessments), the EPQ -Jr was also developed by Eysenck to elicit the same four personality dimensions as the adult version. The child instrument contains 81 items. Our group translated this questionnaire and tested its validity. We found a similar structure to the original version as the four factors could be successfully replicated(*95*). Internal reliability estimates were 0.84 for Neuroticism, 0.74 for both Extraversion and the Lie scale and 0.69 for Psychoticism, respectively.

Child Behavior Checklist (CBCL)

The CBCL is a 130 item questionnaire divided into two sections which measure social competence and behavioral problems(*96*). Subscales were derived from factor analysis. Normative and standardized data which allow the children to be compared to others of their age and sex are available. The overall validity and reliability are high. A French version was developed(*97*) and found to have similar levels of reliability and validity.

CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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Daily Hassles

The Daily Hassles Evaluation Scale was developed by Bolognini et al.(*98*). The 59 items (5-level likert scale) of this questionnaire assess 4 areas of daily hassles: 1) family, 2) school, 3) peers, 4) self-perception.

Pubertal Development Scale

The Pubertal Development Scale was created by Petersen et al.(*99*) The instrument contains 7 questions on growth, height, weight, body hair, skin, breast development, menstruation and voice changes for boys and girls. Validity testing was done by the originators of the scale. Our group established a French translation of the instrument.

Cyclothymic / HypersensitiveTemperament Scale

The French version of the Cyclothymic / Hypersensitive Temperament Scale was created by Kochman et al.(*100*). The instrument contains 25 items on cyclothymic / hypersensitive temperament traits. Validity testing of the scale was conducted by the originators and factor analysis revealed the two series of items to load on separate factors (cyclothymia versus hypersensitivity)(*101*). The two dimensions operationalize the affective nature of temperament including intensity of reactions, switching between extremes, extroversion, impulsivity, energy levels and risk taking behaviors. Such temperament traits have been hypothesized to be precursors or early manifestations of development towards bipolar disorder(*100*).

Other self-rating scales

The other administered self-rating scales have already been described in the section on the baseline assessments. These scales include:

- Child Self Report on Childhood Inhibition (CSRCI)
- Dimensions of Temperament Survey (DOTS) / Dimensions of Temperament Survey – Revised version (DOTS-R)
- Parental Bonding Instrument (PBI-M, PBI-F)
- Family Adaptability and Cohesion Evaluation Scale (FACES III)
- Family Attitude Scale
- Euronet: Problem resolution strategies

III) Complementary information on the second follow-up (FU2) evaluation

1. Somatic part at FU2

1.1. Added investigations (ActiLaus)

ActiLaus (P.I.: Prof. P. Vollenweider)

This sub-study included the following assessments:

- Actigraphy

Sleep and wake activity patterns were measured using a wrist worn accelerometer (*GENEActiv* accelerometer (Activinsights Ltd, United Kingdom)). The device was worn on the wrist of the right rather than the non-dominant hand in our participants because most participants wore watches on the left hand and did not want to miss their watches during the two-week measurement period. Following a short training period, the subjects were asked to

wear the accelerometer for two weeks. They wore the watch during the same time period in which they kept an electronic diary.

- Ecological Momentary Assessments (EMA)

EMA relying on smart phones was used to obtain “on the moment” assessments of the participant's 1) mood, anxiety and subjective energy level, 2) duration and intensity of activity, 3) food and beverage intake, 4) tobacco, analgesic or sedative drug and illicit substance use, 5) positive and negative events, 6) intensity of pain and 7) duration and quality of sleep. Except for sleep (only in the morning) participants provided information four times a day to each of these items during a one-week period. Due to technical problems related to the programming of the smart phones this assessment could only be introduced in 2015.

Electrocardiogram (EKG)

A 12 lead digitalized electrocardiogram was obtained during the somatic examination (Schiller AG, Baar, Switzerland).

1.2. Added self-rating scales

Krupp fatigue severity scale

This instrument contains 9 questions and was initially developed in subject with systemic diseases then extended to other health conditions(*102*). It was validated in a Swiss population(*103*).

Chalder fatigue scale

This instrument containing 14 questions is a measure of perceived fatigue and was validated in a general practice setting(*104*).

The 12-item Short Form Health Survey (SF12)

This instrument(*105, 106*) allows for the computation of a physical health and a mental health summary score. A French version of the scale was developed by Bovier and colleagues(*107*) in Geneva. Indeed, a factor analysis yielded a 2-factor solution as expected, clearly interpretable as representing physical and mental health constructs. The Swiss study also showed that perceived stress is an important risk factor for low mental health and suggested that mastery and self-esteem are important protective factors of mental health among young adults(*107*).

2. Psychiatric part at FU2

2.1. Added investigations (DecibeLaus)

(P.Is.: Prof. M. Bochud, Prof. M. Riediker)

The aim of this sub-study was to investigate the effects of noise on sleep quality assessed by polysomnography and sleep questionnaires; and on psychological risk factors assessed by personal interviews in order to link high-quality data collected in major Swiss population-based epidemiological studies with noise. This sub-study included additional questions about the apartment (floor level, orientation of living and sleeping rooms) during the psychiatric interview and noise measurements in the sleeping room of the participant at random times during day and evening in the subset of participants where the interview is performed at home.

2.2. Added self-rating scales

Siegrist Job Stress Questionnaire

The effort-reward imbalance (ERI) model was introduced by Siegrist(*108*) in order to predict and explain the incidence of CVD explained by job stress. The ERI model implies that the imbalance between high efforts spent and low rewards received at work is likely to produce recurrent negative emotions and sustained stress responses particularly relevant to the pathogenesis of CHD(*109*). Examples of the job stress questionnaire items are "I have constant time pressure due to a heavy workload", "I have many interruptions and disturbances in my job" and "My job promotion prospects are poor". The questionnaire was translated into French and was subsequently validated by Niedhammer and colleagues(*110*).

The Maastricht Vital Exhaustion Questionnaire (MVEQ)

The 9-item short version(*111*) of the original 21-item version(*112*) of the MVEQ questionnaire assesses vital exhaustion or burnout. Items are related to undue fatigue, disturbed sleep, general malaise, irritability, loss of energy and feelings of demoralization. The 9-item version has been found to be associated with metabolic changes induced by acute or chronic stress (*111, 113-117*), with CVD(*118*) and with reduced recovery after CVD(*119*). The MVEQ was translated into French for the study and will subsequently be validated with the data from the study population.

The Maslach Burnout Inventory (MBI)

The original 22-item version of the MBI(*120*) was designed to measure emotional burnout in professionals from human services. A subsequent version of this questionnaire(*120*), which was designed for use with workers in other occupations, is being used in the current study. The questionnaire assesses three aspects of burnout: emotional exhaustion, depersonalization and reduced personal accomplishment. The questionnaire was translated into French for the study and will subsequently be validated with the data from the study population.

3. Additional investigations at FU2

3.1. PneumoLaus

(Spirometry, P.I.: Prof. L. Nicod, Prof. JW. Fitting)

Pulmonary lung function is being measured using SentrySuite Masterscreen PFT equipment (CareFusion, San Diego, USA). Spirometry is being performed according to ATS/ERS recommendations(*121*), using a minimum of three acceptable forced vital capacity (FVC) manoeuvres. An obstructive ventilatory defect has been defined by a reduced FEV1/FVC ratio below the 5th percentile of the predicted value, which corresponds to the lower limit of normal (LLN). In subjects with an FEV1/FVC ratio below the LLN, reversibility testing is being performed according to ATS/ERS recommendations(*121*). Spirometry is being repeated 15 minutes after inhalation of a bronchodilator, i.e. salbutamol delivered in four separate doses at 30 second intervals (total dose 400 μg). This investigation is taking place at the pulmonary function test laboratory of the Service of Pulmonary Medicine of the CHUV.

3.2. OphtalmoLaus

(P.I.: Prof F. Behar-Cohen)

In this sub-study, the following variables have been measured during a visit with an optometrist: visual acuity, automatic refractometry, retina digital photography, choroid thickness (Optical coherence tomography, OCT) and intra-ocular pressure. The main aims are to determine the distribution and the personal, biological and genetic

determinants of these variables in the general population and to assess their associations with cardio-vascular risk factors and mental disorders.

3.3. IRM

Magnetic Resonance Imaging (small nested project of Prof. B. Draganski)

The structural MRI exam of this sub-study relies on a 3 Tesla magnetic resonance imaging (MRI) Siemens Prisma machine. The project allows us to a) characterize specific brain anatomy patterns correlating with the presence of cerebro-vascular risk factors; b) look for shared brain anatomy patterns between cerebro-vascular risk factors and mood disorders; c) identify the main components of inter-individual variability in brain anatomy corresponding to the severity of cerebro-vascular risk factors/psychiatric phenotypes.

3.4. CognoLaus - EEG

EEG (small nested project "Connect'in age" of Prof. JF Démonet, Prof M. Knyazeva)

This sub-study in subjects of 65 years aims at the identification of abnormal functional connectivity based on source EEG synchronization and Event-Related Potential (ERP) responses. This abnormal connectivity could indicate an early stage of Alzheimer's Disease. The project started in fall 2016 and more than 60 subjects could be included.

IV) Complementary information on the third follow-up (FU3) evaluation

1. Somatic part at FU3

1.1. Added investigations

Heart rate variability

We will obtain 24-hour ambulatory recording of heart rate by digital Holter EKG recording (Aria, Del Mar Reynolds Medical, Inc., Irvine, CA). Subjects will have placement of the EKG leads and testing of the device at the end of the somatic assessment, and will wear the device until the next day. The Holter data, stored on electronic media, will be analyzed by standard time- and frequency-domain methods using software provided by the manufacturer for heart rate variability.

Stool material collection for gut microbiota analyses

(Small nested project of Prof. G. Greub)

The gut microbiota has been associated with metabolic(*122*), cardiovascular(*123*) and psychiatric phenotypes(*124*). In this follow-up we will collect stool samples in all willing subjects and freeze them at -80°C for analyses in a collaboration with Prof Gilbert Greub (Institute of Microbiology University of Lausanne)(*125*). Within a small nested project we are planning to conduct microbiota profiling of the first 120 participants according to the following protocol: Next-generation sequencing (NGS) will be prepared using the MiSeq sequencer available at the Institute of Microbiology of the UNIL. Practically, DNA will first be extracted by using the Macherey Nagel® DNA extraction kit, since we got better results with this kit than with other DNA extraction kits such as Qiagen® to extract DNA from Firmicutes and Actinobacteria. Then, library will be prepared using the Illumina® protocol and primers targeting the V3-V4 region. Library quality will be checked using the Fragment analyzer® and the Qubit®, before sequencing with the MiSeq®. Quality controls will be done using the Illumina bioinformatic pipeline and our home-made pipeline for post-PCR metagenomics data. Then, assignment of species, genus, family and order levels will be done by

considering sequence homology cut-offs of 99, 95, 90 and 80%, respectively. Taxonomic assignment will be done using different approaches including a priori and non a priori approaches and different databases including the Greengenes & Silva databases.

1.2. Added self-rating scales

International Physical Activity Questionnaire - Short Form (IPAQ-SF)

Physical activity is assessed using the International Physical Activity Questionnaire - Short Form (IPAQ-SF). The IPAQ-SF is a validated, open-access, internationally used questionnaire assessing physical activity levels of the last seven days(*126, 127*). The different items of the questionnaire were structured to provide separate scores on walking, moderate-intensity, and vigorous-intensity activity.

Health Economic Assessment

Assessed data and assessment tools are provided in the following table:

Summary of data, instruments and variables of the health economic assessment

Data	**Instruments/Tools**	**Information**
Workplace based health assistance or programs	Questionnaire	Consultations with employee health professionals. Participation in workplace health programs. Access to programs to support employment insertion/reinsertion
Electronic Health Applications and devices	Questionnaire	Purchase/use of Mobile Health Applications. Purchase of personal medical devices
Health Care insurance contracts and costs	Questionnaire	Monthly premiums (basic/complementary) Health insurance subsidy (amount, full/part coverage). Deductible, plan type (standard, alternative: telemedicine, gate-keeping family doctor, managed care networks/HMOs.
Invalidity status	Questionnaire	Receive invalidity benefits; assessed degree (%) of incapacity Waiting for assessment by insurance doctor.
Informal care	Questionnaire	Informal care from a member of the family, friends or other community associations
Income benefits and support	Questionnaire	Social support/ and financial assistance: Income support, old age insurance
Lost productivity	Questionnaire	Time unable to work due to ill health. Travel time and time spent away for health care utilization.

Data	Instruments/Tools	Information
Health care resource utilization and expenditure data (out of pocket, and total expenditures).	One-year retrospective collection health care utilization and expenditure data from specific questionnaire and summary accounts of the health expenditures and payments from the participants' health insurer	Number of outpatient consultations with family doctors or specialists, dental practitioners, ophthalmologists or other allied health professionals as well as use of home care services. Diagnostic examinations (imaging, endoscopy, laboratory tests or biopsy/pathology). Hospital admissions (elective/urgent) and length of stay in hospitals including day case procedures. Days in rehabilitation. Days in intermediate or long term care facilities. Prescription drug expenditures (receipts from pharmacy or medical practice prescribers. Over the counter medication and health supplements (e.g. vitamins, probiotics). Complementary medicine other health/wellness therapies. Total health care expenditures (covered by basic insurance, complementary or accident). Out of pocket health care expenditures.

2. Psychiatric part at FU3: added self-rated scales

The Rosenberg Self-Esteem Scale (RSE)

The Rosenberg Self-Esteem 10-item scale measures global self-worth by measuring both positive and negative feelings about the self(*128*). The scale is believed to be uni-dimensional. All items are answered using a 4-point Likert scale format ranging from strongly agree to strongly disagree. The questionnaire was translated into French and was subsequently validated by Vallieres and colleagues(*129*).

V) Complementary information on the forth follow-up (FU4) evaluation

1. Somatic part at FU4: added self-rating scales

SARS-CoV-2

The questionnaire elicits exposure of participants and their relatives to SARS-CoV-2 since January 2020 (number and timing of infections, (length of) symptoms, severity of the disease, (number of) testing by RT-PCR or serology, hospital admission, isolation and quarantine, and vaccination status). In the absence of virological markers, the timing of the infection will allow for an approximate estimation of the involved variant. The majority of the questions overlap with a previous cross-sectional Swiss investigation(*130*).

CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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2. Psychiatric part at FU4: added self-rated scales

The Gender questionnaire

The Gender questionnaire comprises 53 questions on gender identity and gender-related variables, including 25 questions with a coding on a 5-point Likert scale to assess the 7 dimensions of the Stanford Gender-Related Variables for Health Research (GVHR)(*131*). Factors refer to gender norms (caregiver strain, work strain), gender relations (social support and discrimination), and gender-related traits (independence, risk taking, emotional intelligence).

VI) Organization of the CoLaus|PsyCoLaus biobank

The CoLaus|PsyCoLaus biobank includes aliquots of serum, plasma, whole blood and urine samples from all study participants of the baseline and the two follow-up evaluations of CoLaus|PsyCoLaus. Blood was drawn in the fasting state and processed using the same standardized procedures at baseline and follow-up. These procedures ensure low time limits for time to centrifugation and freezing of the samples. The samples are kept in -80oC locked freezers with a CO2 tank back up. All freezers are connected to a centralized alarm center at the CHUV 24/7. The samples are coded in a reversible anonymous manner and are identified by the double labeling of a unique barcode and a participant number. Information identifying subjects is kept in an ACCESS database on a secured server with username and password dependent access. The biobank steering committee ensures that the biobank is run according to current legal dispositions.

CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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Fondo nazionale svizzero
Swiss National Science Foundation

CHUV Centre hospitalier universitaire vaud

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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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Fonds national suisse
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CHUV Centre hospitalier universitaire vaud

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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
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CoLaus Study, CHUV
Rue du Bugnon 19
1011 Lausanne
Switzerland
Phone: +41 21 314 73 61
Fax: +41 21 314 80 37
research.colaus@chuv.ch

PsyCoLaus Study, CHUV
CEPP, Route de Cery 25
1008 Prilly
Switzerland
Phone: +41 21 314 35 52
Fax: +41 21 314 84 69
research.psycolaus@chuv.ch

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