Adolescent depression treatment pathways in Primary Care – a longitudinal Cohort Study Describing Naturalistic Flow of Treatment and Evaluating Effectiveness and Cost-effectiveness of Interpersonal Counseling Compared to Treatment as Usual

Running title: Protocol: treatment of adolescent depression in primary care

Linnaranta, O.[1,2]; Myllyniemi, A. [1,3]; Salusjärvi, E. [1,2,3]; Seilo, N.[2,4]; Kaltiala, R.[5]; Koskinen, T.[6]; Karukivi, M.[7]; Karvonen, J.[8]; Karri, S.[1], Oksanen, J.[1], Heinonen, E.[1,9]; Kiviruusu, O.[1]; Therman, S.[1]; Berg, P. [1,3]; Lahti, J.[11,12]; Rissanen, E.[6]; Lammintakanen, J.[6]; Ranta, K.[5,10,13]; Marttunen, M. [1,10]

[1]Finnish Institute for Health and Welfare, Mental Health Team, Finland

[2]Itla Children's Foundation, Finland

[3]Helsinki University, Finland

[4]Tampere University, Faculty of Medicine and Health Technology

[5]Tampere University, Faculty of Medicine and Health Technology, and Tampere University Hospital Department of Adolescent Psychiatry, Finland

[6]University of Eastern Finland, Finland

[7]Department of Adolescent Psychiatry, University of Turku and Turku University Hospital, Finland

[8]Department of Adolescent Psychiatry, Oulu University Hospital, Oulu, Finland

[9]Department of Psychology, University of Oslo, Norway

[10]Adolescent Psychiatry, University of Helsinki and Helsinki University Hospital, Finland

[11]Department of Psychology and Logopedics, University of Helsinki, Helsinki, Finland

[12]Folkhälsan Research Center, Helsinki, Finland.

[13]Tampere University, Faculty of Social Sciences, Finland.

Corresponding author:

Outi Linnaranta, M.D., Ph.D.

Chief physician, Finnish Institute for Health and Welfare, Finland

Abstract

Background: Implementation of evidence-based interventions is one of the proposed responses to increased demand for prevention and treatment of adolescent depression. While the efficacy of interpersonal psychotherapy (IPT-A) as an intervention to treat depression of adolescents is well established, the effectiveness and cost-effectiveness of the shorter adaptation, adolescent interpersonal counseling (IPC-A) remains open.

Objective: We present a protocol for a prospective evaluation of the naturalistic treatment flow of adolescents with sustained depression, and effectiveness and cost-effectiveness of IPC-A, as compared to treatment as usual or no treatment of sustained depression.

Methods: We will collect a cohort of grade 7 to 9 adolescents (13–16-year-olds) in selected Finnish schools. A universal evaluation of adolescents in a 6-month follow-up will provide information on the proportion of adolescents a) with *sustained depression* over the follow-up period (Patient Health Questionnaire 9 items, PHQ-9-A $\geq$ 10 in two measurements over 6 months), b) with a self-reported need for support due to depressive symptoms, and c) with received therapeutic intervention. We will describe the *treatment received* (number of sessions, therapeutic content) based on reports from adolescents, caretakers, and therapists, as well as electronic patient records. *The primary outcome measure* will be the proportion of adolescents who will receive specialized psychiatric services by 12 months after baseline. *Secondary outcome measures* comparing three groups as defined at 6 months (IPC-A, treatment as usual (TAU), or no treatment group), will include proportion of adolescents who received any support by 12 months after baseline, and longitudinal changes in PHQ-9-A scores by 12 months. *Cost-effectiveness* will be evaluated using survey data at 12 months, and an *economic evaluation* using register data and information on service use 12 months before and 2 and 10 years after baseline.

Results: As this is the prospective registration of a protocol, we do not yet report any results from the trial. Funding was confirmed in 2022. Recruitment is expected to start in March 2024 and is set to finish in May 2025. The expected baseline results will be published in the spring 2026, the 6-month follow-up by 2027, and the 12-month follow-up in 2028. Duration of register follow-up will be dependent on further funding.

Conclusions: The study will describe need for, pathways to, and content of mental health services for depressed adolescents. The results can improve detection and equal access to care, and inform decision -makers about the best practices for prevention, including utility of the implementation of IPC-A.

Keywords: Adolescent, depression, interpersonal counseling, prevention, treatment, effectiveness, economic evaluation

Introduction

Interpersonal psychotherapy (IPT) is a structured intervention, originally developed for adults[1]. IPT for individuals with major depressive disorder has been shown to be highly effective in reducing depressive symptoms and anxiety, as well as improving overall functioning[2,3]. The acceptance and feasibility of IPT through adaptations for a variety of patient groups has been good[1,4].

IPT has been adapted for adolescents (IPT-A) for age sensitivity. However, 12 sessions of IPT-A were not considered to be feasible in primary care[5,6]. A shorter version of IPT-A, interpersonal counseling for adolescents (IPC-A), is composed of 3 to 8 individual sessions[1]. It was developed in an effort to provide a low threshold intervention in primary care and school health services[7]. Feasibility of brief IPT[7] or IPC-A when provided by school and primary level service professionals and healthcare professionals with minimal mental health training has been good in four reports: two school-based, smaller studies[5,7], another study with youth workers [8], and one among undergraduate students[9]. We will conduct an evaluation of IPC-A in primary care after a large-scale national implementation of IPC-A in primary care in 2020-2023. This will include an evaluation of real-world effectiveness and economic evaluation of the IPC-A intervention.

Goal and aims

The overall goal of this research project is to increase knowledge about clinical utility of implementation of evidence-based interventions in primary care. To this end, we propose a protocol to collect a cohort of grade 7 to 9 adolescents (age about 13 to 16 years), using convenience sampling in selected Finnish schools.

Aims

1. We will describe the need for support as well as treatment and naturalistic treatment flow of adolescents during 6 months in a population with no previous treatment of depression
2. In a longitudinal follow-up, we will evaluate the outcome of adolescents with depressive symptoms, including the outcome of those with no treatment, and the effectiveness and cost-effectiveness of IPC-A and treatment as usual (TAU),
3. We will evaluate predictors of the treatment flow and adolescent outcome at 12 months and 2 years after baseline.

Research questions

1. Do young people reporting depressive symptoms have equal access to IPC-A or TAU in a 6-month follow-up, dependent on their risk for depression and independent of their area of residence, gender, or other minority status? (Aim 1)
2. Is IPC-A effective and cost-effective as compared to TAU in a 12-month follow-up? (Aim 2)
3. Can we identify characteristics of young people or therapists which most likely predict treatment benefits from an IPC-A intervention after 12 months and 2 years? (Aim 3)

Hypotheses

1. Availability of IPC-A improves access to treatment. This could be seen as a shorter time to treatment, a larger proportion of or a broader diversity of adolescents with sustained depression being motivated to and/or receiving treatment (Aim 1, RQ1)
2. Adolescents who receive IPC-A have a better outcome, that is, are less likely to be referred to specialized psychiatric services and other support and services than TAU or no treatment group in the 24-month follow-up (Aim 2, RQ 2)
3. Self-reported adolescent inclusion, functionality, positive mental health, and loneliness predict need for a future intervention and outcome, and therapists' sense of skillfulness, satisfaction with implementation, and sense of difficulties is a further predictor of outcome (Aim 3, RQ3)

Methods

Study design

This is a prospective, naturalistic cohort study, where treatment is not under the control of researchers but the sampling is based on a convenience sampling method. Inclusion criteria: We will ***include*** all adolescents attending grades 7 to 9 (age 13 to 16 years) in selected schools. ***Exclusion criteria*** include psychiatric care within the past 12 months or receiving a psychosocial intervention (psychotherapy, IPC-A, any other therapy or support from the same professional for >3 meetings) during the 12 months before baseline, an inability to reliably understand the Finnish, Swedish, English, or Finnish plain language versions of the survey, or an adolescent's or caretaker's report on need for exclusion, such as another medical condition – including a mental disorder – requiring acute current treatment or support. Exclusion will be made by the researcher based on the survey response from the adolescent and caretaker, including confirmatory information by phone where necessary.

Recruitment and eligibility

The recruitment of adolescents will be done from four university clinic areas (Northern, Eastern, Central and Western Finland) to provide a representative national sample based on interest of schools. Two to three municipalities from each university clinic area have consented to the study.

With the consent of the school, all grade 7 to 9 adolescents (age about 13 to 16 years) in the school will have a session about mental health literacy skills (how to talk with friends about mental health, how to know when adult support is needed). The information will be adjusted for their age. During that session, the goals of the study will also be described. A similar session will be held for *caretakers*; the session will be complemented by messaging all parents a link to a video recording and supplementary materials for mental wellbeing online, as well as providing information about the study.

Subsequently, a research assistant (RA) will help adolescents fill in a digital survey questionnaire. Upon agreement with the recruiting school, this can take place either after the information session or in the classroom, in a context of a group discussion at a general level about the dimensions of mental health and wellbeing, and options for help for mental health.

Sample size

To estimate the number of adolescents to be screened, in the absence of available Finnish data, we used the information from the Netherlands Mental Health Survey and Incidence Study (NEMESIS) for incidence[10] and prevalence findings from NEMESIS[11]. Based on these findings, we roughly estimated that the incidence of depressive disorders would be 2%[6].

For the current study, a conservative estimate is to screen 6 000 to 9 000 young people. We estimate this, with a 15% prevalence and 2% incidence, approximately 50% of adolescents not having previous treatment despite prevalent depression at baseline to the cohort, and a 70% consent rate, to recruit a minimum of 100 consenting adolescents to the IPC-A group, 200 consenting adolescents to TAU-group, and 100 to the depressed/no treatment-group. The size of any group might be considerably larger, but we will finish recruitment once the minimum size of all groups has been reached.

Measures and data collection

Data will comprise surveys for adolescents, caretakers, and therapists, as well as register data and complementary information on the timing, duration, and content of psychosocial support and overall treatment of depression (**Table 1**). The respondents will receive an online link they can use to respond at their convenience.

Table 1. Study flow and timing of data sources

Data source	Baseline	3 months	6 months	12 months	Follow-up based on register data at 2, 5 and 10 years
Comprehensive student survey	All	All	All	Those depressed over 6 first months (PHQ-9≥10 twice)	
Biweekly short student survey	x	x	x		
Caretaker's survey	x		x		
Therapists' survey			x		
Intensity of support and treatment	**Medical files, participant and professional's report**				
Register data • Medication • Use of health and social services • Social security benefits • Medical rehabilitation					First completed at 24 months after last participant intake, starting at 12 months preceding intake

A comprehensive adolescent survey

Adolescents will complete a survey on sociodemographic information and self-evaluation measures at baseline and at 3 and 6 months. Those who show ***sustained depression*** (Patient Health Questionnaire 9 items (PHQ-9-A) sum scores ≥ 10 twice during the first 6 months after baseline) will also complete the comprehensive survey at 12 months. The comprehensive adolescent survey is also available as a shorter version in plain Finnish language.

Outcome measures in the adolescents' and caretakers' surveys

We list here the self-report questionnaires (**Table 2**) that will be presented to adolescents and caretakers at the various timepoints. The questionnaires will be presented in Finnish, Swedish, or English, as suitable.

Table 2. A summary of the content of the adolescents' and caretakers' surveys

Name of the scale	Short	Length	Rating	Time frame	Describes
The Patient Health Questionnaire 9 items*[1]	PHQ-9-A	9 items	0 to 3	2 weeks	Depressive symptoms
The child-friendly EQ-5D version[1]	EQ-5D-Y	5 items + VAS	5 items 0 to 2; The EQ VAS	The same day	Quality of life

Generalized Anxiety Disorder Scale-7	GAD-7	7 items	0 to 3	2 weeks	Anxiety
Young Person's Clinical Outcomes in Routine Evaluation-Outcome Measure	YP-CORE	10 items	0 to 4	1 week	Response to therapy
Do you feel lonely?[1]		1 item	0 to 4	No time frame	Perceived loneliness
The Warwick-Edinburg Mental Wellbeing Scale	SWEMWBS	7 items	0 to 4	2 weeks	Positive mental health
Experiences of Social Inclusion Scale	ESIS	10 items	0 to 4	No time frame	Social inclusion
3x10D Survey*	3x10-D	10 items	0 to 10	No time frame	Functionality
Questions about worry as well as need and willingness for treatment*[1]		0 to 10 VAS scales	0 to 10 VAS scale	No time frame	Need and motivation for psychosocial support
Background questionnaire*[1] Sociodemographic information, minority status				NA	
Alcohol and substance use, self-harming behavior*[1]			Yes/no, open field		
Use of health and social welfare services*[1]			Yes/no, open field	12 months	Information to classify as IPC-A, TAU, and no treatment groups

Note. Scales marked with an asterisk (*)will be used in the caretaker's survey as a proxy version. Scales marked with [1] will be included in the shorter plain language version.

The *Patient Health Questionnaire 9 items* (PHQ-9) is a depression severity measure based on DSM criteria. The items are answered according to the frequency of symptoms (0 = not at all, 1= some days, 2 = more than half of the days, 3 = almost every day). A higher score is indicative of greater depressive symptomatology. The PHQ-9 is a unidimensional measure with good internal consistency, also in adolescents[12–15]. In adults, the optimal sum score cut-off is ≥ 10[16]. The PHQ-9 classifies respondents' sum scores into depression severity as follows: 0–4 indicates no depressive symptoms, 5–9 mild depressive symptoms, 10–14 moderate depressive symptoms, 15–19 moderately-severe depressive symptoms, and 20–27 severe depressive symptoms[16]. One study of 442 youth with major depressive disorder (aged 13–17 years) proposed a cut-off of ≥ 11[12]. We will use the PHQ-9-A version according to DSM-5 criteria, including irritated mood for adolescents.

The *child-friendly EQ-5D version* (EQ-5D-Y) is based on the EQ-5D-3L, which is a widely used standardized generic measure of health-related quality of life (HRQoL), originally designed for adults. EQ-5D-3L has been used internationally in many settings, such as in clinical trials and population surveys. The EQ-5D-Y was introduced by the EuroQoL Group in 2009 as a more comprehensible instrument suitable for children and adolescents than the original[17]. The EQ-5D consists of five questions about mobility, looking after oneself, doing usual activities, having pain or discomfort, and feeling worried, sad, or unhappy. Each item has three response alternatives. A question about general health is evaluated on a visual analogue scale (VAS)[18].

The *Generalized Anxiety Disorder Scale-7* (GAD-7) is a seven-item self-rated instrument used to assess symptoms of generalized anxiety. Each item asks the individual to rate the severity of his or her symptoms over the past two weeks. Response options are 0 = not at all, 1 = several days, 2 = more than half the days, 3 = almost every day. GAD-7 scores can be categorized into mild, moderate, and severe anxiety with sum cut-offs of 5, 10, and 15 (score range 0–21). At a cut-off point of 10 or greater, sensitivity and specificity exceed .80[19].

The *Young Person's Clinical Outcomes in Routine Evaluation-Outcome Measure (YP-CORE*) is a ten-item measure designed for use in the 11–16-year age range. It is adapted for young people from *The CORE-Outcome Measure* for adults that has both 34- (CORE-OM) and 10-item versions (CORE-10)[20]. The CORE-OM and CORE-10 were developed as screening measures for psychological distress, including items for well-being, psychological symptoms, functioning, and risk. YP-CORE is well accepted, and the rate of missing values is low. Internal consistency (α = .83–.92) and test-re-test reliability is good (r = .69), and the results of confirmatory factor analysis (CFA) have supported a one-factor model. The YP-CORE showed good concurrent validity against two widely used symptom-specific measures (r = .62–.87). The measure was sensitive to change, showing a larger effect size (d = 0.55) than the Beck Depression Inventory (BDI-21) and Beck Anxiety Inventory (BAI) (d = 0.31-0.50). The Finnish translation of YP-CORE has good psychometric properties[21].

Perceived loneliness is a simple measure of loneliness based on self-assessment including only one question. This single question has been found to have good content validity in older adults[22].

The *Warwick-Edinburgh Mental Wellbeing Scale* (WEMWBS) with both its 14- and short 7- item versions measures positive mental health, that is, holistic aspects of wellbeing, namely eudemonic and hedonic wellbeing as well as psychological functioning[23]. This questionnaire allows for measuring mental wellbeing as a partially separable concept from mental illness, and has favorable psychometric properties, especially an approximate normal distribution in the general population. We will use the 7-item version (the Short WEMWBS; SWEMWBS) that has been validated in a large Finnish dataset[24], and validations in adolescents have proved successful[25–27]. Using the SWEMWBS, we will be able to calculate mental health costs and quality-adjusted life years (QALYs)[28].

Experiences of Social Inclusion Scale (ESIS) is a brief self-evaluation instrument to assess self-reported experiences of social inclusion. It consists of ten statements that map the respondent's feelings of belonging, the significance of what they do, and the possibilities for action. One extreme of the continuum formed by the answers represents the experience of non-participation/social exclusion and the other the experience of inclusion. The participation indicator is calculated by scoring claims: a higher score means a stronger experience of inclusion. The sum score is scaled to a range of 0–100. ESIS has been developed in the Finnish Institute for Health and Welfare (THL) Social Inclusion Coordination Project (Sokra). The theoretical framework is the capability approach (CA). In the validation study of the Finnish version of ESIS in adults, results indicated good internal reliability and consistency ($\alpha = .89$), and factor analyses suggested a one-dimensional factor structure for the ten items of the ESIS[29].

Functionality (3x10D Survey). The 3x10D survey is a quality-of-life mapping metric. The instrument comprises ten dimensions describing the life situation. The dimensions are evaluated in relation to the present moment, their importance, and the future. The young person evaluates areas of life for how important they feel the dimensions are and how satisfied they are with their current state[30]. The scale is awaiting international validation but publications from Finnish datasets are in preparation.

Sociodemographic information

The comprehensive survey will include sociodemographic information collected at baseline after informed consent and will include information on age, self-identified gender, sex assigned at birth, first language, other minority status (language, sexual orientation, ethnic, other), area of residence, and household composition.

Biweekly short survey

Adolescents will respond to a short online survey biweekly over a 6-month follow-up, independent of their mood. This short survey will include PHQ-9-A and questions on their subjective need and motivation for treatment of depression, as well as any received treatment of depression.

Motivation to treatment

Need and motivation to treatment will be asked: Are you worried about your mood (yes/no). Those worried about their mood will further be asked: How willing are you to have help from others to improve your mood? This is done with a VAS with a scale from 1 to 10. *This is complemented by the Motivation for Youth's Treatment Scale (MYTS)*[31], an intrinsic treatment motivation scale for youth. The questionnaire includes 8 questions answered on a scale from 1 (strongly disagree) to 5 (strongly agree), where higher ratings indicate higher motivation. Based on the participants' answers a total scale and two subscales: Problem Recognition (4 items) and Treatment readiness (4 items) are calculated. The internal consistency of all three scales was found to be good ($\alpha = 0.84 – 0.89$) and Confirmatory Factor Analysis supported the two-factor model[31]. These findings were also replicated in another study, although caution in using the total scale is warranted due to low correlation between the subscales[32].

Caretaker's survey

One caretaker, upon acceptance and choice of the adolescent, will be sent a link to consent to and twice fill in a survey using a secure link (within one month from baseline and at 6 months from baseline) (Table 2). The caretaker survey will include sociodemographic information. The scales in the caretaker survey include proxy versions of the PHQ-9, EQ-5D-Y, and 3x10D questionnaires, and questions about the adolescent's mood, need for treatment, and willingness for treatment. We will also ask whether they or the adolescent have sought and received help for the adolescent, and if yes, what kind of support they received; or if not, what kind of support they think would be necessary. At 6 months, where applicable, we additionally ask about benefits and adverse effects of treatment.

The therapist survey

A single survey will be sent to the therapists providing the main psychosocial support, including therapists providing IPC-A and other therapists. For each adolescent, the therapist will report the duration and timing of therapy, content, and response, including benefits and adverse effects of the intervention. We will use the 7-item SWEMWBS to assess their own positive mental health each time they respond to a survey concerning a participating adolescent[23].

The therapist will respond once to a longer survey that will include information on their sociodemographic details, professional training, and specifically, the amount and quality of the training they have had in IPC-A or other psychotherapy. For IPC-A therapists only, we will use the Normalization Measure Development questionnaire (NoMAD)[33] to describe the therapist's view on the implementation process of the IPC-A and their ability to use their IPC-A skills. Furthermore, for all therapists, we will use the *Trainee Current Practice Report,* a comprehensive self-report questionnaire, soliciting information on psychotherapist experiences in their current practice. The therapist skills survey is informed by ongoing work by Professor Erkki Heinonen[34], and was developed to assess how therapists develop during their training in the recently initiated and ongoing SPRISTAD study. The questionnaire features items gauging both subjective skilfulness (10 items) and difficulties (12 items) in therapy work, which are used also in the present investigation. In the Finnish arm of the SPRISTAD study[34], the data of 267 psychotherapist trainees (representing various background professions, therapy training programs, and universities) has yielded good reliabilities (α = .89 and .84) for the two scales, respectively (personal communication).

This information will be used to correlate competence and personal characteristics with the adolescent outcome of IPC-A or other therapy, and to complement knowledge about the impact of training procedures and implementation process.

Benefits and adverse effects due to support or treatment

Benefits and adverse effects due to support or treatment will be estimated with open field questions for the adolescent ("*Do you feel that attending interpersonal counseling was useful for you?" (yes/no), Do you feel that attending interpersonal counseling was harmful for you? (yes/no), "If yes, please describe how".* Open field responses will be analyzed with thematic analysis. Additional statements concerning experience about

treatment were formulated. This format was selected while valid and gold standard instruments for evaluation of adverse effects of therapy have been reported to be lacking[35]. The comprehensive survey at 3, 6 and 12 months contains items for potentially adverse effects (substance use and self-harm). To complement adolescent view, we will ask about benefits and adverse effects in the caretaker and professional's survey with similar questions.

Adolescent follow-up after 6 months

A comprehensive adolescent survey will be repeated at 12 months for those who show sustained depression; no further follow-up will be done for those who were not depressed over 6 months.

A depressed adolescent in subjective need for treatment is an adolescent who reports a need for support or treatment of depression. Depressed adolescents who ***received treatment*** are those who report receiving treatment over 6 months, in the caretaker report at 6 months indicates treatment of the adolescent for depression, or where register data shows contact to social or health care services.

Adolescents with sustained depression (self-reported PHQ-9-A ≥ 10 twice over 6 months, including intake) will be classified in three groups for further follow-up based on adolescent report

(1) Adolescents who received prevention or treatment of depression including IPC-A during 6 months of follow-up as reported by the adolescent or a therapist, or evident from the medical files (aiming at n = 100 recruited in order of identification). If IPC-A is started within six months of the follow-up as reported by the adolescent or a therapist in medical files, the adolescent will be classified into this group (1)

(2) Adolescents who received any other treatment for depression (TAU) (aiming at n = 200).

(3) Adolescents with sustained depression, with no treatment at baseline or during six months of follow-up (aiming at n = 100)

Identifying adolescents who received psychosocial support or treatment is based on the adolescent and caretaker reports and will be complemented from medical records, therapist reports, and/or phone calls to informants.

Description of the intensity of treatment

Description (dosing) of TAU and IPC-A will be based on the adolescent's, caretaker's and therapists' reports. Where necessary, the information might be complemented from medical records, and/or phone calls to informants. This helps in defining the adolescents as three groups (those who received IPC-A, TAU or no treatment), describing the overall use of resources, and calculating intervention cost for cost-effectiveness analysis at 12 months.

Effectiveness of IPC-A intervention. We do not control provision or timing of IPC-A intervention as part of the study. However, adolescents in the IPC-A group will, even if the treatment period continues after six months, complete weekly reports of PHQ-9-A as it is an integral part of treatment, and this information will additionally be collected for the purposes of the study. Thus, even if IPC-A would continue after 6 months after baseline, we will be able to evaluate the response over the IPC-A period.

Register data

Register data will be collected to define health and social care service use and costs. Register-based data will include 12 months prior study to evaluate pre-trends of service use and costs. A further prospective register-based data collection for economic analysis will be done at 2 years, 5 years, and 10 years after baseline.

We will use four Finnish nationwide registers provided by THL: 1) Care Register for Health Care, 2) Register of Primary Health Care visits, 3) Care Register for Social Welfare, and 4) Register of Child Welfare. In addition, we will use the Drug Prescription Register (Statistics on reimbursements for prescription medicines and rehabilitation) from the Social Insurance Institution of Finland (Kela). The data extracted will include use of emergency services and hospitalizations due to suicidality and somatic complications from self-harm as well as for psychiatric indications, use of inpatient and outpatient services, use of primary care, reimbursements for medicine expenses, provision of psychotherapy or neurocognitive rehabilitation, committed suicides, use of child welfare services and use of social services.

Outcome measures comparing three groups of adolescents with sustained depression (IPC-A, TAU or no intervention)

Primary outcome measure

- proportion of adolescents referred to specialized psychiatric services during 12 months after baseline

Secondary outcome measures

- proportion of adolescents with any need for psychosocial or psychiatric treatment or social services at 2, 5, and 10 years after baseline.
- longitudinal changes in PHQ-9-A score by 12 months in each of the three groups in the repeated adolescent surveys

Other outcome measures

- EQ-5D
- GAD-7
- YP-CORE-OM
- loneliness
- SWEMWBS
- ESIS
- 3x10D Survey
- sociodemographic characteristics, including gender and minority status

Complications and harmful behavior during the intervention (surveys and register data)

- alcohol and substance use
- self-harming behavior and suicidality
- hospitalizations during a therapeutic intervention
- drop-out from treatment

All analyses will be *intention-to-treat,* though loss to follow-up will be minimal, due to the outcome measures being comprehensive national registers. Cost-effectiveness will be estimated at 12 months and economic evaluation will be completed at 2 years, 5 years and 10 years after baseline.

Statistical analysis of psychometric measures

For descriptive purposes, we will use both parametric and non-parametric descriptive statistics. Tests for non-parametric measures will be used for testing statistical significance of correlations and between-group differences (IPC-A, TAU, no treatment), with the alpha level set to .05 in each analysis separately. Conventional psychometric characteristics of all measures will be described and compared between self-identified cis-male and cis-female participants. If the size of a subsample is > 20, we will additionally evaluate adolescent groups by gender, sexual orientation, report of ethnic and other minority status, specific groups of first language, or plain language.

To evaluate the validity of each scale, we will analyze the proportion of missing responses. Since there is some indication about limited measurement precision among adolescents for some response options[36], we will use item response theory (IRT) or similar methods to take into account separate probabilities for response option of each item. In the psychometric analysis of the individual scales, we will use confirmatory factor analysis of categorical items to test for psychometric properties. We will also correlate PHQ-9-A with each of the other scales (YP-CORE, perceived loneliness, WEMWBS, EQ-5D-Y, ESIS, and 3x10D Survey). In the longitudinal survey dataset (baseline, bi-weekly measurements over 3 months, comprehensive surveys at baseline, 3, 6, and 12 months), we will estimate test-retest reliability and sensitivity to change of the scales by observing change in PHQ-9-A in relation to changes in other scales.

Statistical analysis of primary and secondary outcomes

Primary outcome: Based on information from adolescent, caretaker and therapist surveys, complementary information and register data, we will determine whether adolescents did or did not receive specialized psychiatric care by 1 year, and from registers between 1 and 2 years We will use descriptive statistics to characterize adolescents with IPC-A, TAU and no treatment, and of main outcome measures in each group.

Secondary outcomes: We will use register data to determine adolescents who received any other support by 2, 5, or 10 years, as indicated by psychosocial or psychiatric treatment, use of social services, or social or medical benefits (yes/no) comparing three groups (IPC-A, TAU, or no treatment group, as defined at 6 months).

PHQ-9-A of IPC-A and TAU groups during the intervention will be compared where data is available.

Predictors of outcome

We will use PHQ-9-A at baseline and mixed linear modelling for individual outcome for PHQ-9-A during the 6 months of follow-up and test whether the three groups (IPC-A, TAU, and no treatment) differ in variation of symptom severity.

We will test whether adolescent-rated SWEMWBS, YP-CORE, perceived loneliness, EQ-5D-Y, ESIS, 3x10D Survey and GAD-7, or membership in some subgroups of >20 adolescents (gender or sex, minority status, functional limitations, first language, area of residence) are predictors of subjective or parent-reported need for treatment, or actually receiving therapy, other TAU, or other support.

IPC-A therapist training and subjective competence will be compared to adolescent response (PHQ-9-A).

Analysis of pathways to care

We will describe the proportion of adolescents who receive any support for depression, who receive IPC-A, and time to treatment or support (Kaplan-Meyer analysis).

We will characterize the schools and municipalities of recruitment based on the number of therapists rained and providing IPC-A and other professionals providing public social and health care services to the age group as compared to the number of adolescents at the school or municipality. This information will be used to evaluate the impact of availability of IPC-A therapists on likelihood of receiving any treatment for depressive symptoms, time to therapy/TAU treatment, and outcome of adolescents recruited to the study (Hypothesis 1). This will provide the estimate of utility and added value of implementation of IPC-A.

The bi-annual School Health Survey (SHS) is a national survey, with the last round completed in spring 2023. Where possible, we have included the same questions as the SHS and will thus be able to estimate how representative our cohort is compared to mean values in the municipality. In addition to two first items of PHQ-9-A, the SHS survey provides information on the proportion of adolescents reporting that they have a subjective need for support and that they have sought support, which will allow comparing the results in the current study to the general finding in the SHS.

Economic evaluations of IPC-A

The overall goal of the economic evaluation of IPC-A is to estimate costs and cost-effectiveness of the IPC-A intervention to provide information for health and social care decision-makers. The aim is to evaluate whether the IPC-A is cost-effective as compared to TAU and no intervention in a 6- and 12-month follow-up from a societal perspective. Also, we aim to evaluate the IPC-A intervention's effect on health and societal care service use and costs of adolescents with depressive symptoms in 2-, 5-, and 10-year follow-ups compared to TAU and no treatment. The cost-effectiveness of the IPC-A intervention will be evaluated together with the effectiveness study at 12 months and therefore the study design will be as described previously. We will use the effectiveness data and registers of health and social care services and medical purchases collected as described above.

The cost-effectiveness evaluations will combine both effectiveness and costs information of the IPC-A as compared to TAU and no treatment. Two separate analyses will be conducted. First, we will use EQ-5D-Y-based QALYs as the effectiveness outcome. Second, we will use PHQ-9-A scores as the effectiveness outcome. We will apply the limited societal cost perspective including, for instance, intervention costs with relevant use of both health and social care services and medicine purchases from national registers. To enable the use of micro-costing, we will collect the resource uses from multiple sources and use National unit costs for health and social care services in monetarization[30]. Multiple imputations[37] will be performed for missing effectiveness outcomes and cost items if needed.

We will use standard methods of cost-effectiveness analyses, and will, for instance, apply incremental analysis of the effects and costs. First, we will assess dominance of the intervention, that is, whether an intervention is more effective and less costly. In case without clear dominance, we will calculate incremental net health benefit or net monetary benefit comparing the alternatives with 95% confidence intervals[38].

Data management

Data entry: Data will be collected using the THL in-house questionnaire engine Lomakepalvelu (questionnaire service).

Data coding: All participants will receive automatically generated identifiers and additional, automatically generated identifiers for caretakers and professionals. All survey data will be stored using this research ID.

Register data including person IDs will be managed using the Findata Kapseli service. Sensitive personal information will be stored separately from any questionnaire data. All other data will be stored pseudonymized.

Data storage: Data will be stored on the THL database system OLAP server, where the survey data, sample data, and register data will be collected for analysis. Participant identifier data will be stored separately on the THL research and scheduling service "*Tutkimus ja ajanvarauspalvelu* TAP".

Data confidentiality: Subjects have no access to information provided from other linked persons. Data access is restricted by user roles with permission of PI.

Data monitoring committee will be comprised of the senior researchers in the team (Linnaranta, Marttunen, Ranta, Lammintakanen, Heinonen, Lahti, Koskinen, Karvonen, Kaltiala, Oksanen) and will monitor the number of participants every three months (adolescents with subsequent depression who received IPC-A, TAU or no treatment, caretakers and professionals) and missing data. They will make the final decision about finishing recruitment or changing procedures to enrich recruitment for any group to reach sufficient power to respond to the research questions. If necessary, these modifications will be reported to the ethics committee and in scientific reports. Additionally, the same committee will audit data collection procedures every 6 months. No independent auditing committee is nominated since the treatment is not under control of researchers.

Results

We expect to start recruitment of the prospective cohort in March 2024 and will finish 12-month prospective sampling and data collection by the end of 2025. We expect to collect the first register data at the end of 2026. We expect to report psychometric properties and intercorrelations of measures in the baseline survey data in spring 2025, 6-month follow-up data in late 2025, and 12-month follow-up data in 2027. We expect to describe treatment flow by 12 months, treatment (IPC-A, TAU) effectiveness, and predictors of 12-month treatment outcome in late 2026 or in 2027. We expect to report economic evaluation of 12-month-data in 2027. The economic analyses at 2-, 5- and 10-year follow-ups will be reported as the data is ready to be collected from registers. All main results will be reported as peer-reviewed articles in suitable international journals.

Discussion

This will be a large prospective and nationally representative cohort of up to 9000 adolescents. The overall goal of this project is to increase knowledge about the actual, naturalistic provision, effectiveness, and cost-effectiveness of treatment for adolescent depression in primary care. This will inform further improvements in detecting adolescents who would benefit from early prevention of depression and improving equal access to treatment of depression.

Ethics approval

The protocol was approved by Helsinki University Hospital Ethics board (#HUS/1485/2023).

Informed consent

The adolescents will receive oral and written information about the study. Informed consent from the adolescent will be obtained digitally after the self-evaluation at baseline. While all adolescents are asked to fill in the survey forms, only the digital survey data of those adolescents who provide informed consent to participate in the study will be stored and used for research purposes. For those whose age at baseline is below 15 years, a caretaker's informed consent is necessary; data without caretaker's consent within 2 weeks of adolescent consent will not be stored. The consenting adolescents will have an option to decline and withdraw from the study at any point afterwards by sending an SMS, by email, or by using a link on the study site.

The caretakers and therapists receive both oral and written information about the study. They will provide informed consent digitally before being provided the digital survey. Separate consent to the caretaker survey will be requested from all caretakers, independent of the age of the adolescent.

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Conflict of interest

Tarja Koskinen is an accredited IPT-A, IPC-A psychotherapy trainer (IPT-A, IPC-A). Max Karukivi, Tarja Koskinen, Klaus Ranta and Jari Lahti are accredited CBT psychotherapy trainers. Klaus Ranta, Mauri Marttunen and Outi Linnaranta have received author subventions from Duodecim for articles and as editors or authors in a book on IPT-A and IPC-A (published in 9/2023) and a book on Psychiatry. The other authors report no financial relationships with competing interests.

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