

Protocol for literature review on psychotropic drug use in children

Revised 2018/03/20

This protocol is designed to answer the following research questions:

1. What recent studies have examined the use of psychotropic medication in children ages 0-18, including (a) prevalence or (b) predictors of use (using either predictive models or subgroup comparisons)?
2. What geographies and populations have been examined by prevalence studies, and what were the resulting prevalence estimates?
3. What predictors of use have been identified? For each predictor, what is the nature of the relation with use and the strength of evidence?

Inclusion and exclusion criteria

The review will include studies meeting the following criteria:

- Journal article, white paper, research or evaluation report, dissertation, or master's thesis
- Published between 2011-2015 inclusive (We will not examine gray literature, seek recommendations from authors, or hand-search journals. We searched databases using the original 2000-2015 date range, which we later amended due to limited resources.)
- Examines prevalence or predictors of using psychotropic medication in general or a category of psychotropic medication (e.g., anticonvulsants, antidepressants, antimanic drugs, hypnotics, mood stabilizers, sedatives, stimulants, tranquilizers) (Note: This includes studies of prevalence or predictors of use among children with a specific diagnosis such as ADHD, but not among children at the end of life. Prevalence studies must be quantitative, but studies of predictors of use may be either quantitative or qualitative.)
- Includes U.S. children ages 0-18 (may also include older individuals, as long as results are reported separately for children 0-18)

Clarifications about the definition of "using psychotropic medication:"

- Studies with medication adherence, discontinuation, or continuation as an outcome are included as studies of medication use.
- Studies focusing on receipt of guideline-concordant psychotropic treatment or medication monitoring as an outcome are also included.
- Studies merely mentioning psychotropic medication use or predictors of use as background information, but not having use as an outcome, are not included.
- Studies of medication provided in preparation for, or in conjunction with, inpatient medical care or procedures are excluded. Specifically, studies of perioperative

medication (pre- or post-procedure drugs such as anesthesia and analgesia) are excluded.

- Similarly, studies of trauma care and end-of-life care are excluded.
- Studies that examine mental health treatment in general (e.g. of caregivers' willingness for children to receive mental health treatment), but not psychotropic use in particular, are excluded.
- Case studies are excluded.
- Studies of overdose or poisoning are excluded.

Clarification about "inclusion of U.S. children ages 0-18"

- Studies of caregivers, providers, etc., are included, as long as the study focuses on psychotropic use in U.S. children. Because applying the age restriction to such studies might result in a large amount of information loss, we will not apply the age restriction to otherwise relevant studies whose participants are not children.

Databases

We will run several database searches (described in the numbered list below), beginning with a search for previous reviews (#1) and proceeding to a combined search through EBSCOhost (#2). We will search PubMed separately in order to use MeSH terms and explode the term for "psychotropic drugs" (i.e., include all MeSH terms below this term). When we search EMBASE (#3), we will exclude items indexed in PubMed.

This section lists databases to be used for the review.

1. Review databases
 - a. [Cochrane Library](#) [link through UNC; also available at NCSU]
 - b. [Joanna Briggs Institute EBP Database](#) [link through UNC]
2. EBSCOhost
 - a. [Global Health](#) [link through UNC; NC State has temporary access, which may expire soon]
 - b. Health Source: Nursing/Academic Edition
 - c. PsycINFO
 - d. Social Work Abstracts
 - e. [CINAHL Plus with Full Text](#) [link through UNC; not available at NCSU]
 - f. [not MEDLINE; search PubMed separately]
3. [PubMed](#) [link through UNC; also available at NCSU; use MeSH headings]
4. [EMBASE](#) [Elsevier; link through UNC; exclude items indexed in PubMed]
5. Web of Science
 - a. Social Sciences Citation Index
6. ProQuest
 - a. ProQuest Dissertations and Theses
 - b. Social Services Abstracts

Procedure

We will complete the steps enumerated below. Steps described in italics are expected to occur after May 2016. Because we are addressing broad research questions, we may adjust and re-publish the protocol at any step.

1. Search the review databases, using the search criteria described below, in order to identify any previous reviews published between 2011-2015. Use any previous reviews found as the basis for forward citation searches in Google Scholar and Web of Science. For each of these two forward citation searches, document the number of records retrieved and export the results, including title and abstract.
2. Search each of the remaining databases, using the search criteria described below and documenting the number of records retrieved from each search. At least for the first database search, check to make sure that studies known to be eligible (see below) are included in the search results. Export the results of each search, including title and abstract, to a separate file. With exported files: (a) use software to convert to CSV format, (b) create a program to de-duplicate records, (c) import into Excel, and (d) create identical spreadsheets to facilitate title and abstract screening.
3. For each study, at least two independent reviewers will review the title and abstract and will document whether the study meets the inclusion criteria (estimates prevalence, examines predictive model, examines predictors using subgroups, examines outcomes, quantitative, qualitative, includes U.S. children ages 0-18). For records without abstracts, we will attempt to screen based on the title and, if necessary and feasible, we will obtain the abstract and screen based on the title and abstract together. There may be overlap between prevalence and predictive studies. The principal investigator will evaluate at least a representative subsample of studies. Any disagreements about whether to retain an article for further screening will be resolved through discussion. If consensus is not reached, the principal investigator will decide how to proceed.
4. Create an initial flow diagram documenting the number of ineligible studies and reasons for ineligibility, the number of duplicates, and the number of eligible studies by category (i.e., prevalence, predictive, both).
5. For studies classified as prevalence studies:
 - a. Obtain the full text. Re-evaluate the paper based on the full text. Document the findings as described above. At least two individuals will evaluate each study, and the principal investigator will evaluate at least a representative subsample. Any discrepancies in findings will be resolved through discussion. If consensus is not reached, the principal investigator will decide how to proceed.
 - b. For prevalence studies that remain eligible, document the following:
 - i. sample size
 - ii. geographic coverage (list of states (or "US"), with indicator for partial coverage of a single state)

- iii. age range
 - iv. distribution of sex (% male if available; otherwise % female)
 - v. distribution of race/ethnicity (% for each race/ethnicity category; categories may vary by study and therefore may require later consolidation)
 - vi. distribution of income/SES (% for each SES category; categories may vary by study and therefore may require later consolidation)
 - vii. inclusion/exclusion criteria (e.g., Medicaid enrollment) (text field)
 - viii. data source (text field - e.g., Medicaid claims, parent interviews)
 - ix. study population (indicators for children, parents, providers; text for other)
 - x. drugs or drug types examined (indicators for psychotropic drugs overall and for individual categories listed below)
 - xi. prevalence period (e.g., annual, quarterly)
- c. Update the flow diagram documenting the number of ineligible studies and reasons for ineligibility, the number of duplicates, and the number of eligible studies by category (i.e., prevalence, predictive, both).
 - d. Summarize the prevalence findings in a paper.
6. *For studies classified as predictive studies:*
- a. *Obtain the full text. Re-evaluate the paper based on the full text. Document the findings as described above. At least two individuals will evaluate each study, and the principal investigator will evaluate at least a representative subsample. Any discrepancies in findings will be resolved through discussion. If consensus is not reached, the principal investigator will decide how to proceed.*
 - b. *For predictive studies that remain eligible, document the following:*
 - i. *variables 5(b)(i) - 5(b)(x)*
 - ii. *one column for each predictor examined, indicating direction of association with use (1, -1, 0)*
 - c. *Update the flow diagram documenting the number of ineligible studies and reasons for ineligibility, the number of duplicates, and the number of eligible studies by category (i.e., prevalence, predictive, both).*
 - d. *Summarize the predictive findings in a paper.*

Search criteria

General instructions: Search using the database-specific search strings and database-specific instructions listed in the “search string” column. Convert files using the database-specific instructions highlighted in green in the “Database” column.

Database	search string
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[Cochrane](#)

Exports to a text file. Import into RefWorks using the "Wiley Interscience" import format, then export using the "Bibliographic Software" format. If the download does not occur automatically, it may be necessary to right-click the link and choose "Save Link As..." Save the exported file in the refworks_exports folder within the shared Google Drive folder.

((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*)
OR ((CNS OR (central NEXT nervous NEXT system) OR (anti NEXT anxiety) OR ADHD OR (attention NEXT deficit NEXT hyperactivity NEXT disorder*) OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) NEXT (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental NEXT health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*)

search title, abstract, keywords

include Cochrane reviews (all, including protocols), other reviews, and economic evaluations

limit to 2000-2015

Approximate # records to expect based on testing: **218**

[Joanna Briggs](#)

Check "all," then
click Export (to
RIS).

1:
(anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR
anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR
neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz*
OR tranquilis*)

2:
((CNS OR (central ADJ1 nervous ADJ1 system) OR (anti ADJ1 anxiety)
OR ADHD OR (attention ADJ1 deficit ADJ1 hyperactivity ADJ1 disorder*)
OR psychiatric OR ((behavior OR behavioral OR behavioural OR
emotional) ADJ1 (disorder* OR problem* OR diagnosis OR diagnoses))
OR psychotherapeutic OR (mental ADJ1 health)) AND (agent* OR
medication* OR drug* OR pharmacotherapy OR
psychopharmacotherapy))

3:
(administration OR "use" OR utilization OR utilisation OR prescri* OR
prevalence OR incidence OR initiation OR rate* OR receipt OR
treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR
juvenile* OR pediatric OR paediatric OR young OR youth*)

search all fields

(1 or 2) and 3
limit 4 to yr="2000 - 2015"

include evidence summaries, systematic review protocols, and systematic
reviews

Approximate # records to expect based on testing:

1: 504

2: 617

3: 2319

(1 or 2) and 3: 457

limit 4 to ((evidence summaries or "systematic review protocols" or
systematic reviews) and yr="2000 - 2015"): **385**

EBSCOhost 1
([CINAHL Plus with Full Text](#),
PsycINFO)

Export limit
25,000. Request
link via email,
with RIS format.
If download is
missing some
records,
document this
and make up to
3 total attempts.

TI (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*)) OR AB (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*)) OR SU (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*))

limit to 2000-2015

limit to English language

CINAHL - limit to "all child;" exclude MEDLINE records

PsycINFO - limit to childhood (0-12), neonatal (0-1), infancy (2-23 mo), preschool age (2-5), school age (6-12), adolescence (13-17)

	11,350
<p>EBSCOhost 2 (Global Health, Health Source: Nursing/Academic Edition, Social Work Abstracts)</p> <p>Export limit 25,000. Request link via email, with RIS format. If download is missing some records, document this and make up to 3 total attempts.</p>	<p>TI (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*)) OR AB (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*)) OR SU (((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central w0 nervous w0 system) OR (anti w0 anxiety) OR ADHD OR (attention w0 deficit w0 hyperactivity w0 disorder*) OR psychiatric OR ((behavioral OR behavioural OR emotional) w0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental w0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*))</p>

	<p>limit to 2000-2015 limit to English language</p> <p>Approximate # records to expect based on testing: 5,013</p>
<p>Embase</p> <p>Can export up to 10K to RIS format (use drop-down menu labeled "Select number of items," then click Export).</p>	<p>((('anticonvulsant' OR 'anticonvulsants' OR 'antidepressant' OR 'antidepressants' OR 'antimanic' OR 'antimanics' OR 'antipsychotic' OR 'antipsychotics' OR 'anxiolytic' OR 'anxiolytics' OR 'hypnotic' OR 'hypnotics' OR 'mood stabilizer' OR 'mood stabilizers' OR 'mood-stabilizing' OR 'mood stabiliser' OR 'mood stabilisers' OR 'mood-stabilising' OR 'neuroleptic' OR 'neuroleptics' OR 'psychotropic' OR 'psychotropics' OR 'sedative' OR 'sedatives' OR 'stimulant' OR 'stimulants' OR 'tranquilizer' OR 'tranquilizers' OR 'tranquiliser' OR 'tranquillisers' OR ('cns' OR 'central nervous system' OR 'anti-anxiety' OR 'adhd' OR 'attention-deficit hyperactivity disorder' OR 'attention-deficit disorder' OR 'attention deficit disorder' OR 'psychiatric' OR 'behavior disorder' OR 'behavior disorders' OR 'behavior problem' OR 'behavior problems' OR 'behavior diagnosis' OR 'behavior diagnoses' OR 'behavioral disorder' OR 'behavioral disorders' OR 'behavioral problem' OR 'behavioral problems' OR 'behavioral diagnosis' OR 'behavioral diagnoses' OR 'behavioural disorder' OR 'behavioural disorders' OR 'behavioural problem' OR 'behavioural problems' OR 'behavioural diagnosis' OR 'behavioural diagnoses' OR 'emotional disorder' OR 'emotional disorders' OR 'emotional problem' OR 'emotional problems' OR 'emotional diagnosis' OR 'emotional diagnoses' OR 'psychotherapeutic' OR 'mental health' AND ('agent' OR 'agents' OR 'medication' OR 'medications' OR 'drug' OR 'drugs' OR 'pharmacotherapy' OR 'psychopharmacotherapy')) AND ('administration' OR 'use' OR 'utilization' OR 'utilisation' OR 'prescription' OR 'prescriptions' OR 'prescribing' OR 'prescribed' OR 'prevalence' OR 'incidence' OR 'initiation' OR 'rate' OR 'rates' OR 'receipt' OR 'treatment' OR 'treatments')) OR (('psychotropic agent' OR 'antidepressant agent' OR 'tranquilizer' OR 'anxiolytic agent' OR 'neuroleptic agent' OR 'mood stabilizer' OR 'central nervous system agents' OR 'hypnotic agent' OR 'sedative agent' OR 'central stimulant agent' OR 'central depressant agent' OR 'anticonvulsive agent' OR 'attention deficit disorder' OR 'mental disease' OR 'problem behavior') AND ('drug therapy' OR 'drug utilization')) AND 'human'/de AND ('article'/it OR 'review'/it) AND ([infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR [adolescent]/lim OR [child]/lim) AND [2000-2015]/py AND [english]/lim NOT [medline]/lim</p> <p>on mapping tab of advanced search, uncheck all boxes</p>

	<p>Approximate # records to expect based on testing: 5,483</p>
<p>Web of Science (Social Sciences Citation Index)</p> <p>Export 500 records at a time, "full record," using "other reference software" format; will result in 26 files; name files wos_00001_005 00 etc.)</p>	<p>TS=(((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood stabilizer* OR mood stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR (central NEAR/0 nervous NEAR/0 system) OR (anti NEAR/0 anxiety) OR ADHD OR (attention NEAR/0 deficit NEAR/0 hyperactivity NEAR/0 disorder*) OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) NEAR/0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR (mental NEAR/0 health)) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*))</p> <p>limit to English limit to 2000-2015 Approximate # records to expect based on testing: 12,996</p>
<p>ProQuest (ProQuest Dissertations and Theses Global, Social Services Abstracts)</p> <p>To export >100 records, select 1-100, then go to page 2 and select 101-200, etc. After selecting all desired records, go to "More..." and export.</p> <p>Export to Excel format.</p>	<p>all(((anticonvulsant* OR antidepress* OR antimanic* OR antipsychotic* OR anxiolytic* OR hypnotic* OR mood-stabilizer* OR mood-stabiliser* OR neuroleptic* OR psychotropic* OR sedative* OR stimulant* OR tranquiliz* OR tranquilis*) OR ((CNS OR central-nervous-system OR anti-anxiety OR ADHD OR attention-deficit-hyperactivity-disorder* OR psychiatric OR ((behavior OR behavioral OR behavioural OR emotional) NEAR/0 (disorder* OR problem* OR diagnosis OR diagnoses)) OR psychotherapeutic OR mental-health) AND (agent* OR medication* OR drug* OR pharmacotherapy OR psychopharmacotherapy))) AND (administration OR use OR utilization OR utilisation OR prescri* OR prevalence OR incidence OR initiation OR rate* OR receipt OR treatment*) AND (neonat* OR infan* OR child* OR teen* OR adolesc* OR juvenile* OR pediatric OR paediatric OR young OR youth*)) AND la(English)</p> <p>limit to 2000-2015 Approximate # records to expect based on testing: 2,385</p>

[PubMed](#)

Export to XML
format.

("Anticonvulsants/therapeutic use"[Mesh] OR "Narcotics/ therapeutic use"[Mesh] OR "Central Nervous System Depressants/ therapeutic use"[Mesh:NoExp] OR "Hypnotics and Sedatives/ therapeutic use"[Mesh] OR "Tranquilizing Agents/ therapeutic use"[Mesh] OR "Central Nervous System Stimulants/ therapeutic use"[Mesh:NoExp] OR "Wakefulness-Promoting Agents/ therapeutic use"[Mesh] OR "Psychotropic Drugs/ therapeutic use"[Mesh]) OR ("Anticonvulsants/statistics and numerical data"[Mesh] OR "Narcotics/statistics and numerical data"[Mesh] OR "Central Nervous System Depressants/statistics and numerical data"[Mesh:NoExp] OR "Hypnotics and Sedatives/statistics and numerical data"[Mesh] OR "Tranquilizing Agents/statistics and numerical data"[Mesh] OR "Central Nervous System Stimulants/statistics and numerical data"[Mesh:NoExp] OR "Wakefulness-Promoting Agents/statistics and numerical data"[Mesh] OR "Psychotropic Drugs/statistics and numerical data"[Mesh]) AND (drug therapy[mesh] OR "drug therapy"[sh] OR utilization OR "prevalence" OR "incidence")

limit to 2000-2015

limit to English

limit to Child 0-18

Approximate # records to expect based on testing: **17,997**