UTAH DEPARTMENT OF HEALTH & HUMAN SERVICES
CONTRACT AMENDMENT

Utah Department of Health & Human Services

PO Box 144003, Salt Lake City, Utah 84114
288 North 1460 West, Salt Lake City, Utah 84116

2102110	212701484
Department Log Number	State Contract Number

1. CONTRACT NAME: The name of this contract is Pharmacy DUR and P and T Support Amendment 1.

2. CONTRACTING PARTIES: This contract amendment is between the Utah Department of Health & Human Services (DEPARTMENT) and Office of Sponsored Projects University of Utah (CONTRACTOR).

PAYMENT ADDRESS
Office of Sponsored Projects University of Utah
201 S Presidents Circle Rm 406
Salt Lake City UT, 84112

MAILING ADDRESS
Office of Sponsored Projects University of Utah
201 S Presidents Circle Rm 406
Salt Lake City UT, 84112

Vendor ID: VC0000162160
Commodity Code: 99999

3. PURPOSE OF CONTRACT AMENDMENT: The purpose of this amendment is to incorporate additional reports and add funding.

4. CHANGES TO CONTRACT:

   1. The contract amount is being changed. The original amount was $2,000,000. The funding amount will be increased by $150,000 in state funds. New total funding is $2,150,000.
   2. Attachment B, effective 4/17/2023, is replacing Attachment B, which was effective 1/1/2021.
   3. Attachment D, effective 4/17/2023, is being added.

All other conditions and terms in the original contract and previous amendments remain the same.

5. EFFECTIVE DATE OF AMENDMENT: This amendment is effective 04/17/2023.

6. DOCUMENTS INCORPORATED INTO THIS CONTRACT BY REFERENCE BUT NOT ATTACHED:
   A. All other governmental laws, regulations, or actions applicable to services provided herein.
   B. All Assurances and all responses to bids as provided by the CONTRACTOR.

7. This contract, its attachments, and all documents incorporated by reference constitute the entire agreement between the parties and supersedes all prior written or oral agreements between the parties relating to the subject matter of this contract.

IN WITNESS WHEREOF, the parties enter into this agreement.

CONTRACTOR

By: _____ 04/19/2023
Brent Brown Date
Director, Office of
Sponsored Projects

STATE

4/29/2023

By: _____ _____
Tracy S. Gruber Date
Executive Director, Department
of Health & Human Services

Attachment B

University of Utah – Utah Medicaid

Pharmacy DUR and P&T Support

Special Provisions

Effective Date: April 17, 2023

I. Parties

CONTRACTOR: University of Utah College of Pharmacy, Drug Regimen Review Center

DEPARTMENT: Utah Department of Health, Division of Medicaid & Health Financing, Bureau of Healthcare Policy & Authorization, Medicaid Pharmacy Team.

As of July 1, 2022, the Department shall be known as the Utah Department of Health and Human Services, Division of Integrated Healthcare, Office of Healthcare Policy & Authorization, Medicaid Pharmacy Team.

II. Effective Date and Duration

The period of this Agreement is five years, from January 1, 2021, through December 31, 2025, unless terminated or extended by agreement in accordance with the terms and conditions of this contract. The DEPARTMENT may extend this contract annually two times by means of an amendment to this contract. Any extension must be in writing.

III. Purpose

The purpose of this Agreement is to establish requirements for which the DEPARTMENT will pay the CONTRACTOR to provide evidence-based recommendations to the Drug Utilization Review Board (DUR) and the Pharmacy & Therapeutics Committee (P&T), and submit Additional Reports as requested by the DEPARTMENT.

IV. Definitions

A. Additional Reports means any report requested under section V.C.

B. Contractor means the “Sub-recipient” or the person who delivers the services or goods described in this Contract, other than the state or the Department.

C. Drug means any substance recognized by the United States Food and Drug Administration to diagnose, cure, mitigate, treat or prevent disease.

D. Drug and Criteria Review means a written and oral report of analyses of literature, Medicaid Data and Patient and/or Provider reviews, including recommendations to the Drug Utilization Review Board.

E. Drug Utilization Review Board means a group of individuals designated to perform Drug Utilization Review duties as described in Utah Code 26-18-2 sections 102 and 103. The Board holds at least 10 open public hearings per calendar year.

F. Medicaid means the State of Utah Department of Health, Division of Medicaid and Health Financing.

G. A Hierarchy of Evidence approach means that evidence for DUR criteria set reviews and P&T reports will be gathered by starting at the top of the evidence pyramid, which means that if there are high-quality systematic reviews and meta-analyses that answer the question sufficiently, we will cite only that evidence. If not, we will move down the evidence pyramid to experimental studies, then observational studies, then expert opinion. XXXX

H. Patient means a Utah Medicaid client who receives any service reimbursed by a fee- for-service pharmacy program(s).

I. Pharmacy & Therapeutics Committee means a group of individuals designated to perform Pharmacy and Therapeutics activities as described in Utah Administrative Code R414-60B. The committee meets at least once quarterly.

J. Provider means Pharmacists and/or Prescribers involved in a Patient’s medical care.

K. Scope of Services

The CONTRACTOR shall perform pharmacy drug information services for the DUR Board and the P&T Committee on behalf of the DEPARTMENT, specifically:

1. DUR Board Reports: Performs criteria set reviews of proposed drugs or drug classes to analyze the evidence for pharmacologic drug utilization, comparative efficacy and safety, and evaluation and proposal of prior authorization criteria.

2. P&T Committee Reviews: Perform systematic reviews of the evidence for comparative safety and efficacy for medications under consideration for inclusion on Medicaid's Preferred Drug List (PDL). This includes place in therapy and considerations for special populations with respect to drugs within a given class. Provide evidence-based recommendations to the Utah Medicaid P&T Committee in the form of written reports and oral presentation at P&T Committee meetings, under the direction of DMHF.

The CONTRACTOR shall also perform pharmacy drug information services to develop Additional Reports as requested by the DEPARTMENT.

V. Requirements

A. DUR Board Reviews

1. CONTRACTOR and DEPARTMENT staff shall meet quarterly to collaboratively plan and update future DUR topics. The proposed topics must be approved by the Bureau Director.

a. Topic selection may be based on new therapeutic options, safety considerations, appropriate use, appropriate limitations, or other areas of concern to the DEPARTMENT. In order to meet all timeline requirements, topic selection must be finalized no later than 18 weeks before the presentation date, including Bureau Director approval.

2. The CONTRACTOR shall conduct preliminary searches to identify key areas of focus and work with DEPARTMENT personnel to finalize the scope of the reports, no later than 14 weeks before the presentation date. The scope will include finalizing the specific details of any utilization data to be included in the report.

3. The CONTRACTOR shall perform a literature review according to a hierarchy of evidence (HOE) strategy.

a. Depending on the type and availability of evidence needed, common search locales include Medline (PubMed); the US Food and Drug Administration (FDA) website (including product labeling information); Lexicomp; World Health Organization; national associations governing research and treatment of the disease state; and other drug databases. Reference lists from search results are screened for additional relevant publications.

4. For each report, the CONTRACTOR shall evaluate usage patterns of the medication(s) being reviewed. Utah Medicaid utilization data will be extracted using Utah Medicaid classification (0812*) and will be included in the report.

a. Other data centers such as the Centers for Disease Control and prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), Public Health Indicator Based Information System (IBIS) Utah's Public Health Data Resource, the FDA website, Micromedex, Lexicomp, UpToDate, Pharmacist's letter, Cochrane Library and PubMed may also be searched for specific information to help inform the drug utilization extraction.

5. The CONTRACTOR shall submit the completed report, including utilization data, to the DUR Board manager and the bureau director no later than 3:00 pm local time 21 calendar days prior to the DUR meeting date.

6. No later than 14 calendar days prior to the DUR meeting date, CONTRACTOR staff shall meet with DEPARTMENT staff to finalize key points for the presentation. No later than 3:00 pm local time 7 calendar days prior to the meeting, a presentation slide deck of the report that is to be presented shall be submitted to the same DEPARTMENT staff.

B. P&T Committee Reviews

1. CONTRACTOR and DEPARTMENT staff shall meet quarterly to collaboratively plan and update future P&T topics. The proposed topics must be approved by the Bureau Director.

a. P&T reviews may be based on new drugs, new drug classes, and re-review of previously presented topics in order to assess the safety and efficacy of the medications. In order to meet all timelines specified in this proposal, topic selection will be finalized no later than 18 weeks before the presentation date, including Bureau Director approval.

2. For each approved topic, the CONTRACTOR shall perform a literature search to inform the CONTRACTOR and DEPARTMENT regarding the precise scope of the report.

a. Two methodological filters shall be used: one for systematic reviews/meta-analyses (SRMAs) and another for randomized controlled trials (RCTs). Results shall be limited to English language studies from 2010 to present for SRMAs and from 2015 to present for RCTs. Reference lists of related systematic reviews and other relevant websites shall be screened for further information. At least two review authors shall screen titles and abstracts and conflicts shall be resolved via discussion between reviewers or a third person. The full texts for all citations receiving 2 inclusion votes shall be retrieved and reviewed. Evidence shall be selected according to the HOE by the lead author. High quality SRMAs may be sufficient to answer the questions of comparable safety and efficacy; when necessary, evidence to the level of direct RCT comparisons shall be included. In these cases, SRMAs of RCTs and RCTs providing direct head-to-head efficacy and/or safety comparisons shall be prioritized.

3. The CONTRACTOR shall submit completed reviews to the P&T manager and the bureau director no later than 3:00 pm 21 calendar days prior to the P&T Committee meeting date.

4. No later than 14 calendar days prior to the DUR meeting date, CONTRACTOR staff shall meet with DEPARTMENT staff to finalize key points for the presentation. No later than 3:00 pm 7 calendar days prior to the meeting, a presentation slide deck of the report that is to be presented shall be submitted to the same DEPARTMENT staff.

C. Work Orders for Additional Reports

1. Within ten business days of receiving a written work order from the DEPARTMENT for an Additional Report, the CONTRACTOR shall submit a written proposal including timeline and budget for the Department's consideration and feedback. The CONTRACTOR shall notify the DEPARTMENT in writing if additional time is required to develop and submit the proposal.

2. Once accepted by the DEPARTMENT, the parties shall negotiate the specific proposal language and amend this contract to include the proposal, provisions, and any funds as necessary.

3. The CONTRACTOR shall complete the report and submit it to the DEPARTMENT by the agreed upon timeline found in the accepted proposal. If additional time is required, the CONTRACTOR shall request additional time in writing with at least 10 business days

advanced noticed. The DEPARTMENT shall approve or deny the request in writing within five business days. A contract amendment shall not be required to adjust the timeline.

VI. Evaluation, Reporting, and Outcomes

A. The CONTRACTOR shall deliver a total of 10 DUR Board reports per year. Each report shall be delivered 3 weeks before each DUR Board meeting. A DRRC staff pharmacist or faculty member will attend the DUR Board meeting and present a summary of the contents of the report, and will remain to answer questions and provide additional insight in support of the DUR Board discussion.

B. The CONTRACTOR shall deliver a total of 4-12 P&T Committee reviews per year, depending on scope of each report. This will include between 1-3 reports at each quarterly P&T Committee meeting, depending on scope. Each review shall be delivered 3 weeks before each P&T Committee meeting. A DRRC staff pharmacist or faculty member will attend the P&T Committee meeting and present a summary of the contents of the written report. The staff pharmacist will remain to answer questions and provide additional insight in support of the P&T Committee discussion.

C. The CONTRACTOR shall deliver Additional Reports according to the timeline agreed upon in amendments as provided in section V.

D. The DEPARTMENT shall organize quarterly meetings for the DEPARTMENT and CONTRACTOR to discuss and identify interventions and MTMS already completed and to be completed in the future, as well as to discuss Additional Reports requested by the DEPARTMENT.

E. The CONTRACTOR shall provide to the DEPARTMENT annual reports containing a summary and impact assessment of the CONTRACTOR's activities. The report shall include:

1. Data from the previous Federal fiscal year (October 01 through September 30), and shall be submitted to the Department on or before March 01 of the following year. For example, a report regarding Federal fiscal year 2015 (October 01, 2014 to September 30, 2015) must be submitted on or before March 01, 2016.

2. A brief overview of the Drug and Criteria Reviews and any other reports or presentations prepared and/or presented in the previous Federal fiscal year.

3. Analyses of fee-for-service drug claims and costs.

4. Any other information that the CONTRACTOR believes the DEPARTMENT will find useful or noteworthy.

VII. Data

A. Contractor's Access to Data

1. Individuals employed by the CONTRACTOR shall access Patients' personal health information (prescription and other health claims) Data via a secure, encrypted internet connection. Patients' personal health information will be accessed and used according to the Utah Department of Health and Human Services Business Associate Agreement. The DEPARTMENT shall provide technical assistance to the CONTRACTOR in order to facilitate access to prescription and health claims Data.

2. Each interaction and consultation with the CONTRACTOR will be documented in an Access Database. This Database will be able to link to Medicaid prescription claims. This will provide the ability to review prior requests and actions taken in making decisions for additional requests.

B. Contractor's Use of Data

1. The CONTRACTOR agrees that any and all Data exchanged must be used expressly and solely for the purposes set forth in this contract.

2. The CONTRACTOR shall ensure that any agents, including subcontractors, to whom it may transmit, exchange or provide the Data agrees to the same restrictions and conditions set forth in this Agreement.

C. Data Transmission

The DEPARTMENT shall provide the CONTRACTOR with access to or a copy of Data in a method to be determined by the Department. Unless otherwise agreed upon by the DEPARTMENT, the CONTRACTOR agrees that any and all electronic transmission or exchange of Data with the DEPARTMENT or any other parties must take place via secure means (using HTTPS or SFTP or equivalent).

D. Data Security and Confidentiality

1. The use, storage and transmissions of Data are implemented, maintained and monitored according to the best business practices and standards established by each party. The parties jointly agree to determine the specific technical, regulatory or administrative rules or regulations that govern the technical use of Data or Data transmission.

2. The CONTRACTOR shall establish safeguards to protect the confidentiality of the Data and to prevent unauthorized access to the Data provided by the DEPARTMENT. Safeguards include, but are not limited to:

a. Maintaining adequate physical controls and password protections for any server or system on which the Data may reside

b. Ensuring the Data is not stored on a device or transmitted electronically unless it is secure or encrypted

c. Taking any other measures reasonably necessary to prevent any use or disclosure of the Data other than as provided in this Agreement.

3. The CONTRACTOR acknowledges the need to maintain and negotiate changes affecting the sharing of Data in a manner that does not compromise the administrative, physical, and technical safeguards that the CONTRACTOR implements and maintains to secure the integrity, safety and privacy of Data.

4. This duty of confidentiality shall be ongoing and survive the term of the contract. The data will remain the property of the DEPARTMENT and will continue to be subject to and protected by GRAMA and HIPAA. Upon termination of the contract, the CONTRACTOR agrees to hold in confidence the information obtained from the DEPARTMENT and will take reasonable and prudent action to safeguard the data from the initial receipt of the information through the end of the disposal process.

E. Breach of Privacy or Security Obligations

The CONTRACTOR shall immediately notify the DEPARTMENT upon discovery of any use or disclosure not authorized hereunder. Such report shall be made to the DEPARTMENT as soon as reasonably possible, but in no event, later than 3 business days from the date on which CONTRACTOR becomes aware that the Data has been used or disclosed in a manner not provided for by this Agreement. The

CONTRACTOR agrees to fully cooperate with any remediation that the DEPARTMENT, in its sole discretion, determines is necessary to:

1. Address any applicable reporting requirements, and
2. Mitigate any effects of such unauthorized use or disclosure of the Data.

F. Data Ownership

The parties mutually agree that the DEPARTMENT retains all ownership rights to the Data and that CONTRACTOR does not obtain any right, title, or interest in any Data furnished by the DEPARTMENT.

G. Disposition of Data

The CONTRACTOR agrees that upon expiration or termination of this Agreement, it shall erase, destroy and render unreadable all Data and certify in writing to the DEPARTMENT that these actions have been completed within 30 days of the expiration or termination of this Agreement or within 7 days of the request of the DEPARTMENT, whichever shall come first.

H. Risk Assessments and Audits

1. The DEPARTMENT may require the CONTRACTOR to conduct a risk assessment that addresses administrative, technical and physical risks, if reasonable and appropriate. If requested by the DEPARTMENT, the CONTRACTOR shall provide a copy of the risk assessment findings and results.

2. The DEPARTMENT or a DEPARTMENT-appointed audit firm may conduct audits of the CONTRACTOR during normal working hours to observe the practices for protecting the privacy and security of Data.

I. Terms and Termination

The terms of this section shall remain in effect as long as CONTRACTOR retains the Data.

J. Health and Human Services Records

Pursuant to 42 U.S.C. Section 1395x (V) (1) (I) with respect to any services furnished under the terms of this Agreement, the value or cost of which is $10,000.00 or more over a 12-month period, until the expiration of four (4) years after termination of this Agreement, the CONTRACTOR and the

DEPARTMENT shall make available upon request to either the United States Department of Health and Human Services or the United States Comptroller General, and their representatives, a copy of this Agreement and such other documents and records as are necessary to certify the nature and extent of the costs of the services provided by the CONTRACTOR under this Agreement.

K. HIPAA Compliance

The DEPARTMENT and the CONTRACTOR mutually acknowledge that in the performance of this Agreement each may have access to patient medical records and other protected health information, the confidentiality of which is protected by law. Neither party nor its employees shall disclose to any third party, except where permitted or required by law or where such disclosure is expressly approved in writing by the other party, any patient or medical record information regarding transferred patients. Both parties shall comply with all Federal and State laws and regulations, and all rules, regulations, and policies regarding the confidentiality of such patient information, including without limitation the Health Insurance Portability and Accountability Act (HIPAA). Each party represents and warrants to the other that it is in compliance with the privacy provisions of HIPAA as found under 45 CFR, parts 160 and 164: Standards for Privacy or Individually Identifiable Health Information, commonly known as the "Final Privacy Rule." Each party shall cooperate with the other in implementing such Business Associate Agreement or other Agreements as HIPAA may require. Each party shall indemnify and hold the other party harmless from any liability, costs, awards, judgments, penalties, or fees (including reasonable attorney's fees) arising out of a breach of its confidentiality or other obligations under this Paragraph. However, nothing in this contract shall constitute a waiver of any defense available to either under the Utah Governmental Immunity Act.

VIII. Billing and Payments

A. DUR Board Reviews and P&T Committee Reviews: Up to a maximum of $400,000 per year ($2,000,000 for the duration of the contract), the DEPARTMENT shall compensate the CONTRACTOR at the following rates, based on the requirements outlined above. Charges for all reports will be based on an hourly rate of $105 per hour. The final price for each report will be calculated when the scope is finalized, 14 weeks before the presentation date. A worksheet for estimating charges for DUR and P&T reports will be used (see Appendix 1).

B. Work Orders for Additional Reports: The DEPARTMENT shall compensate the CONTRACTOR at the rates agreed to in any amendments to this contract.

C. The DEPARTMENT shall reimburse the CONTRACTOR for all travel beyond the borders of Salt Lake County (including airfare, car rental, food, and lodging), and other expenses reasonably incurred by the CONTRACTOR in providing these services, if approved in advance by the DEPARTMENT.

D. The CONTRACTOR shall submit quarterly invoices to the DEPARTMENT for services provided under this Agreement. All invoices must provide a description of the services, a statement of hours worked, and an itemization of any expenses incurred.

E. The DEPARTMENT shall pay invoices submitted by the CONTRACTOR within 15 business days of receipt of each invoice.

IX. Limitations

A. Intellectual Property

Notwithstanding Article VIII, Information Ownership, of the Utah Department of Health and Human Services General Provisions for the University of Utah, the DEPARTMENT grants to the CONTRACTOR a non-exclusive right to use all intellectual property conceived or developed by the CONTRACTOR in the performance of the services specified in Paragraph V - VII above.

B. Publication

The DEPARTMENT shall place no restrictions upon the CONTRACTOR's ability to publish any portion of the intellectual properties that result from performance of services specified by this Contract. The DEPARTMENT will publish class reviews online as part of the Pharmacy and Therapeutics Committee meeting materials.

C. Disclaimer of Warranties

The DEPARTMENT acknowledges that the individual use and application of the intellectual properties may involve complex medical decisions and factual circumstances beyond the knowledge of the CONTRACTOR. Although the CONTRACTOR shall exercise its best professional judgment in developing the drug reviews, the CONTRACTOR makes no representations or warranties whatsoever, express or implied, including, but not limited to, any implied warranty of merchantability and/or fitness for a particular purpose, with respect to the intellectual properties, and specifically disclaims all such warranties. The DEPARTMENT and other users of the drug reviews are advised that decisions regarding the use of drugs and drug therapies are complex medical decisions, and that in using these drug reviews each user must exercise his/her own independent professional judgment. Neither the DEPARTMENT nor the CONTRACTOR assumes any liability for persons administering or receiving drugs or other medical care in reliance upon these drug reviews, or otherwise in connection with the services rendered. Neither the DEPARTMENT nor the CONTRACTOR endorses or recommends the use of any particular drug.

Attachment D: Gender Dysphoria Report Proposal

COLLEGE OF PHARMACY
UNIVERSITY OF UTAH
L. S. SKAGGS PHARMACY INSTITUTE

GENDER-AFFIRMING MEDICAL TREATMENTS FOR PEDIATRIC PATIENTS WITH GENDER DYSPHORIA

Proposal

Submitted to

Jennifer Strohecker, PharmD, BCPS
Medicaid Director
Director, Division of Integrated Healthcare
Utah Department of Health and Human Services
jstrohecker@utah.gov

Submitted by

Joanne LaFleur, PharmD, MSPH
Director, Drug Regimen Review Center
Associate Professor, Department of Pharmacotherapy
University of Utah, College of Pharmacy
Joanne.LaFleur@pharm.utah.edu

February 27, 2023

BACKGROUND

In recent years, there has been a growing public awareness about the challenges faced by individuals suffering from *gender dysphoria*. According to the 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-VI), this condition is defined as a disparity between an individual's perceptions about their own gender identity relative to their assigned gender at birth, resulting in psychological distress. The incorporation of the diagnostic term *gender dysphoria* into the DSM-5 is relatively new; it was added in 2013.[1] However, that diagnostic term was preceded by the term *gender identity disorder* in the DSM-3, published in 1980,[2] and the condition itself has been reported in the medical literature as long ago as the 1800s.[3] Outside the medical literature, transgender individuals have been mentioned in western literature for more than 2 thousand years; for example, as early as the 1st century BCE, the Roman poet Ovid wrote a collection of stories and myths, The Metamorphoses, which included a myth about a transgender figure, Tiresias.[4]

The recent increase in public awareness has coincided with a great deal of public discourse in which individuals from across the political spectrum have opined publicly and privately about whether gender dysphoria should be medically treated, and if so, how. Much of the discourse has focused on the issue of whether transgender children should receive the same medical interventions that are offered to adult patients.[5,6] A 2018 guideline by the American Academy of Pediatrics (AAP) advocated for the importance of gender-affirming medical care in transgender children,[7] citing evidence that gender-affirming care may reduce depression, anxiety, eating disorders, self-harm, and suicide.[8-14]

Despite the AAP's advocacy,[15] Utah state legislators passed a law on January 28, 2023 prohibiting newly-diagnosed transgender and gender-diverse minors from receiving gender-affirming medical interventions;[17] Utah is the 5th state to pass legislation banning gender-affirming care for transgender minors.[16] Senate Bill (SB) 16 refers to the ban as a *moratorium*, and charges the Utah Department of Health and Human Services (UDHHS) to undertake a systematic review of the medical evidence about gender-affirming hormonal and hormone- blocking agents, and to use that as the basis for making a recommendation to the legislature about whether the moratorium on use of these treatments in minors should be lifted.[17]

Objective

To support the UDHHS in its charge, we propose a phased approach to conducting a systematic, world-wide search for medical evidence addressing the safety and efficacy of hormonal and hormone-blocking prescription drugs used in pediatric patients with gender dysphoria, including relevant sources to answer the following questions:

Research questions

1. What hormones and hormone blockers are used in gender-affirming care of pediatric patients?

   What is the regulatory status of the treatments? (ie, are they approved by the US Food and Drug Administration [FDA] for use in pediatric patients?)

   What are the indications and contraindications for their use?

   What are off-label pediatric indications listed in pharmacy compendia for hormones and hormone blockers?

2. What recent clinical practice guidelines address medical interventions for gender-affirming treatment in pediatric gender dysphoria patients?

   What recommendations are made in the guidelines?

   What are the levels of evidence (LOEs) that support the guideline recommendations?

3. What systematic reviews and meta-analyses (SRs/MAs), randomized controlled clinical trials (RCTs), and observational studies address short- and long-term safety and efficacy outcomes of hormonal and hormone-blocking agents in pediatric gender-affirmation care patients?

   What are the primary and secondary findings of the studies?

   What is the quality (or risk-of-bias [ROB]) of the evidence?

4. Among pediatric patients who initiate a hormone or hormone blocker, what are the short- and long-term rates of discontinuation?

APPROACH

Standard tertiary databases (eg, MicroMedex, UpToDate, and the FDA Orange Book) will be searched to identify a comprehensive list of all drug product hormones and hormonally active agents that are used in gender dysphoria, transgender, and gender-diverse children in the United States. Information in these databases that addresses the relevant question above will be extracted; for example, the FDA Orange Book will be the primary source for identifying FDA-approved indications.

Remaining questions will be addressed by a comprehensive search of at least 2 standard bibliographic medical databases, including Medline and Embase, and Cochrane CENTRAL if time allows. Search strategies used for bibliographic databases will be conducted according to minimum best-practice standards, and will employ both structured vocabulary (eg, medical subject headings [MeSH] for Medline and EmTree for Embase), and unstructured keyword terms in relevant database fields. The searches will be limited to relevant citations published since 2010 to ensure that studies preceding the 2013 addition of the term *gender dysphoria* to the DSM-VI are retrieved. Search strategies will use validated, high-quality filters for publication types (ie, guidelines, systematic reviews, experimental studies, observational studies, and descriptive studies.) Potentially relevant citations will be screened for eligibility in duplicate.

Evidence tables will be created to summarize evidence in relevant citations, including a summary of each study (all publication types) and an evaluation of the quality of the evidence (all publication types except descriptive studies).

The work will be conducted in 2 phases:

- The **initial phase (Phase I)** will include the identification of all hormonal and hormone-blocking agents used or recommended for gender-affirming care in the US, based on secondary and tertiary literature sources. For each drug, the table will list FDA-approved pediatric indications, relevant off-label uses, and contraindications.

  Phase I will also include a summary of recent clinical practice guidelines (since 2010) that address treatment of gender dysphoria, evidence tables of SRMAs identified in bibliographic database searches, including a summary of their findings and an appropriate risk-of-bias (ROB) assessment for each review, and a bibliography of all relevant studies identified in bibliographic databases, grouped into relevant publication types, including the following:

  - Guidelines
  - Systematic reviews and meta-analyses
  - Experimental studies
  - Observational studies
  - Descriptive studies

- **Phase II** will include the delivery of evidence tables for all explanatory studies, including experimental and observational studies; the evidence tables will summarize primary and secondary safety and efficacy findings as well as a ROB assessment. Phase II will also include summaries of all relevant descriptive studies identified in bibliographic database searches.

BUDGET, TIMELINE, AND DELIVERABLES

The total budget for the proposed work in this Attachment D will be $150,000 in direct costs for work to be completed by July 31, 2023. Invoices will be submitted no earlier than July 2023, and will be submitted for work performed, as shown in the table of project milestones, deliverables, deliverable dates, and charges:

Table: Payment milestones, deliverables, and budget for the proposed work

Phase	Payment Milestones/Deliverables	Completion Date	Payment Amount *(Percentage of total budget)*
0	Contract signed	April 17, 2023	$37,500 *(25%)*
I	A. Table of hormonal and hormone-blocking agents used in pediatric gender dysphoria patients, their regulatory status, and indications/contraindications for their use	May 1, 2023	$22,500 *(15%)*
	B. Table of clinical practice guidelines, their recommendations, and LOE for supporting evidence C. Evidence tables: Systematic review findings and ROB assessment	June 30, 2023[a]	$30,000 *(20%)*
	D. Bibliography of relevant publications since 2013, categorized broadly by publication type: guidelines, SRMAs, RCTs, observational studies, and descriptive studies	July 31, 2023[a]	$37,500 *(25%)*
II	A. Evidence tables: Experimental and observational study findings and ROB assessment	July 1, 2023[a]	$15,000 *(10%)*
	B. Evidence tables: Descriptive study findings	July 31, 2023[a]	$7,500 *(5%)*
	C. Additional evidence as it arrives: Evidence-table updates. Some relevant citations may be added after the July deadline. (For example, some citations require Interlibrary Loan [ILL]).	TBD[b]	–

Total			**$150,000**

[a] *Evidence tables for relevant citations retrieved by a comprehensive search (including all relevant structured vocabulary terms and/or keyword terms) in 1-2 bibliographic databases (ie, Medline and Embase) will be completed and delivered by July 1, 2023. We anticipate that this will comprise at least 90% of the relevant citations.*

[b] *Late retrievals will be added to the deliverables as they arrive, with delivery of all Phase I and II evidence tables from a complete and comprehensive search with all relevant structured vocabulary and keyword search terms in at least 2 bibliographic databases (ie, Medline, Embase, and/or Cochrane CENTRAL. All updates will be provided no later than September 30, 2023.*

REFERENCES

1. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders Text Revision (DSM-5-TR).* 5th ed. American Psychiatric Association; 2022. doi:10.1176/appi.books.9780890425763 Last Updated 2022. Accessed July 12, 2022. Available at https://www.appi.org/Products/DSM-Library/Diagnostic-and-Statistical-Manual-of-Mental-Di-(1)

2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders - Revised (DSM-III-R).* American Psychiatric Association; 1980. doi:10.1176/appi.books.9780890420188.dsm-iii-r Accessed February 27, 2023. Available at https://dsm.psychiatryonline.org/doi/book/10.1176/appi.books.9780890420188.dsm-iii-r

3. Koh J. [The history of the concept of gender identity disorder]. *Seishin Shinkeigaku Zasshi*. 2012;114(6):673-680. https://www.ncbi.nlm.nih.gov/pubmed/22844818

4. 43 BCE-17 AD or 18 AD Ovid. *Ovid metamorphoses*. Tarrant RJ, ed. Oxford University Press; 2004.

5. Kaufman E. What We Owe Children Contemplating a Gender Transition. *Wall Street Journal*. August 23, 2022. Accessed February 27, 2023. Available at https://www.wsj.com/articles/trans-gender-transition-medical-surgery-hormones-affirm-therapy-conversion-academy-pediatrics-aap-11661289032

6. Bazelon E. The Battle over Gender Therapy. *New York Times Magazine*. June 15, 2022. Accessed February 27, 2023. Available at https://www.nytimes.com/2022/06/15/magazine/gender-therapy.html

7. Rafferty J, Committee On Psychosocial Aspects Of C, Family H, et al. Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents. *Pediatrics*. 2018;142(4)doi:10.1542/peds.2018-2162 https://www.ncbi.nlm.nih.gov/pubmed/30224363

8. Almeida J, Johnson RM, Corliss HL, Molnar BE, Azrael D. Emotional distress among LGBT youth: the influence of perceived discrimination based on sexual orientation. *J Youth Adolesc*. 2009;38(7):1001-1014. doi:10.1007/s10964-009-9397-9 https://www.ncbi.nlm.nih.gov/pubmed/19636742

9. Clements-Nolle K, Marx R, Katz M. Attempted suicide among transgender persons: The influence of gender-based discrimination and victimization. *J Homosex*. 2006;51(3):53-69. doi:10.1300/J082v51n03_04 https://www.ncbi.nlm.nih.gov/pubmed/17135115

10. Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: results from a longitudinal study. *Psychoneuroendocrinology*. 2014;39:65-73. doi:10.1016/j.psyneuen.2013.09.029 https://www.ncbi.nlm.nih.gov/pubmed/24275005

11. Haas AP, Eliason M, Mays VM, et al. Suicide and suicide risk in lesbian, gay, bisexual, and transgender populations: review and recommendations. *J Homosex*. 2011;58(1):10-51. doi:10.1080/00918369.2011.534038 https://www.ncbi.nlm.nih.gov/pubmed/21213174

12. Maguen S, Shipherd J. Suicide risk among transgender individuals. *Psychology and Sexuality*. 2010;1(1):34-43. doi:10.1080/19419891003634430 Accessed February 27, 2023. Available at https://www.researchgate.net/publication/233355000_Suicide_risk_among_transgender_individuals

13. Connolly MD, Zervos MJ, Barone CJ, 2nd, Johnson CC, Joseph CL. The Mental Health of Transgender Youth: Advances in Understanding. *J Adolesc Health*. 2016;59(5):489-495. doi:10.1016/j.jadohealth.2016.06.012 https://www.ncbi.nlm.nih.gov/pubmed/27544457

14. Grossman AH, D'Augelli AR. Transgender youth and life-threatening behaviors. *Suicide Life Threat Behav*. 2007;37(5):527-537. doi:10.1521/suli.2007.37.5.527 https://www.ncbi.nlm.nih.gov/pubmed/17967119

15. Belloni G. Transgender Youth Care Targeted in Culture Battle Sweeping US. *Bloomberg Law*. February 21, 2023, 2023. Accessed February 27, 2023. Available at https://news.bloomberglaw.com/health-law-and-business/transgender-youth-care-targeted-in-culture-battle-sweeping-us

16. Sands L. Utah banned gender-affirming care for trans kids. What does that mean? *Washington Post*. February 1, 2023. Accessed February 27, 2023. Available at https://www.washingtonpost.com/nation/2023/02/01/utah-gender-affirming-care-ban/

17. Transgender Medical Treatments and Procedures, S.B. 16, 65th Leg., Gen. Sess. (Utah 2023). Accessed February 27, 2023. Available at https://le.utah.gov/~2023/bills/static/SB0016.html