Journal of Eating Disorders

RESEARCH

Open Access

Exploring markers of feasibility for a pragmatic study of biomarkers in adolescents with eating disorders: steps towards a precision psychiatry approach

Mark L. Norris[1,2,3*†], Krista A. Power[4,5†], Wendy Spettigue[3,6], Niana Lavallée[3], Madeline J. Gertler[3], Dawson B. H. Livingston[3,4], Alexane F. Rodrigue[3,4], Janessa E. Porter[3], Lori Pope[3], Megan Harrison[1,2,3], Nuray Kanbur[1,2], Gary S. Goldfield[2,3], Leanna Isserlin[6], Amy Robinson[1,2] and Nicole Obeid[3,6]

Abstract

Objective To examine markers of feasibility for a pragmatic interdisciplinary multi-axial study of biomarkers in adolescents with eating disorders (EDs).

Method The study included the collection of medical and clinical variables, psychometric measures, dietary logs, sensory and sleep assessments, and biological samples (i.e., blood and stool collection) for biomarker analyses. Adolescents between the ages of 11 to 17 diagnosed with a restrictive ED, along with control participants were enrolled between November 2021 to July 2024. Participants with EDs underwent concurrent treatment while enrolled in the study. Time points for low-weight patients included baseline, 4, 12, and 26 weeks, depending on the biological marker. Control subjects and patients over 90% treatment goal weight were assessed once. Feasibility was evaluated using clinical participant recruitment efficiency and uptake, adherence to the study protocol, rates of study completion, and self-reported ratings of acceptability.

Results In total, 100 participants with an ED, and 52 controls participated. We observed high rates of clinical participant enrolment, high adherence with most protocol collection procedures, modest dropout for longitudinal clinical participants (17% at 12 weeks), and positive feedback returned on surveys. We observed higher dropout at the 26-week timepoint (33%). Food log and sleep assessments were hindered by several contributing factors, resulting in completion rates of 31–70% and 40–87%.

Discussion Overall, results suggest acceptable feasibility for most variables assessed. Protocols requiring participation beyond 12 weeks, and utilizing dietary logs and sleep assessments, should be powered accordingly to account for lower completion rates. Further studies are needed to determine methods to optimize dietary and sleep assessments. This study provides valuable insights that can inform future precision psychiatry ED research strategies.

†Mark L. Norris and Krista A. Power are co-principal authors.

*Correspondence:
Mark L. Norris
mnorris@cheo.on.ca

Full list of author information is available at the end of the article

Plain English Summary

In this study, we report on the feasibility of collecting biomarker samples in adolescents with eating disorders (ED) to help inform a platform of precision psychiatry research. We included standardized questionnaires, dietary logs, sleep, sensory, and pharmacogenetic assessments, and collected blood and stool samples. Depending on the biomarker and grouping of participants, we collected data at 1, 3 or 4 timepoints. We evaluated feasibility using rates of recruitment, adherence to the protocol, timepoints and study completion, and overall acceptability. We recruited 100 participants with an ED and 52 controls. We observed high rates of clinical enrolment and adherence to most collection procedures, low rates of drop out over the first 12 weeks, and positive feedback returned on surveys. Dietary log completion and sleep assessments were the most challenging research tasks, with the highest rates of non-completion. Our results suggest that most participants followed longitudinally completed testing up to twelve weeks. Protocols requiring participation beyond this timeframe should account for substantial dropout. Further studies are required to investigate the optimal method to track nutritional intake and assess sleep characteristics for research purposes in adolescents with EDs.

Keywords Precision psychiatry, Feasibility, Adolescents, Anorexia nervosa, Eating disorders

Eating disorders (EDs), including anorexia nervosa (AN), are psychiatric illnesses that often begin in adolescence and are associated with dangerous medical and psychiatric sequelae, chronicity, comorbidity, and death [2]. Relapses are common and long-term outcomes are often poor, with large proportions of individuals continuing to experience symptoms many years after initial diagnosis [15]. Research on best practices for treating youth with AN suggests that evidence-based treatments demonstrate only modest efficacy, with a recognized need for further treatment advances [11, 26, 28].

Recent trends in medical research have focused on precision approaches, which utilize an individual's genetic, biological and psychosocial factors to influence medical treatment to optimize individual outcomes (Delpierre & Lefèvre, 2023). Although these approaches have revolutionized cancer care and other medical conditions [40], precision medicine research involving psychiatric conditions remains in its infancy [17]. Due to the complex etiology of mental health (MH) disorders, creating and implementing effective treatments can be difficult [38]. Precision psychiatry offers theoretical solutions to these challenges by utilizing tailored and personalized approaches for treating psychiatric conditions [5, 32, 38]. In MH trials, biomarkers such as high-sensitivity c-reactive protein (hs-CRP) have shown promise in improving precision by stratifying patients into biologically relevant subgroups and assessing measurable outcomes of treatment efficacy (Raison et al., 2013).

Although several potential biomarkers of interest have been demonstrated within the field of EDs, evidence of adoption and implementation into clinical practice remains scarce, with the majority of research focusing on adults with AN [28]. Biological research has focused on the identification of biomarkers that aim to inform the disease process and response to treatments [1, 37, 45]. Increased biomarker research involving neurobiological contributors to ED onset and maintenance may also help advance discoveries of novel therapeutic targets (Steinglass & Walsh, 2016). As an example, research has suggested that leptin may act as a disease-specific biomarker given alterations beyond what would be expected for weight-related effects in patients with EDs [9]. To date, ED studies have concentrated on biomarkers associated with starvation status and medical acuity, with research on the utility of broader disease-specific biomarkers currently in their incipient stage of development (Malcolm et al., 2021).

Despite a wide breadth of research in various domains with relevance to precision psychiatry, a recent review failed to identify comprehensive research programs focusing on multi-axial biomarker collection in adolescent ED populations [28]. This may be in part due to the lack of collection of clinical measurements and data required to advance this work [32]. The integration of biomarker collection into practice has the potential to transform clinical care by offering more precise phenotyping and, as a result, more precise treatment options. Given the complexity of EDs, it is highly unlikely that a single biomarker will offer sufficient sensitivity or specificity to provide definitive diagnostic or prognostic value. Instead, the development of composite biomarker profiles is more likely to improve clinical utility and support greater precision psychiatry interventions [16].

Several broad biological areas of biomarker collection in EDs have been identified, mainly in adults, including: (1) the gut microbiome, (2) serum markers (immune and endocrine mediators, e.g., interleukin 6 [IL-6] and leptin), (3) olfaction and taste perception profiles, and (4) genetics and genomics [22, 28]. We are unaware of any study in pediatric EDs that has attempted to integrate these biomarkers into a single study protocol, nor are there any guidelines as to the feasibility of integrating this type of multiple biomarker collection into treatment programs and routine clinical care.

The primary objective of this study was to use a pragmatic design to report on the feasibility of collecting multiple biomarkers in youth in treatment for an ED. We sought to learn about recruitment efficiency and uptake, adherence to the measurement protocol, and acceptability of collecting several biomarkers at once, including smell and taste (using sensory collection kits), sleep (using a wearable device), cytochrome p450 genetic assays (using a commercially available psychopharmacogenetic test), blood (markers of immune, endocrine, and appetite signalling), and stool (examining stool microbiome diversity, composition, and metabolites). Ultimately, we seek to better understand and describe how biomarker collection can be integrated into clinical practice to allow for precision psychiatry approaches in youth with EDs to be realized.

Methods

Protocol development

The protocol was developed in a stepwise fashion using a collaborative, interdisciplinary approach. Our initial funding was awarded before the COVID-19 pandemic and focused on the collection of variables associated with the microbiome (stool, dietary logs, and standardized measures). Additional funding was received thereafter (before the initial study launched), which resulted in the protocol expanding to include further biomarkers (sensory assessment, sleep assessment, blood collection, and pharmacogenetic testing; see Fig. 1).

To learn of the feasibility of enrolling patients at varying stages of treatment and weight presentations and to understand the impact of malnutrition and illness state on biomarker collection, we divided participants into four groups: (1) participants with an ED under 90% treatment goal weight (TGW) at enrolment, (2) participants with an ED over 90% TGW at enrolment, (3) healthy controls, and (4) siblings of participants with an ED (Fig. 1). We included sibling controls given the recognized importance of environmental and genetic influence on the microbiome [14]. To help understand the impact that weight recovery had on biomarker collection and findings, those with an ED and under 90% TGW were asked to complete the biomarker collection up to 4 timepoints: baseline, 4, 12 and 26 weeks.

To help address issues with potential anxiety and/or discomfort, participants were given the choice to provide stool, blood, or both, depending on their comfort level. Given the differences in timing and structure of funding, participants who consented to stool but not blood collection were administered questionnaires, diet logs and stool collection kits at baseline, 4, 12, and 26 weeks (Fig. 1). Participants who consented to blood but not stool collection were given the same standardized measures and diet logs, and had blood collected and sensory

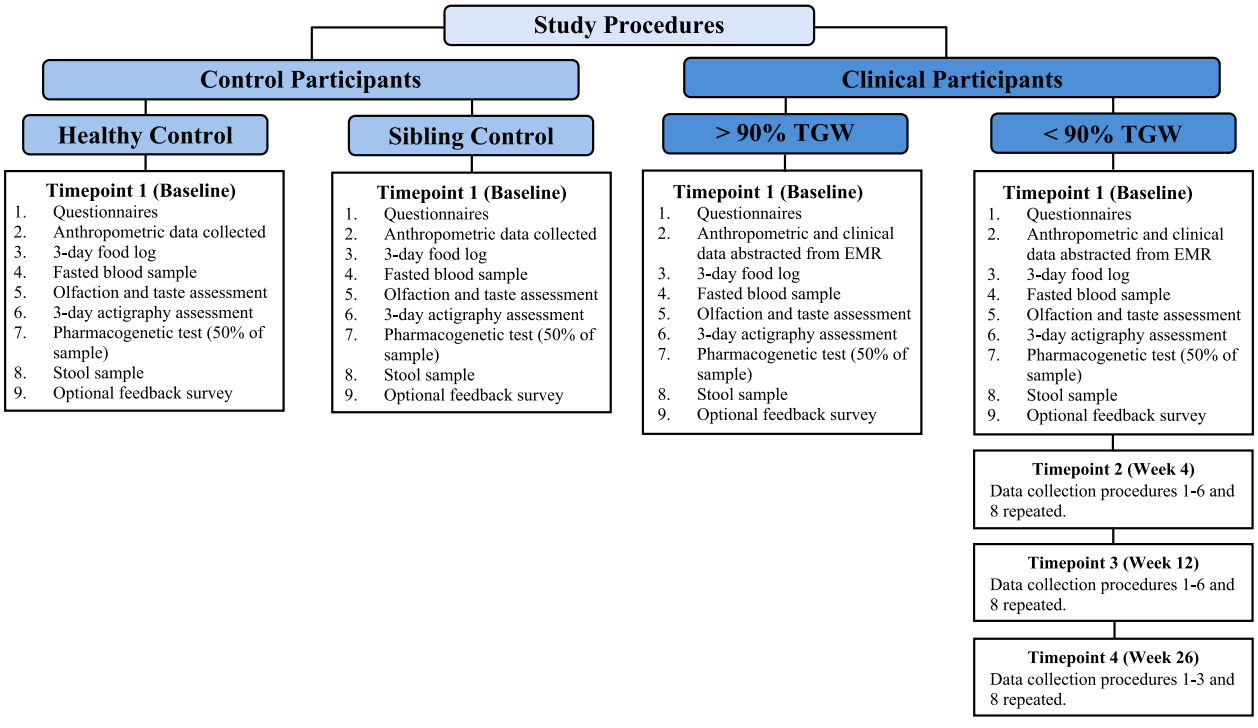

Fig. 1 Study Procedures. *TGW* Treatment goal weight, *EMR* Electronic medical records. All participants completed procedures 1–3; Participants who consented to 4 also completed 5–7; Those who provided stool samples (collection procedure 8) provided a separate consent. Feedback survey added retrospectively in March 2023

and sleep assessments completed at baseline, 4, and 12 weeks. Due to the high cost of pharmacogenetic testing (which focused on cytochrome p450 metabolism) and budgetary constraints, testing was randomized to approximately 50% of participants enrolled in this arm.

The study was approved by the hospital and university research ethics boards.

Participants

Inclusion criteria included a diagnosis of a restrictive ED (i.e., AN—restrictive type, AN—binge-purge type, other specified feeding and eating disorder (atypical AN subtype), unspecified feeding and eating disorder or avoidant restrictive food intake disorder (ARFID) and receiving inpatient and outpatient treatment within our ED program. Exclusion criteria included the presence of comorbid autoimmune-mediated medical conditions or conditions known to influence inflammatory pathways (e.g., rheumatoid arthritis, lupus, inflammatory bowel disease, celiac disease, etc.); pregnancy; treatment in the last two months with steroids, probiotics, or antibiotics (for those participating in the collection of stool for microbiome examination); participants who, in the course of their medical work-up relating to diagnosis of an ED were found to have evidence of any condition outlined above.

Participants seeking ED treatment were categorized based on their percentage TGW at recruitment (individually determined by the clinical team based on developmental history and other factors associated with one's premorbid weight, nutritional, medical, mental health, and menstrual history [29]. We used a convenience sample and based recruitment efforts on an estimation that 60% of patients receiving treatment in our program (approximately 220 patients) would be less than 90% of their TGW, and the majority (>75%) would have a diagnosis of AN [42]. With a hypothesized enrolment rate of 50%, we aimed to recruit 90–100 individuals over 2 years. We also aimed to recruit 25–30 sex and age-matched (within 2 years) control participants and 25–30 sibling participants.

As our primary objective focused on patient enrollment, study completion, adherence, and acceptability, we did not collect enrollment-related information for control subjects or siblings. The total targeted sample size for this study was 150–160 individuals.

Procedure

Eligible participants were identified by a medical clinician (i.e., physician, nurse practitioner or nurse) working in the program at any point after initial assessment had been completed, and an ED diagnosis meeting the inclusion criterion was provided. Diagnoses were provided after initial assessment, and clinical interviews were completed either by a physician, nurse practitioner, or psychologist. If eligible and interested, participants completed informed consent. Control participants were recruited through informal referrals (e.g., from clinical and research staff), promotional posters in outpatient clinics, and online social media announcements. Siblings were recruited by word of mouth and through email outreach facilitated by the research team. In-person recruitment, combined with telephone screening for controls and participants with EDs not receiving inpatient treatment, supported study recruitment efforts.

Patients receiving intensive hospital-based care had blood collected by inpatient hospital staff, and outpatients had blood collected in the hospital's outpatient laboratory. Patients receiving intensive outpatient (or inpatient) care provided stool samples in the hospital or at home (depending on disposition and patient preference), and outpatients collected samples at home. Inpatients completed sleep assessments on the inpatient unit, whereas outpatients and controls were given an actigraphy watch to take home. Measure completion, sensory assessments, and pharmacogenetic assays were completed on the inpatient unit or in the outpatient clinic, depending on participant type and disposition.

Participants were compensated up to $85 CAD and received up to two volunteer service hours per time point (i.e., $50 CAD for completing validated questionnaires, providing a blood sample, and completing sensory, sleep, and cytochrome p450 metabolism assay; $35 CAD for providing a stool sample). Upon study completion, participants were asked to complete a survey exploring feedback relating to their study participation and received one volunteer hour service for the time and effort required to complete the survey.

Measurement

Anthropometric and clinical measurement

Participants' weight, height, duration of illness, comorbidities, menstrual status, and medication history were collected. Weight and height were captured at study baseline for controls only, and all anthropometric and clinical measurements were abstracted for participants with an ED from the medical charts (e.g., clinician reports).

Psychometric measures

Eating disorder examination questionnaire-adolescent [8] Eating disorder symptoms were measured using the Eating Disorder Examination Questionnaire-Adolescent (EDEQ-A [8]). The EDEQ-A is a reliable, validated 36-item instrument that generates four subscale scores: restraint, eating concern, shape concern, weight concern, and a global score. Respondents rate each item on a 7-point Likert-scale (0 = *no days* to 7 = *every day*) and indicate how many of the past 14 days an ED behaviour, atti-

tude or feeling occurred. Scores of 2.8 or higher indicate clinical significance [8, 44]. A global score is calculated by summing the subscale scores and then dividing the value by four [8, 44]. The internal consistency in the EDEQ-A has been shown to be acceptable among clinical and general population samples [8, 44].

Revised children's anxiety and depression scale [10] Anxiety and depression symptoms were captured using the Revised Children's Anxiety and Depression Scale (RCADS; [10]). The RCADS is a reliable and validated 47-item instrument that has been used in a variety of clinical paediatric samples [10]. The measure subscales correspond to social phobia, obsessive/compulsions, panic disorder, generalized anxiety disorder, separation anxiety and major depressive disorder. Participants are asked to rate each statement (e.g., "I worry about things") based on a 4-point Likert scale (i.e., 0 = *never* to 3 = *always*). When comparing the RCADS to other traditional measures, it corresponds to specific diagnoses and shows favourable validity (Chorpita et al., 2002). Calculated T-scores below 65 are considered normal range, while T-scores between 65 to 69 are considered borderline clinical range, and T-scores above 70 are in the clinical range (Carlander et al., 2007).

Short health scale for gastrointestinal symptoms [46] Impact of GI symptoms was assessed using the Short Health Scale for Gastrointestinal Symptoms (SHS-GI [46]). The SHS-GI is a validated short form general measure used to assess the impact of GI symptoms on quality of life, (e.g. "Do your bowel problems interfere with your activities in daily life?") Respondents answer a four-item questionnaire using a 100 mm visual analog scale which ranges from no issue (0 mm) to extreme symptomology/discomfort (10 0 mm). The sum of the four items is taken and is scored out of 400. The SHS-GI is a validated and brief measure that is suitable for capturing the impact of GI symptoms in both patient and general populations [46].

Toronto obsessive compulsive scale [33] Obsessive–compulsive (OC) symptoms were assessed using the Toronto Obsessive Compulsive Scale (TOCS; [33]). The 21-item measure includes six subscales: (a) cleanliness and contamination, (b) symmetry and ordering, (c) counting and checking, (d) rumination, (e) superstition and f) hoarding. Each item is scored on a 7-point Likert scale (-3 = *far less often* to 3 = *far more often).* Responses with a value of two or three are summed for a total score, which indicates the presence or absence of OC symptoms among children and adolescents [33].

Sensory measures

Taste assessment The "Taste Strips" test (Burghart Messtechnik GmbH) was used to assess participants' taste ability (Mueller et al., 2003). The test comprises of paper strips that have varying concentrations of sweet, sour, salty and bitter chemicals, with some containing no taste (Mueller et al., 2003). Participants were asked to identify the taste they perceive on the given strip (Mueller et al., 2003). Each correct response is one point, with a maximum total of 16 [19], Mueller et al., 2003). False identifications may be used to diagnose parageusia in participants. Normative values for scoring have been provided by the manufacturer. This test has been shown to have good reproducibility in clinical settings [19].

Olfaction assessment The "U-Sniff" test (Burghart Messtechnik GmbH) was used to capture participants' olfaction abilities (Gellrich et al., 2017). The test consists of 12 scented pens and participants are asked to identify the presented odor from a choice card with four options (Gellrich et al., 2017). The olfaction test can be used to examine normosmia and reduced smell ability in children [39]. This measure has demonstrated suitability and high test re-test reliability in pediatric populations [39, 47].

Sleep assessment

The Actiwatch-2 (AW2; Philips Respironics, Murrysville, Pennsylvania, United States) is a lightweight ambulatory actigraphy device used to capture participants' sleep patterns. The AW2 provides data on participant' sleep schedule variability, sleep quantity and quality, physical activity levels, and ambient white light levels. The actigraphy assessments were based on device availability. Participants who received a sleep watch were asked to wear the device on the wrist for three consecutive days at each timepoint. The data were exported from the Actiware version 6.3.0. software (Philips Respironics, Murrysville, Pennsylvania, United States) for preliminary processing using the default wake threshold and immobility settings. Epochs were set at 15-s intervals. Estimated sleep onset and end was calculated by using the Philips sleep interval detection algorithm and was set to register if immobile for more than 10 min. AW2 has been validated among pediatric and adolescent samples and performed adequately against the gold standard polysomnography [24, 35].

Blood collection and storage

Fasted blood samples were collected by the hospital's phlebotomy team. Samples included 4 mL lithium heparin vacutainer tubes for quantification of serum C-reactive protein (CRP), cortisol and ferritin by the hospital laboratory and 4 mL K2 EDTA-coated vacutainer tubes

for a complete blood count (CBC) test. Additional 8.5 mL samples were collected in a P800 blood collection tube (BD, Mississauga, ON, CAN, #366420), containing a proprietary mix of protease inhibitors, to ensure biomarker stability and allow accurate measurement of inflammatory, endocrine, and metabolic markers (lipopolysaccharide (LPS), interleukin-6 (IL-6), tissue necrosis factor-alpha and tissues necrosis factor-beta (TNF-α and β), interleukin-1 beta (IL-1β), interleukin-10 (IL-10), interleukin-15 (IL-15), interleukin-17 (IL-17), brain derived neurotrophic factor (BDNF), leptin, ghrelin, neuropeptide y (NPY), oxytocin, vaspin, (glucagon like peptite-1 (GLP-1), gastric inhibitory polypeptide (GIP), and adiponectin). These samples were stored on ice and transported by trained research members for aliquoting and storage at − 80 until later analysis.

Stool collection and storage

Participants were provided with a stool collection kit, assembled and delivered by the research team. The kit included a specialized specimen collection container (nuns cap), protective gloves, specimen collection vial and ice packs. The participants were asked to provide a 10 ml sample, collected using the provided spoon from several areas of the stool. Stool samples collected from participants were directed to be immediately frozen at − 20 °C and kept on ice packs for transport to the laboratory for storage at − 80 °C. The stool sample collection was facilitated by the hospital's internal courier system for participants receiving inpatient treatment or by a local medical laboratory courier service for individuals who completed sample collection outside of the hospital. Participants who visited the hospital infrequently or lived outside of the designated courier system's pickup radius were asked to freeze their samples until they could be returned. The stool samples were collected from the central lab by research team members and stored at − 80 until later assessment of the fecal microbiota diversity, composition, and function.

Dietary record and assessment

Research participants (and/or caregivers where appropriate) were instructed to complete a three-day food log aligning with the time of blood and/or stool sample collection. Patients undertaking cognitive behavioural therapy filled out their own forms, whereas for patients receiving family-based treatment, parents and caregivers or staff completed the logs. As required and appropriate (depending on the stage of treatment), a registered dietitian within the EDP assisted in data collection for dietary records. Questions pertaining to meal preparation methods, amounts eaten, and food descriptions were collected. Food logs underwent quality control parameters based on metrics of portion size, description of items, and time of consumption [20]. Nutritional itemization and dietary assessment were completed using the nutrition tracking program, Cronometer (Cronometer Software Inc., 2025).

OptimalRx plus® pharmacogenetic assay

Participants completed buccal self-swabs, which were processed by Dynacare, a commercial laboratory. The analysis primarily focused on cytochrome p450 metabolism related to psychotropic medications, including SSRIs, SNRIs, SGAs. Standardized reports were returned to the investigator and participants. Assay results are categorized based on degree of metabolism for each gene tested (i.e., normal metabolizer, fast metabolizer, etc.).

Variables relating to study feasibility

Study feasibility was assessed using established feasibility guidelines for design and evaluation [6, 34, 43], which were adapted to address considerations specific to the adolescent ED population under investigation. This assessment included measures of recruitment efficiency and patient uptake (this was not completed for control subjects), adherence to the measurement protocol (for all participants), study dropout (for patients in the longitudinal arm of study), and the acceptability of the overall protocol (for all participants).

Recruitment efficiency and study dropout

Recruitment efficiency was measured by recording the number of patients approached by the research team, including ineligible individuals, eligible individuals who declined to participate, and participants who enrolled in the study. An overall recruitment efficiency percentage was calculated by dividing the number of enrolled participants by the total number of youths approached. Study dropout (for those in the longitudinal arm of study) was calculated at each time point by dividing the number of participants in the longitudinal study arm who completed that time point by the number initially enrolled at baseline (in that specific arm of study).

Adherence to measurement protocol

Adherence to the measurement protocol was calculated by examining the average number of days between each participant's initially scheduled research appointment within a ± 3-day window and the actual date of measurement and by calculating the percentage of participants who adhered to the measurement protocol.

Study acceptability

To evaluate study acceptability, an optional online feedback survey was introduced to the study procedures in March 2023. The survey assessed participants' overall satisfaction and acceptability of the study across

three primary domains: the informed consent process, data collection procedures, and communication with the research team. Each domain included items rated on 5-point Likert scales (e.g., 1 = *strongly disagree* to 5 = *strongly agree*). Open-text responses were also provided to allow participants to elaborate on their experiences and offer suggestions for study improvement (e.g., "Please provide any suggestions as to how the stool kit and the return process could be improved"). Scores were calculated by averaging item responses within each domain. A total acceptability score was calculated by averaging the domain scores. For participants enrolled in the longitudinal arm, the survey was administered at the third timepoint (i.e., approximately 12 weeks after the baseline assessment), while single timepoint participants completed the survey following their research appointment.

Data analysis

Markers of study feasibility were analyzed using Microsoft Excel and IBM SPSS Statistics (Version 30.0). Descriptive statistics were calculated, including measures of central tendencies (mean, median), variability (standard deviation, range), sample size, and percentages. Outliers were identified and retained, as they provided relevant insights into study feasibility and implementation of biomarker collection within this population. Optional open-ended text responses were inductively coded and thematically presented.

Results

Study feasibility

Recruitment efficiency, timepoint completion, and study dropout

A total of 127 patients were approached for the study, of which 100 enrolled (78.74%; $n = 70 < 90\%$ TGW; $n = 30 > 90\%$ TGW). In addition, 29 healthy controls ($n = 24$ [82.76%] consented to providing all samples; $n = 5$ [17.24%] consented to providing all samples except stool) and 23 sibling controls ($n = 15$ [65.22%] consented to providing all samples; $n = 6$ consented to providing all samples except stool [26.09]; $n = 2$ [8.7%] consented to providing stool samples only) enrolled, bringing the total number of participants to 152 (see Fig. 2).

The longitudinal study arm ($n = 70$) included 41 participants (58.57%) who consented to providing all samples, 25 participants (35.71%) who consented to providing all samples except stool, and four participants (5.71%) who consented to providing stool samples only. The single time point > 90% TGW ($n = 30$) included 22 participants (73.33%) who consented to providing all samples, seven participants (23.33%) who consented to providing all samples except stool, and one participant (3.33%) who consented to providing stool samples only. All patients and controls attended baseline timepoints ($n = 152$). Dropout for patients enrolled in the longitudinal study arm from baseline ($n = 70$) to timepoint two (4 weeks; $n = 63$ completed) was 10%, timepoint three (12 weeks; $n = 58$ completed) was 17.14%, and time point four (26 weeks; $n = 30$ of 45 participants with a timepoint at 6 months completed) was 33.33%. Reasons for dropout are provided in Fig. 2.

Adherence to measurement protocol

On average, the time between the healthy controls' initially scheduled research appointment (± 3-day window) and the actual date of timepoint completion was approximately three days ($M = 2.69$, $SD = 13.34$, range = 0–73 days). Two healthy controls (6.9%) had differences in their initially scheduled appointments of 73 days and eight days, respectively. There was no difference in the sibling controls scheduled and actual timepoint completion dates when accounting for the ± 3-day window. The mean number of days between the scheduled research appointment and the actual date of timepoint completion for the > 90% TGW participants was approximately one day ($M = 0.77$, $SD = 4.2$, range = 0–23 days). Only one participant had a 23-day difference between the scheduled research appointment and the actual date the timepoint was completed. For the < 90% TGW participants, the mean number of days between the scheduled research appointment and the actual date of measurement for timepoint one was approximately one day ($M = 0.03$, $SD = 0.24$, range = 0–2 days), three days ($M = 2.86$, $SD = 5.97$, range = 0–25 days) for timepoint two, five days ($M = 4.76$, $SD = 15.20$, range = 0–105 days) for timepoint three, and five days ($M = 4.8$, $SD = 7.98$, range = 0–32 days) for timepoint four. Additionally, the average number of days between the final timepoint and stool collection was approximately 10 days ($M = 9.77$, $SD = 20.88$, range = 0–84 days).

At baseline, protocol adherence was high, with $\geq$ 94% completion for psychometric measures, sensory assessments, blood and stool collection, and $\geq$ 86% for pharmacogenetic testing (see Table 1). Dietary log and sleep assessment completion exhibited the highest rates of non-completion across all timepoints. Despite the anticipated suitability of the actigraphy device, we encountered several challenges over the study duration. As examples, device malfunctions, delays associated with software updates, and subsequent discontinuation of the actigraphy model limited the number of devices available as the study progressed. This resulted in missed opportunities for measurement. We also experienced delays in participants returning devices after at-home assessments were complete, which prevented the optimization of handover of the device from one patient to another. While the

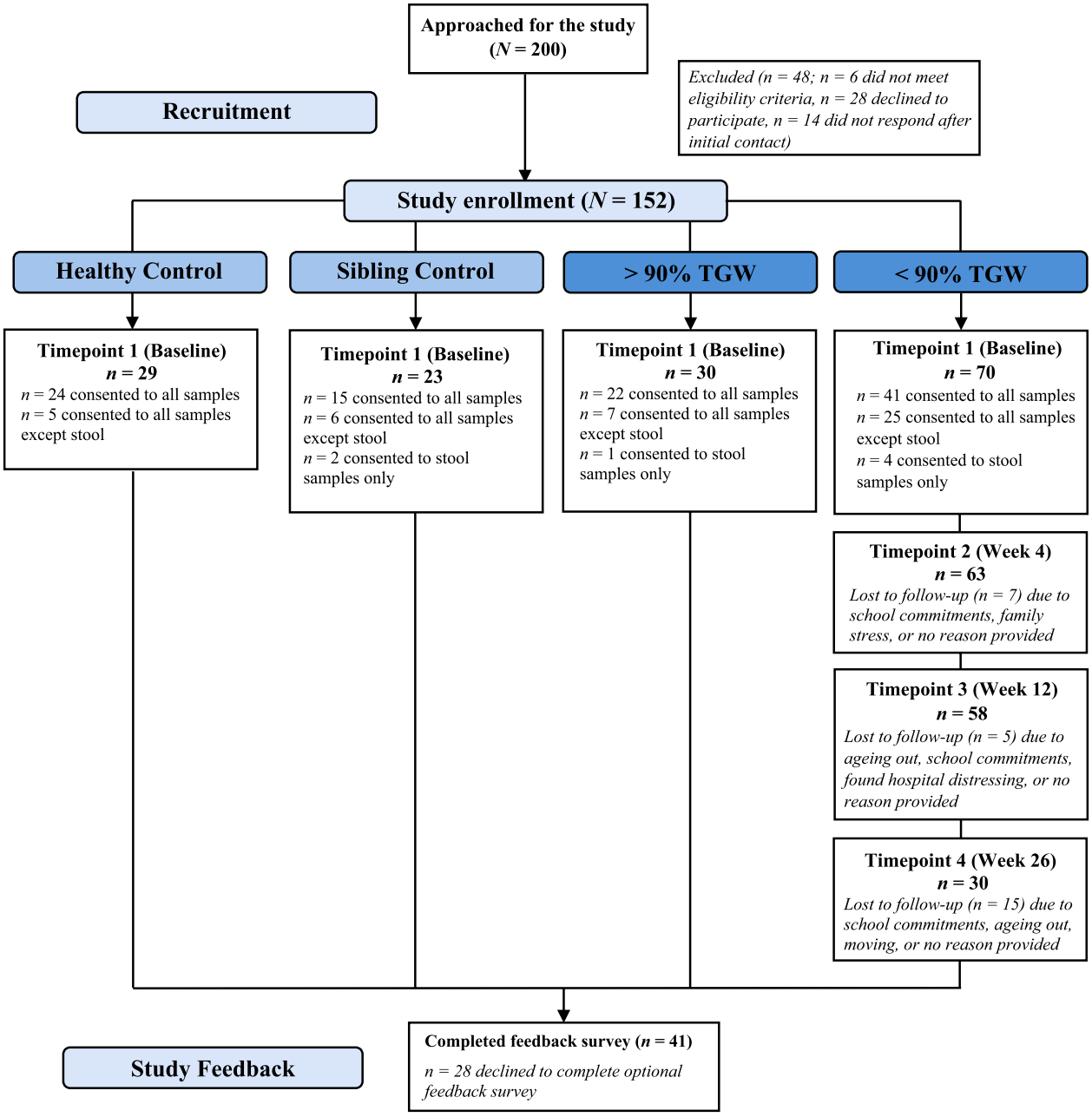

Fig. 2 Participant Consort Table. *TGW* Treatment goal weight

diet logs were intended to capture and track nutritional intake, participants (and parents) noted difficulties providing accurate and sufficiently detailed records.

Aside from challenges with sleep assessments and dietary log completion, the single timepoint groups (i.e., controls, siblings, and > 90% TGW participants) demonstrated a high degree of procedure task adherence. While the < 90% TGW group achieved high procedure adherence and study completion at baseline, increased deviations were noted at 4, 12 and 26 weeks (see Table 1). Deviations included a limited number of stool samples that were thawed during the return process ($n = 3$).

Study acceptability

Forty-one of 69 participants who were offered an opportunity to complete the feedback survey did so (59.42% completion). Results demonstrated agreement across key components of the study, including the informed consent process ($M = 4.52$, $SD = 0.71$), biomarker data collection procedures ($M = 4.08$, $SD = 0.69$), and communication with the research team ($M = 4.44$, $SD = 0.69$). Similarly, the total score for study acceptability was 4.35 ($SD = 0.64$). Open-text responses provided additional insights into participants' experiences. While many responses endorsed the current study protocol (e.g., four

Table 1 Adherence to Study Measurements

Participant	Adherence to measurement													
	Core measurement				Measurement for blood								Measurement for stool	
	Questionnaire		Food log		Blood		Taste		Smell		Sleep		PGT		Stool	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Healthy control																
Timepoint 1 (baseline)	29	100	24	82.76	29	100	29	100	29	100	9	31.03	13	86.67	24	100
Sibling control																
Timepoint 1 (baseline)	23	100	16	69.57	21	100	21	100	21	100	8	38.1	14	100	16	94.12
> 90% TGW																
Timepoint 1 (baseline)	30	100	23	76.67	29	100	29	100	29	100	10	34.48	15	93.75	23	100
< 90% TGW																
Timepoint 1 (baseline)	70	100	61	87.14	66	100	66	100	66	100	46	69.7	35	92.11	45	100
Timepoint 2 (week 4)	63	90	43	61.43	59	89.4	59	89.4	59	89.4	36	54.54	–	–	42	93.33
Timepoint 3 (week 12)	58	82.86	36	51.43	53	80.3	53	80.3	53	80.3	30	45.46	–	–	36	80
Timepoint 4 (week 26)	28	62.2	18	40	–	–	–	–	–	–	–	–	–	–	30	66.67

TGW Treatment goal weight, *PGT* Pharmacogenentic testing, % percent completion. Sleep measurements were collected conditionally based on availability of wearable devices. Pharmacogenetic testing was randomized to approximately 50% of each cohort and conducted at a single timepoint

participants noted the study procedures were well organized and engaging), others (who completed the survey early during the study trial) offered feedback aimed at improving the study's suitability for youth with EDs. For example, two participants indicated the dietary records were "stressful" and "tough" to fill. The preliminary feedback of the dietary records also cited insufficient space for detailed entries and lack of clear instructions as concerns. As the study progressed, the log was amended accordingly. Participants also initially expressed concerns about the small size of the tube provided as part of the stool collection kit; larger tubes were subsequently ordered to address these concerns.

Discussion

To effectively guide the development of precision-psychiatry treatments for EDs, it will be essential to establish protocols and procedures that collect, integrate, analyze, and provide feedback on biomarkers alongside psychological characteristics, behavioural patterns, and social determinants. Given the inherent complexity associated with this task, our research team sought to prospectively examine feasibility markers associated with a multi-axial precision psychiatry study of biomarker collection for patients with EDs. Rates of study recruitment among patients, adherence to outlined protocols, study completion, and participant satisfaction were selected as primary outcome variables.

Given the multidimensional nature of the proposed protocol and sample collection methods, as well as previous research highlighting challenges associated with study recruitment for adolescent patients with EDs, we estimated that approximately 50% of eligible patients would consent to participate [27],Ali et al., 2022; [30, 31]. We observed a much higher overall rate of study enrolment in eligible patients (nearly 80%). It is possible (given the varied proportions of participants who consented to all samples being collected, all samples except stool, or only stool collection) that the flexible nature of the study design helped bolster recruitment. Feedback from participants suggested that feeling at ease during the study recruitment and consenting process likely contributed to this success, with many valuing the flexibility to review the informed consent documents at their own pace and schedule a later discussion if desired. Recruitment efficiency was enabled through collaboration with program staff and the support from the hospital's research integration initiatives. Although not tracked, anecdotal observations from research staff suggested that patient and family stress associated with treatment initiation often resulted in patients and families requiring additional time before consenting to being approached by research staff. Future research efforts should consider additional means by which consent procedures can be facilitated at the

time of treatment initiation, including working with the treatment team at the time referrals are reviewed and initial assessments booked.

To date, few studies have looked at recruitment and retention in ED research as primary outcomes [7]. Unfortunately, high dropout rates have long been recognized in studies of treatment outcomes for individuals with AN [13]. A recent systematic review of ED studies involving cognitive behavioural therapy (CBT) reported an overall dropout of 24% among RCTs, although study designs varied widely as did definitions of dropout [21]. Not surprisingly, dropout rates vary considerably across ED studies, with many citing high overall rates of dropout [4, 18] but others noting high completion rates [7]. Our previous experience with a highly rigorous RCT protocol investigating the utility of olanzapine as an adjunct treatment for AN also highlighted numerous barriers to patient participation and study completion, suggesting a variety of factors likely influence research participation [31]. Overall, results from the present study suggest that recruiting and retaining (a majority of) patients with severe restrictive EDs into multi-axial studies of biomarkers can be accomplished with protocols that utilize single or as many as three timepoints over 12 weeks. Protocols that require biomarker collection beyond this timeframe should factor higher rates of dropout into appropriate power calculations.

Participants' engagement and adherence to most study procedures were observed for all participant cohorts at baseline. Lower rates of sleep assessments and dietary log completion were noted across the entire study. Given the array of issues we faced with the actigraphy devices, additional studies are required to investigate sleep characteristics among adolescents with EDs and the feasibility of integrating sleep variables into a larger protocol involving biomarker collection. In hindsight, the noted difficulties with diet log completion are not necessarily surprising given that clinical research measuring dietary intake has long been recognized as extremely challenging (Bailey, 2022). Our findings suggest additional considerations and modifications are needed to improve how nutritional data is captured and to reduce potential participant burden. Privacy concerns limited the ability of the research team to utilize apps that stored data outside of Canada. Although not in use currently, it is possible that the use of pre-printed descriptions of meal plans for patients undertaking hospital-based treatment might decrease burden and increase completion rates. As the team navigated these issues, there were also questions about whether asking participants to photograph their meals and snacks would be appropriate and offer a possible solution. As research involving the microbiome in EDs increases, it will be important for investigators to understand which method of nutritional data capture (including digital and mobile methods that leverage technology) is suited to best meet the needs of individual studies (Bailey, 2022).

Procedure adherence and participant acceptability in those completing one timepoint suggested that the collection of blood and stool, sensory assessments, pharmacogenetic test completion, and standardized questionnaires were feasible. Allowing participants to provide feedback and suggest adjustments to study procedures during the initial stages of the study development (e.g., increasing the vial size for the stool samples, creating additional writing space in the dietary assessments) also helped streamline study processes. Collecting blood for biomarkers that are subject to degradation (e.g., GLP-1) proved exceptionally costly, as temperature-sensitive vials containing enzyme inhibitors were required for sample collection. Measurement of appetite-regulating hormones (i.e., leptin, ghrelin, neuropeptide Y) and GLP-1 required fasting blood samples, which complicated scheduling due to the rigid nature of the treatment meal schedule. Given the absence of trained phlebotomists on our research team, we relied on hospital personnel for blood collection. As a result, delays occurred regularly, with patients waiting (at times) up to one hour for phlebotomy staff, and thus for breakfast.

For many participants, this study marked their first experience providing a stool sample. The take-home stool collection kit and flexible return process likely increased autonomy and comfort for participants and their families, as they were not required to complete the stool collection during the research appointment. Our research team normalized the data collection process by encouraging questions and reviewing the stool sample kits at each appointment. Verbal, written, and electronic instructions were provided to clearly communicate the stool collection procedures, including stool volume and sampling techniques necessary for accurate microbiome assessment. The flexible stool sample return methods, while designed to accommodate participants, resulted in some minor challenges. In a few isolated examples, there were delays in sample receipt, and as a result, the sample quality was compromised. Moving ahead, consideration could be given to using collection kits containing stabilizers to help minimize these issues.

Collecting sensory data was well accepted by participants. The olfaction and taste assessments required minimal time to administer. While most participants had no concerns with the sensory assessments, a minority of patients ($n < 5$) expressed reservations about the caloric content of the taste strips. Participants were able to consume water during the taste assessment, though it was not required between each taste strip. This deviation from the standardized procedures was necessary for study as water consumption is monitored for some

patients. The order of data collection varied at times; some participants were asked to complete the sensory tasks and psychometric questionnaires while waiting for their blood draw, while other had their blood drawn first when phlebotomy was available. It is possible these modifications and variability in the task sequences may impact study results.

We did not experience any meaningful issues with the pharmacogenetic assay completion. We utilized a commercial assay with preprinted instructions for kit completion and delivery of the sample. Results of the assays were returned to participants and the ordering physician, and the results were transcribed into our database.

After baseline collections were completed, we noted increased deviations from the protocol timing and higher rates of dropout for those in the longitudinal arm. As participants transitioned through different facets of treatment (inpatient, partial hospitalization and outpatient care), arranging research appointments alongside outpatient clinic appointments became more challenging. Study dropout increased as the number of weeks from baseline increased, with 10% of patients dropping out by 4 weeks, 17% dropping out by 12 weeks, and 33% of those with a 6-month timepoint failing to complete collection. Pressures relating to school were often provided as a reason for dropout, although it is unclear how other undocumented factors, including research fatigue or other clinical, treatment, and/or psychosocial factors, impacted these rates, as well as rates of study task completion.

Finally, although outside the primary objective of this study, our experience suggests that some procedures, such as collecting fasting blood samples, manually completing dietary logs, and arranging for courier delivery of outpatient stool samples, added substantially to the cost and operational complexity of trial implementation and completion.

Limitations

Several limitations should be considered in the context of this study. First, markers of study feasibility were assessed using a convenience sample of individuals receiving care through our program, representing a selection bias. Our findings are based on a limited sample and may not be representative of a larger population of adolescents with EDs. Future research should consider broadening inclusion criteria for clinical participants and controls, and explore mechanisms to increase sample size and standardize intake assessments, including the administration of structured interviews. The strict inclusion criteria for controls created recruitment challenges, primarily due to the requirement that participants had not received active treatment for or been diagnosed with a MH condition within the past year at the time of study enrollment. The fact that these patients may have experienced MH conditions prior to this timeframe should also be considered a potential confounder and limitation. Further, as it was not a primary outcome, we did not track the proportion of siblings available for study enrolment or the reasons for or against sibling participation.

Second, the feedback survey was developed and incorporated after the study launched. While having some participants' feedback on the consent and data collection procedures and overall acceptability of the novel study design was helpful, subsequent studies should incorporate validated feasibility measures at study onset to evaluate the suitability of multi-dimensional sample collections amongst this population. The novelty of this research program led to several amendments in the study procedures (e.g., changes to the dietary assessments, stool collection vitals, etc.). Future research should consider flexible windows for data collection (e.g., scheduling data collection while routine blood is being taken) and incorporate other validated sensory and dietary assessments. Finally, optimization of biomarker collection within ED populations would benefit from streamlined laboratory access for biomarker preparation, storage, and analysis, as well as a dedicated phlebotomist for blood sample collection.

Conclusion

The study results suggest multi-axial biomarker research that employs short-term (up to 12 weeks) protocols among adolescents with EDs are feasible, although not without issue, as assessed by high rates of study enrolment, acceptable rates of dropout, adherence to a majority of study procedures, and positive feedback obtained from patients. Protocols that extend testing beyond 12 weeks and up to 6 months, as well as those that rely on dietary logs, should be sufficiently powered to account for higher rates of dropout and noncompletion. Challenges with actigraphy function and availability prevented meaningful conclusions relating to sleep assessment.

Findings from this study can serve to inform the development of future precision psychiatry approaches for ED assessment and treatment in adolescents. The completion of biomarker research is essential to evaluate whether the evolution of ED care into a more analytics-guided, individualized discipline can improve outcomes (Norris, Obeid & El-Emam, 2024). Further research should aim to recruit larger and more diverse sample sizes across all participant groups, explore mechanisms to facilitate study enrolment at the time of treatment initiation, incorporate flexible windows for data collection, and explore additional methods that optimize the measurement of variables relating to sleep and dietary intake. As the body of research investigating questions that pertain to precision psychiatry for EDs grows, it will be important for researchers to share experiences with

study design, implementation, data collection and results to ultimately optimize the success of such trials.

Abbreviations

AN	Anorexia nervosa
AI	Artificial intelligence
ARFID	Avoidant restrictive food intake disorder
AW2	Philips Respironics Actiwatch-2
CBC	Complete blood count
CHEO	Children's Hospital of Eastern Ontario
CRP	C-reactive protein
EDs	Eating disorders
EDP	Eating Disorder Program
EDEQ-A	Eating Disorder Examination Questionnaire-Adolescent
EMR	Electronic medical records
GC	Gas chromatography
GLP-1	Glucagon-like peptide-1
IL-6	Interleukin
MH	Mental health
ML	Machine learning
PMH	Precision mental health
TGW	Treatment goal weight
RCADS	Revised Children's Anxiety and Depression Scale
RD	Registered dietitian
rRNA	Ribosomal ribonucleic acid
SCFAs	Short-chain fatty acids
SHS-GI	Short Health Scale for Gastrointestinal Symptoms
SSRIs	Selective serotonin reuptake inhibitors
SNRIs	Selective serotonin and norepinephrine reuptake inhibitors
SGAs	Second-generation atypical antipsychotics
TOCS	Toronto Obsessive Compulsive Scale

Acknowledgements
Chase Groulx, Melissa King, April McColeman.

Author contributions
MLN, KAP, NO: conceptualization; methodology; analysis; writing—review and editing. WS, LP: conceptualization; methodology; writing—review and editing. NL: project administration; data collection; data analysis; writing. MJG: project administration, data collection; data analysis; writing. DBHL, AFR: data collection; writing. JEP: project administration; writing. NK: conceptualization; methodology; supported data collection; writing. GG: methodology; writing. MH, LI, AR: supported data collection; writing.

Funding
This research was made possible thanks to the Waverley House Foundation through the CHEO Foundation, and in partnership with SickKids, and the Children's Hospital Academic Medical Organization (CHAMO) Innovation Fund at CHEO.

Availability of data and materials
The datasets generated during the study are not publicly available due to analyses of biomarker outcomes being underway. For further information on the data availability, please contact the corresponding author.

Declarations

Ethics approval and consent to participate
The study was approved but the Research Ethics Board at the Children's Hospital of Eastern Ontario (CHEOREB# 22/43X, 22/20X) and the University of Ottawa Research Ethics Board (REB # H-04–22-7917).

Consent for publication
Consent to publish the de-identified study data was obtained by participants who consented to participate in the study.

Competing interests
The authors declare no competing interests.

Author details
[1]Division of Adolescent Medicine, Department of Pediatrics, Children's Hospital of Eastern Ontario, 401 Smyth Ave, Ottawa, ON, Canada
[2]Department of Pediatrics, Faculty of Medicine, University of Ottawa, Ottawa, Canada
[3]Children's Hospital of Eastern Ontario Research Institute (CHEO RI), Ottawa, Canada
[4]Department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ottawa, Canada
[5]School of Nutrition Sciences, Faculty of Health Sciences, University of Ottawa, Ottawa, Canada
[6]Department of Psychiatry, Faculty of Medicine, University of Ottawa, Ottawa, Canada

Received: 16 May 2025 / Accepted: 28 November 2025
Published online: 12 December 2025

References

1. Agüera Z, Jiménez-Murcia S. Advances in eating disorders. J Clin Med. 2020;9(12):4047. https://doi.org/10.3390/jcm9124047.
2. Auger N, Potter BJ, Ukah UV, Low N, Israël M, Steiger H, et al. Anorexia nervosa and the long-term risk of mortality in women. World Psychiatry. 2021;20(3):448–9. https://doi.org/10.1002/wps.20904.
3. Bailey RL. Overview of dietary assessment methods for measuring intakes of foods, beverages, and dietary supplements in research studies. Curr Opin Biotechnol. 2021;70:91–6. https://doi.org/10.1016/j.copbio.2021.02.007.
4. Breton É, Dufour R, Côté SM, Dubois L, Vitaro F, Boivin M, et al. Developmental trajectories of eating disorder symptoms: a longitudinal study from early adolescence to young adulthood. J Eat Disord. 2022;10(1):84. https://doi.org/10.1186/s40337-022-00603-z.
5. Bickman L, Lyon AR, Wolpert M. Achieving precision mental health through effective assessment, monitoring, and feedback processes. Adm Policy Ment Health. 2016;43(3):271–6. https://doi.org/10.1007/s10488-016-0718-5.
6. Bowen DJ, Kreuter M, Spring B, Cofta-Woerpel L, Linnan L, Weiner D, et al. How we design feasibility studies. Am J Prev Med. 2009;36(5):452–7. https://doi.org/10.1016/j.amepre.2009.02.002.
7. Brownstone L, Anderson K, Beenhakker J, Lock J, Le Grange D. Recruitment and retention in an adolescent anorexia nervosa treatment trial. Int J Eat Disord. 2012;45(6):812–5. https://doi.org/10.1002/eat.22010.
8. Carter JC, Stewart DA, Fairburn CG. Eating disorder examination questionnaire: norms for young adolescent girls. Behav Res Ther. 2001;39(5):625–32. https://doi.org/10.1016/S0005-7967(00)00033-4.
9. Cassioli E, Lucherini Angeletti L, Rossi E, Selvi G, Riccardi E, Siviglia S, et al. Leptin levels in acute and recovered eating disorders: an arm-based network meta-analysis. Eur Eat Disord Rev. 2025;33(3):525–37. https://doi.org/10.1002/erv.3163.
10. Chorpita BF, Moffitt CE, Gray J. Psychometric properties of the revised child anxiety and depression scale in a clinical sample. Behav Res Ther. 2005;43(3):309–22. https://doi.org/10.1016/j.brat.2004.02.004.
11. Couturier J, Kimber M, Szatmari P. Efficacy of family-based treatment for adolescents with eating disorders: a systematic review and meta-analysis. Int J Eat Disord. 2013;46(1):3–11. https://doi.org/10.1002/eat.22042.
12. Cronometer Software Inc. [Nutrition Tracking Application]. (2025). Retrieved from https://cronometer.com/
13. Dejong H, Broadbent H, Schmidt U. A systematic review of dropout from treatment in outpatients with anorexia nervosa. Int J Eat Disord. 2012;45(5):635–47. https://doi.org/10.1002/eat.20956.
14. Dong TS, Gupta A. Influence of early life, diet, and the environment on the microbiome. Clin Gastroenterol Hepatol. 2019;17(2):231–42. https://doi.org/10.1016/j.cgh.2018.08.067.
15. Eddy KT, Tabri N, Thomas JJ, Murray HB, Keshaviah A, Hastings E, et al. Recovery from anorexia nervosa and bulimia nervosa at 22-year follow-up. J Clin Psychiatry. 2017;78(2):184–9. https://doi.org/10.4088/JCP.15m10393.
16. Fernandes BS, Karmakar C, Tamouza R, Tran T, Yearwood J, Hamdani N, et al. Precision psychiatry with immunological and cognitive biomarkers: a multi-domain prediction for the diagnosis of bipolar disorder or schizophrenia using machine learning. Transl Psychiatry. 2020;10(1):162. https://doi.org/10.1038/s41398-020-0836-4.

17. Fernandes BS, Williams LM, Steiner J, Leboyer M, Carvalho AF, Berk M. The new field of 'precision psychiatry.' BMC Med. 2017;15(1):80. https://doi.org/10.1186/s12916-010849-x.
18. Halmi KA, Agras WS, Crow S, Mitchell J, Wilson GT, Bryson SW, et al. Predictors of treatment acceptance and completion in anorexia nervosa: implications for future study designs. Arch Gen Psychiatry. 2005;62(7):776–81. https://doi.org/10.1001/archpsyc.62.7.776.
19. Landis BN, Welge-Luessen A, Brämerson A, Bende M, Mueller CA, Nordin S, et al. "Taste strips"—a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. J Neurol. 2009;256(2):242–8. https://doi.org/10.1007/s00415-009-0088-y.
20. Leeming ER, Mompeo O, Turk P, Bowyer RCE, Louca P, Johnson AJ, et al. Characterisation, procedures and heritability of acute dietary intake in the Twins UK cohort: an observational study. Nutr J. 2022;21(1):13. https://doi.org/10.1186/s12937-022-00763-3.
21. Linardon J, Hindle A, Brennan L. Dropout from cognitive-behavioral therapy for eating disorders: a meta-analysis of randomized, controlled trials. Int J Eat Disord. 2018;51(5):381–91. https://doi.org/10.1002/eat.22850.
22. Malcolm A, Phillipou A. Current directions in biomarkers and endophenotypes for anorexia nervosa: a scoping review. J Psychiatr Res. 2021;137:303–10. https://doi.org/10.1016/j.jpsychires.2021.02.063.
23. Malcolm A, Toh WL, Crocker K, Phillipou A. The contribution of sleep to anorexia nervosa severity. Eat Weight Disord. 2022;27(4):1563–8. https://doi.org/10.1007/s40519-021-01286-2.
24. Meltzer LJ, Wong P, Biggs SN, Traylor J, Kim JY, Bhattacharjee R, et al. Validation of actigraphy in middle childhood. Sleep. 2016;39(6):1219–24. https://doi.org/10.5665/sleep.5836.
25. Mills R, Hyam L, Schmidt U. A narrative review of early intervention for eating disorders: barriers and facilitators. Adolesc Health Med Ther. 2023;14:217–35. https://doi.org/10.2147/AHMT.S415698.
26. Monteleone AM, Pellegrino F, Croatto G, Carfagno M, Hilbert A, Treasure J, et al. Treatment of eating disorders: a systematic meta-review of meta-analyses and network meta-analyses. Neurosci Biobehav Rev. 2022;142:104857. https://doi.org/10.1016/j.neubiorev.2022.104857.
27. Norris ML, Spettigue W, Obeid N. Pragmatic clinical trials to advance research in children and adolescents with eating disorders. Int J Eat Disord. 2024;57(6):1350–6. https://doi.org/10.1002/eat.24209.
28. Norris ML. Exploring biologically oriented precision mental health initiatives for the care of patients with eating disorders: a narrative review. Eur Eat Disord Rev. 2024. https://doi.org/10.1002/erv.3114.
29. Norris ML, Hiebert JD, Katzman DK. Determining treatment goal weights for children and adolescents with anorexia nervosa. Paediatr Child Health. 2018;23(8):551–551. https://doi.org/10.1093/pch/pxy133.
30. Norris ML, Spettigue W, Buchholz A, Henderson KA, Obeid N. Factors influencing research drug trials in adolescents with anorexia nervosa. Eat Disord. 2010;18(3):210–7. https://doi.org/10.1080/10640261003719468.
31. Norris ML, Spettigue W, Buchholz A, Henderson KA. Challenges associated with controlled psychopharmacological research trials in adolescents with eating disorders. J Can Acad Child Adolesc Psychiatry. 2007;16(4):167–72.
32. Obeid N, Lavallée N, Bradley AHM, Norris M, L. Considerations for informing precision psychiatry in eating disorders: foundations for future practice. J Eating Dis. 2025;13:162. https://doi.org/10.1186/s40337-025-01351-6.
33. Park LS, Burton CL, Dupuis A, Shan J, Storch EA, Crosbie J, et al. The Toronto obsessive-compulsive scale: psychometrics of a dimensional measure of obsessive-compulsive traits. J Am Acad Child Adolesc Psychiatry. 2016;55(4):310-318.e4. https://doi.org/10.1016/j.jaac.2016.01.008.
34. Pearson N, Naylor PJ, Ashe MC, Fernandez M, Yoong SL, Wolfenden L. Guidance for conducting feasibility and pilot studies for implementation trials. Pilot Feasibility Stud. 2020;6(1):167. https://doi.org/10.1186/s40814-020-00634-w.
35. Pesonen A-K, Kuula L. The validity of a new consumer-targeted wrist device in sleep measurement: an overnight comparison against polysomnography in children and adolescents. J Clin Sleep Med. 2018;14(4):585–91. https://doi.org/10.5664/jcsm.7050.
36. Rajadhyaksha V. Conducting feasibilities in clinical trials: an investment to ensure a good study. Perspect Clin Res. 2010;1(3):106–9.
37. Rossi E, Cassioli E, Gironi V, Idrizaj E, Garella R, Squecco R, et al. Ghrelin as a possible biomarker and maintaining factor in patients with eating disorders reporting childhood traumatic experiences. Eur Eat Disord Rev. 2021;29(4):588–99. https://doi.org/10.1002/erv.2831.
38. Scala JJ, Ganz AB, Snyder MP. Precision medicine approaches to mental health care. Physiology. 2023;38(2):82–98. https://doi.org/10.1152/physiol.00013.2022.
39. Schriever VA, Agosin E, Altundag A, Avni H, Cao Van H, Cornejo C, et al. Development of an international odor identification test for children: the universal sniff test. J Pediatr. 2018;198:265-272.e3. https://doi.org/10.1016/j.jpeds.2018.03.011.
40. Singh D, Dhiman VK, Pandey M, Dhiman VK, Sharma A, Pandey H, et al. Personalized medicine: an alternative for cancer treatment. Cancer Treat Res Commun. 2024;42:100860. https://doi.org/10.1016/j.ctarc.2024.100860.
41. Smith S, Charach A, To T, Toulany A, Fung K, Saunders N. Pediatric patients hospitalized with eating disorders in Ontario, Canada, over time. JAMA Netw Open. 2023;6(12):e2346012. https://doi.org/10.1001/jamanetworkopen.2023.46012.
42. Spettigue W, Norris ML, Douziech I, Henderson K, Buchholz A, Valois DD, et al. Feasibility of implementing a family-based inpatient program for adolescents with anorexia nervosa: a retrospective cohort study. Front Psychiatry. 2019;10:887. https://doi.org/10.3389/fpsyt.2019.00887.
43. Teresi JA, Yu X, Stewart AL, Hays RD. Guidelines for designing and evaluating feasibility pilot studies. Med Care. 2022;60(1):95–103. https://doi.org/10.1097/MLR.0000000000001664.
44. Velkoff EA, Brown TA, Kaye WH, Wierenga CE. Using clinical cutoff scores on the eating disorder examination-questionnaire to evaluate eating disorder symptoms during and after naturalistic intensive treatment. Eat Disord. 2023;31(5):464–78. https://doi.org/10.1080/10640266.2023.219148.
45. Verebi C, Nectoux J, Duriez P, Gorwood P, Ramoz N, Bienvenu T. The value of plasma cell-free DNA levels as biomarker in patients with eating disorders: a preliminary study. Psychoneuroendocrinology. 2024;160:106918. https://doi.org/10.1016/j.psyneuen.2023.106918.
46. Walter S, Jones MP, Sjödahl J, Stjernman H, Hjortswang H, Andreasson A. Measuring the impact of gastrointestinal inconvenience and symptoms on perceived health in the general population—validation of the short health scale for gastrointestinal symptoms (SHS-GI). Scand J Gastroenterol. 2021;56(12):1406–13. https://doi.org/10.1080/00365521.2021.1974087.
47. Zou L, Dworschak A, Alizadeh R, Kamrava SK, Alwashahi M, Bock MA, et al. U-Sniff"- the international odor identification test for children: an extension of its normative database and study of global reliability. Rhinology J. 2020;58(5):471–6. https://doi.org/10.4193/Rhin19.355.

Publisher's Note