AHRQ EPC PROGRAM RESEARCH GAPS SUMMARY: WOMEN'S HEALTH

An AHRQ publication summarizing evidence gaps identified across recent EPC reviews for select healthcare topics

Prepared by:
Angela Carr, R.N., M.H.A.
Suchitra Iyer, Ph.D.
Jill Huppert, M.D.
Christine Chang, M.D., M.P.H.
Craig A. Umscheid, M.D., M.S.

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This report is based on research conducted by AHRQ staff. The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare researchers and funders of research make well informed decisions in designing and funding research and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of scientific judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical research and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new healthcare technologies and strategies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

An important part of evidence reports is to not only synthesize the evidence, but also to identify the gaps in evidence that limit the ability to answer the systematic review questions. This information is provided for researchers and funders of research.

If you have comments on this document, they may be sent by mail to the AHRQ staff named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

Robert "Bob" Otto Valdez, Ph.D., M.H.S.A.
Director
Agency for Healthcare Research and Quality

Arlene S. Bierman M.D., M.S.
Director
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Craig A. Umscheid, M.D., M.S.
Director
Evidence-based Practice Center Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Angela Carr, R.N., M.H.A.
Stakeholder Engagement Coordinator for the USPSTF and EPC Programs
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

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Introduction

The AHRQ Evidence-based Practice Center (EPC) Program supports the quality of healthcare by providing the best available evidence on medications, devices, and healthcare services with the goal of helping healthcare professionals, patients, policymakers, and healthcare systems make informed and evidence-based healthcare decisions. Women's Health research supports the overall AHRQ mission of producing evidence to make healthcare safer, higher quality, more accessible, equitable, and affordable, and to work within the U.S. Department of Health and Human Services and with other partners to make sure that the evidence is understood and used. Identifying gaps in women's health research can inform future studies and outline areas that need to be addressed to inform clinical practice to improve the Nation's overall health and well-being.

To identify evidence gaps to inform women's health, the AHRQ EPC program examined all reviews conducted by an AHRQ EPC from December 2017 through February 2022 that addressed a research topic in women's health. Women's health is defined as a health topic that exclusively affect women (e.g., reproductive health) or other health conditions of particular relevance to women (e.g., chronic pain).

The 13 identified reports are presented in descending order, by date. The purpose, key messages, and evidence gaps identified in each review are summarized. Evidence gaps are organized by population, intervention, study design, and outcomes to facilitate ease of use. Detailed descriptions of the gaps are also available in the original report as provided in hyperlinks.

The women's health gaps identified in the following pages are provided to inform research funders, researchers, and policymakers about the types of questions that need to be addressed and the types of studies necessary to address these questions.

Breast Reconstruction After Mastectomy
July 14, 2021
https://effectivehealthcare.ahrq.gov/products/breast-reconstruction-mastectomy/research

Purpose

This systematic review evaluates breast reconstruction options for women after mastectomy for breast cancer (or breast cancer prophylaxis).

Key Findings

- Compared with implant-based reconstruction (IBR), autologous reconstruction (AR) is probably associated with clinically better sexual well-being and patient satisfaction with breasts, but comparable general quality of life and psychosocial well-being.
- Compared with IBR, AR probably poses greater risk of deep vein thrombosis or pulmonary embolism.
- Compared with AR, although results in the short term (1 to 1.3 months) are inconsistent, IBR probably poses greater risk of reconstructive failure in the long term (1.5 to 4 years). IBR may also pose a greater risk of breast seroma.
- Conducting IBR either before or after radiation therapy may result in comparable physical well-being, psychosocial well-being, sexual well-being, and patient satisfaction with breasts.
- Conducting IBR either before or after radiation therapy probably results in comparable risk of implant failure/loss or need for explant surgery.
- Silicone or saline implants may result in clinically comparable patient satisfaction with breasts.
- Acellular dermal matrices (ADM) use probably increases the risk of implant failure/loss or need for explant surgery and may increase the risk of infections not explicitly related to the implants or ADM. The risks of seroma or of unplanned repeat surgery for revision probably are comparable with or without ADM use; The risks of seroma or of unplanned repeat surgery for revision probably are comparable with or without ADM use.
- AR with either deep inferior epigastric perforator (DIEP) or latissimus dorsi (LD) flaps may result in comparable patient satisfaction with breasts.

Evidence Gaps

Study Populations

- Studies that predominantly enroll women undergoing mastectomy for prophylactic purposes:
  - Risk-benefit assessments for reconstruction choices
  - Perceived (subjective) benefits and harm
- More studies that include diverse groups of women, such as by age group, race, ethnicity, and socioeconomic status.

Interventions

- Research on comparison of implant materials (for IBR), anatomic planes of implant placement (for IBR), and choice of flaps (for AR).

Study Design

- Research to address timing of IBR and AR in relation to chemotherapy and radiation therapy.

Outcomes

- Evaluate outcomes not adequately reported in identified evidence:
  - Quality of life
  - Number of planned surgeries for reconstruction
  - Incidence and duration of unplanned repeat hospitalizations and surgeries
  - Analgesic use
  - Animation deformity
  - Complications that may delay other cancer-related treatments

Maternal, Fetal, and Child Outcomes of Mental Health Treatments in Women: A Systematic Review of Perinatal Pharmacologic Interventions

April 15, 2021

https://effectivehealthcare.ahrq.gov/products/mental-health-pregnancy/research

Purpose

For women who are currently or planning to become pregnant or are breastfeeding, a critical question is whether the benefits for mother and fetus of treating psychiatric illness with pharmacologic interventions outweigh the harms; a systematic review will help clarify the balance of benefits and harms.

Key Messages

- Brexanolone probably improves depressive symptoms and may increase risk of sedation, leading to dose interruption or reduction.
- Sertraline may improve response, remission, and depression and anxiety symptoms.
- Mood stabilizers may reduce recurrence and increase time to recurrence.
- Although associations may exist between psychotropic medications and adverse events, causality cannot be inferred.
- First-trimester exposure to lithium is more likely to be associated with overall congenital and cardiac anomalies than first-trimester exposure to lamotrigine, which can inform the decision to switch a medication in a successfully treated individual.
- The paucity of evidence does not mean that pharmacotherapy is not beneficial, nor that harms do not exist; rather, it underscores the absence of high-quality research.

Evidence Gaps

Study Populations

- Clinical trials that include pregnant and lactating women (regulatory barriers have been removed) evaluating—
  - efficacy and effectiveness of pharmacologic mental health treatments
  - comparative benefits and harms from potential congenital anomalies in the fetus
  - studies that include minority populations

Study Design

- Future observational studies should address confounding adequately.
- Pragmatic trial designs and collaborative care models that allow ongoing data collection may permit greater rigor while addressing confounding.

Outcomes

- More high-quality studies on harms of pharmacotherapy.
- Not enough eligible evidence on congenital anomalies for triazolam, alprazolam, valproate, carbamazepine, clonazepam, and topiramate, although evidence is available from studies of other populations ineligible for this review.

Cervical Ripening in the Outpatient Setting
March 22, 2021
https://effectivehealthcare.ahrq.gov/products/cervical-ripening/research

Purpose

To assess the comparative effectiveness and potential harms of cervical ripening in the outpatient setting (vs. inpatient, vs. other outpatient interventions) and of fetal surveillance when a prostaglandin is used for cervical ripening.

Key Findings

- The highest strength of evidence for outcomes of outpatient cervical ripening found in this report was low, with several important outcomes having insufficient evidence.
- Low-strength evidence suggested that outpatient cervical ripening with dinoprostone (intravaginal insert or intracervical gel) or single-balloon catheters (30–50 ml fill) were not significantly different for: cesarean delivery, fetal/neonatal infection (with dinoprostone) and maternal infection, birth trauma, or shoulder dystocia (with single-balloon catheters) when compared with the same intervention in the inpatient setting.
- Low-strength evidence suggested that cesarean delivery and postpartum hemorrhage were not significantly different between cervical ripening with catheters (double-balloon or single-balloon) in the outpatient setting and dinoprostone in the inpatient setting.
- The evidence on outpatient cervical ripening with misoprostol, double-balloon catheters, or hygroscopic dilators was insufficient.
- Low-strength evidence suggested that the risk of cesarean delivery with dinoprostone intracervical gel 2.5 mg versus 5.0 mg, and with silicone versus latex single-balloon catheters in the outpatient setting was not significantly different.
- Low-strength evidence suggested that in the outpatient setting, the risk of cesarean delivery with prostaglandins was not significantly different than placebo, expectant management, and membrane sweeping. The incidence of meconium aspiration syndrome, shoulder dystocia, and uterine infection (with dinoprostone) were not significantly different than placebo.

Evidence Gaps

Study Populations

- Randomized controlled trials to evaluate differential effectiveness and harms of outpatient cervical ripening in important maternal characteristics such as parity, maternal age (including women over 30 or 35), group B streptococcus (GBS) status, diabetes, hypertension, fetal growth restriction, race, body mass index, gestational age categories.

Interventions

- Explore additional factors (e.g., augmentation of labor with synthetic oxytocin, epidural anesthesia).
- Studies comparing methods of fetal surveillance (e.g., intermittent heart rate auscultation vs. electronic monitoring) during cervical ripening with prostaglandins

Study Design

- Randomized controlled trials to corroborate findings on—
  - misoprostol and double-balloon catheters (comparing each in the outpatient versus inpatient settings)
  - direct comparisons of single- and double-balloon catheters and catheters versus prostaglandins
  - hygroscopic dilators
  - various formulations and routes of administration of dinoprostone or misoprostol
- Large, prospective, cohort studies using robust methods to control for variation in baseline risk of women studied (e.g., propensity score matching) and large, case control studies to evaluate the risk of rare harms.
- Quality improvement studies and registry studies to evaluate rare harms and explore process questions.

Outcomes

- Larger registry cohort studies to evaluate harm outcomes of cervical ripening in all settings.

Management of Primary Headaches in Pregnancy
November 12, 2020
https://effectivehealthcare.ahrq.gov/products/headaches-pregnancy/research

Purpose

To evaluate the literature on pharmacologic and nonpharmacologic interventions to prevent or treat attacks of primary headaches (migraine, tension headache, cluster headache, and other trigeminal autonomic cephalgias) in women who are pregnant (or attempting to become pregnant), postpartum, or breastfeeding.

Key Findings

- Prevention of primary headache – Venlafaxine, tricyclic antidepressants (any), benzodiazepines (any), beta blockers (any), prednisolone, and oral magnesium use during pregnancy may have increased risk of fetal/child adverse effects, but calcium channel blockers (any, but nifedipine in particular) and antihistamines (any) may have a low risk of adverse effects (indirect evidence).
- Pharmacologic treatment of acute attacks of primary headache – Use of triptans for migraine during pregnancy may not be more harmful than their use before pregnancy. Compared with nonuse, triptan use may not be associated with spontaneous abortions or congenital anomalies, but may be associated with worse child emotionality and activity outcomes at 3 years of age.
- Systematic reviews of harms (regardless of indication) report that acetaminophen, prednisolone, indomethacin, ondansetron, antipsychotics (any), and intravenous magnesium use during pregnancy may be associated with fetal/child adverse effects, but low-dose aspirin use may not be associated with increased risk of adverse effects.

Evidence Gaps

Interventions

- Studies addressing prevention or treatment of cluster headache and other primary headache disorders in pregnant women.

Study Design

- Given the concern regarding exposing the fetus to potentially harmful pharmacologic interventions, when observational studies using patient registries are conducted, they should be adequately designed and analyzed to compare treatments and measure fetal/neonatal outcomes.
- Future studies should either randomize patients (after considering the ethical issues in this population) to minimize selection bias, or report between-arm estimates of treatment effect that adequately account for important confounders, such as age and severity of headache attack (or of history of headaches). Studies should also, where feasible, conduct blinding of participants, care providers, and outcome assessors to minimize the likelihood of performance and detection biases.

Outcomes

- Since registry data will likely continue to be important in identifying harms, researchers should report more details about disease severity, intervention doses, durations, and frequencies.
- Evaluate maternal outcomes, such as headache-related symptoms (e.g., photosensitivity), quality of life, functional outcomes (e.g., impact on employment/school attendance), and patient satisfaction with intervention; adverse effects on breastfeeding, such as decreased milk supply; and fetal/child adverse outcome.

Labor Dystocia
May 14, 2020
https://effectivehealthcare.ahrq.gov/products/labor-dystocia/research

Purpose

To review the evidence on the definition of "normal" labor progression and the comparative effectiveness of different strategies for treating labor dystocia in women with otherwise uncomplicated pregnancies.

Key Messages

- Use of partograms did not impact important maternal or neonatal outcomes.
- Amniotomy plus oxytocin decreases duration of labor without increasing cesarean delivery rates.
- Emotional support interventions may reduce cesarean deliveries and instrumental deliveries.
- Much of the evidence on different interventions came from studies performed outside the United States. Differences in patient, provider, health system, and other characteristics may affect the applicability of these results to a U.S. setting.

Evidence Gaps

Interventions

- High-quality observational studies that evaluate specific labor management strategies (including the use of partograms) derived from contemporary data sources such as the Consortium on Safe Labor evaluation should include—
  - Comparison of methods and timing of augmenting labor (oxytocin administration, artificial rupture of the membranes)
  - Fetal monitoring
  - Impact of supportive therapies (massage, fluids, nutrition, positioning) on mode of delivery

Study Design

- Clinical research is needed on the creation of separate labor curves (partograms) derived from contemporary U.S. data for women with spontaneous onset of labor, no augmentation with oxytocin or other pharmacologic agents, and vaginal delivery of healthy baby, stratified by parity, as well as for women with augmented labor.
- Exploration of tools/methods, with validated measures, to capture maternal and paternal decision-making preferences.

Outcomes

- Discrete choice experiments developing tools for estimating patient preferences for the process and maternal and neonatal outcomes of labor.

Opioid Treatments for Chronic Pain
April 16, 2020
https://effectivehealthcare.ahrq.gov/products/opioids-chronic-pain/research

Purpose

To assess the effectiveness and harms of opioid therapy for chronic noncancer pain, alternative opioid dosing strategies, and risk mitigation strategies.

Key Messages

- Opioids are associated with small improvements versus placebo in pain and function, and increased risk of harms at short-term (1 to <6 months) followup; evidence on long-term effectiveness is limited, and there is evidence of increased risk of serious harms that appear to be dose dependent.
- At short-term followup, evidence showed no differences between opioids versus nonopioid medications in improvement in pain, function, mental health status, sleep, or depression.
- Evidence on the effectiveness and harms of alternative opioid dosing strategies and the effects of risk mitigation strategies is lacking, although provision of naloxone to patients might reduce the likelihood of opioid-related emergency department visits, a taper support intervention might improve functional outcomes compared to no taper support, and coprescription of benzodiazepines and gabapentinoids might increase risk of overdose.
- No instrument has been shown to be associated with high accuracy for predicting opioid overdose, addiction, abuse, or misuse.

Evidence Gaps

Study Populations

- Benefits and harms in special populations (older adults, cancer survivors, patients at higher risk for opioid use, patients with history of or current opioid use, mental health disorders, and medical comorbidities).
- Clinical trials focused on patients with conditions characterized by nociplastic pain (e.g., fibromyalgia).

Interventions

- Studies exploring the effectiveness of different dosing methods and risk mitigation strategies.
- Comparative effectiveness trials of alternative tapering strategies and outcomes associated with concomitant use of cannabis or gabapentinoids with opioids.

Study Design

- Studies exploring how underlying pain mechanisms (e.g., nociceptive, neuropathic, and nociplastic), presence of specific pain conditions (e.g., autoimmune, congenital, sickle cell, hypermobility, or other) and presence of genetic polymorphisms affecting opioid metabolism impact effectiveness of therapies.
- Develop and validate instruments for accurately predicting risk of opioid use disorder or misuse, and determining how using risk prediction instruments impacts treatment decisions and, ultimately, patient outcome.

Outcomes

- Comparative effectiveness studies on harms of opioid therapy for chronic pain, different opioids or formulations, and different prescribing methods and formulations.
  Long-term outcome studies, including newer or emerging harms potentially associated with long-term opioid use.

Nonopioid Pharmacologic Treatments for Chronic Pain
April 16, 2020
https://effectivehealthcare.ahrq.gov/products/nonopioid-chronic-pain/research

Purpose

Evaluate the benefits and harms of nonopioid drugs in randomized controlled trials of patients with specific types of chronic pain, considering the effects on pain, function, quality of life, and adverse events.

Key Messages

- In the short term, improvement in pain and function was small with specific anticonvulsants, moderate with specific antidepressants in diabetic peripheral neuropathy/post-herpetic neuralgia and fibromyalgia, and small with nonsteroidal anti-inflammatory drugs (NSAIDs) in osteoarthritis and inflammatory arthritis.
- In the intermediate term, evidence was limited, with evidence of benefit for memantine in fibromyalgia and for serotonin norepinephrine reuptake inhibitor (SNRI) antidepressants in low back pain and fibromyalgia.
- In the long term, evidence was too limited to draw conclusions. In general, evidence on quality of life was limited and no treatment achieved a large improvement in pain or function.
- Small to moderate, dose-dependent increases in withdrawal due to adverse events (WDAE) were found with SNRIs duloxetine and milnacipran, anticonvulsants pregabalin and gabapentin, and NSAIDs. Large increases in WDAE were seen with oxcarbazepine. NSAIDs have increased risk of serious gastrointestinal, liver, and cardiovascular adverse events.

Evidence Gaps

Study Populations

- Trials in older patients to better understand possible age-related difference in treatment effect and in patients of non-White race.
- More trials in patients with chronic headache, low back pain, and sickle cell disease.

Study Design

- Good quality/low risk of bias studies since many trials suffered from poor reporting (e.g., unclear randomization and allocation concealment techniques), baseline differences between randomized groups, lack of blinding, and high attrition.
- Studies with consistent use of recognized standard measures of pain and function to facilitate comparisons across trials.

Outcomes

- Comparative effectiveness trials that evaluate intermediate- and long-term treatment duration, long-term health outcomes (including quality of life), and make direct comparisons among key interventions both within and across classes.

Noninvasive Nonpharmacological Treatment for Chronic Pain
April 16, 2020
https://effectivehealthcare.ahrq.gov/products/noninvasive-nonpharm-pain-update/research

Purpose

To assess noninvasive nonpharmacological treatments for common chronic pain conditions.

Key Messages

- Interventions that improved function and/or pain for ≥1 month:
  - Low back pain: Exercise, psychological therapy, spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, acupuncture, multidisciplinary rehabilitation (MDR).
  - Neck pain: Exercise, low-level laser, mind-body practices, massage, acupuncture.
  - Knee osteoarthritis: Exercise, cognitive behavioral therapy (CBT).
  - Hip osteoarthritis: Exercise, manual therapies.
  - Fibromyalgia: Exercise, CBT, myofascial release massage, mindfulness practices, tai chi, qigong, acupuncture, MDR.
  - Tension headache: Spinal manipulation.
  - Some interventions did not improve function or pain.
  - Serious harms were not observed with the interventions.

Evidence Gaps

Study Populations

- Studies in pregnant and breastfeeding women with chronic pain.

Interventions

- Research leading to standardization of techniques and their delivery and understanding best combinations of intervention.
- Pragmatic trials comparing interventions with pharmacological treatments.

Study Design

- Traditional (explanatory) and pragmatic trials with long-term followup and use of methods to enhance recruitment, retention and adherence are needed as are documentation of adherence and studies with sufficient sample size designed to evaluate differential effectiveness and safety of treatments in subpopulations of interest.

Outcomes

- Standardized protocols for types of outcomes to be assessed (including harms) would facilitate evaluation and comparison across studies.
- Use of measures that incorporate understanding of pathophysiological mechanisms and address multiple domains of pain.
- Reporting of the proportions of patients achieving a clinically meaningful improvement for measures of pain and function (i.e., responders) as well as outcomes related to change in use of opioids, healthcare utilization and quality of life.

Management of Infertility
May 14, 2019
https://effectivehealthcare.ahrq.gov/products/infertility/research

Purpose

The purpose of this review was to evaluate the comparative effectiveness and safety of treatments for common causes of infertility.

Key Messages

- The ability to compare the effectiveness of treatments would be enhanced by greater consistency in reporting of outcomes, particularly live birth rates, as well as reporting of diagnosis-specific outcomes for treatments, such as assisted reproductive technology, that are used for multiple diagnoses.
- Letrozole most likely results in more live births with lower multiple births than clomiphene alone in women with polycystic ovary syndrome.
- For women with unexplained infertility, there is most likely shorter time to pregnancy for women with immediate in vitro fertilization (IVF) than for those who undergo other treatments prior to IVF. For the outcomes of live birth, multiple births, ectopic pregnancy, miscarriage, low birthweight, and ovarian hyperstimulation syndrome, there may be no difference between the two groups.
- Across all diagnoses, elective single-embryo transfer results in slightly lower live birthrates but substantially lower multiple birth rates than multiple-embryo transfer.

Evidence Gaps

Study Populations

- Short- and long-term intervention studies performed in patients with different underlying diagnoses, reporting results by diagnosis.

Study Design

- Comparative effectiveness studies focused on diversity of infertility causes and treatment options.
- In identifying future infertility research priorities, the following areas of consensus should be established:
    - Limits of acceptability for specific quantitative harms (e.g., preterm birth) and clinically meaningful differences in benefits (e.g., live birth).
    - Potential role of cost effectiveness in decision making, including issues of willingness to pay and appropriate choice of outcome.
    - Issues related to study design, including potential tradeoffs between risk of bias, efficiency, ability to measure all relevant potential confounders and effect modifiers, and appropriateness of alternative approaches such as Zelen randomization.
    - Issues related to data reporting, including reporting results separately by indication in both randomized trials and large observational studies.

Outcomes

- Short- and long-term outcomes of oocyte donation.

Long-Term Drug Therapies and Drug Holidays for Osteoporosis Fracture Prevention
April 23, 2019
https://effectivehealthcare.ahrq.gov/products/osteoporosis-fracture-prevention/research

Purpose

- To summarize the effects of long-term osteoporosis drug treatment (ODT) and ODT discontinuation and holidays on fractures and harms.
- This report was used to inform a NIH Pathways to Prevention workshop, Appropriate Use of Drug Therapies for Osteoporotic Fracture Prevention.

Key Findings

- Evidence on the effects of long-term osteoporosis drug treatment and drug continuation versus discontinuation is mostly limited to White, healthy, postmenopausal women.
- Long-term alendronate reduces radiographic vertebral and nonvertebral fractures in women with osteoporosis; long-term zoledronate reduces vertebral and nonvertebral fractures in women with osteopenia or osteoporosis.
- Long-term bisphosphonates may increase atypical femoral fractures and osteonecrosis of the jaw, although both are rare.
- In women with osteoporosis, long-term raloxifene reduces vertebral fractures, but not hip or nonvertebral fractures, and increases venous thromboembolism.
- Long-term oral hormone therapies reduce hip and clinical fractures but increase multiple serious harms.
- Continuing bisphosphonates after 3–5 years versus discontinuation reduces some measures of vertebral fractures, but not nonvertebral fractures.

Evidence Gaps

Study Populations

- Studies of osteoporosis drug treatment in populations such as men, frail individuals with multiple comorbidities, non-White women, the oldest old, and those with absence of osteoporosis by either BMD, past hip fracture, or prevalent vertebral fracture criteria.

Study Design

- Studies that examine how patients and clinicians make decisions about these treatments.
- Randomized controlled trials comparing risk of clinical fracture endpoints for osteoporosis drugs, including ibandronate, risedronate, and denosumab.
- Randomized controlled trials comparing risk of clinical fracture endpoints to compare sequential therapy, including denosumab, bisphosphonate therapy, and anabolic therapy (e.g., teriparatide or abaloparatide).
- Randomized controlled trials comparing risk of clinical fracture endpoints to compare anabolic therapy (e.g., teriparatide or abaloparatide) followed by antiresorptive therapy versus antiresorptive therapy alone.
- Retrospective and prospective cohort studies to estimate the risk of rare harms associated with antiresorptive osteoporosis drug treatment.

Outcomes

- Research to estimate the magnitude and duration of risk for post-denosumab vertebral and nonvertebral fractures, clarify whether post-denosumab fracture risk only appears increased because of removal of an effective treatment or truly is increased compared with if patients had not received denosumab at all, and evaluate the efficacy of different post-denosumab antiresorptive regimens for fracture prevention.

Nonsurgical Treatments for Urinary Incontinence in Women
August 8, 2018
https://effectivehealthcare.ahrq.gov/products/urinary-incontinence-update/final-report-2018

Purpose

Compare nonpharmacological and pharmacological interventions in adult women with urinary incontinence.

Key Findings

- The nonpharmacological and pharmacological interventions studied, except hormones and periurethral bulking agents, result in better urinary incontinence (UI) outcomes than no treatment.
- For stress UI, among treatments commonly used as first- or second-line interventions, behavioral therapy is more effective than either alpha agonists or hormones. Combination behavioral therapy and hormones are more effective than alpha agonists. Alpha agonists, in turn, are more effective than hormones.
- For urgency UI, among treatments commonly used as first- or second-line interventions, behavioral therapy is more effective than anticholinergics.
- Onabotulinum toxin A may be more effective than neuromodulation as third-line therapy for women with urgency UI.
- Dry mouth is the most common side effect of pharmacological interventions, particularly with anticholinergics. Duloxetine is associated with numerous constitutional adverse effects such as nausea, insomnia, and fatigue.
- Serious adverse events are rare for all interventions. Onabotulinum toxin A is associated with risk of urinary tract infections and urinary retention. Periurethral bulking agents are associated with erosion in a small percentage of women.

Evidence Gaps

Study Populations

- Studies to examine specific subpopulations (e.g., athletes, younger and older, military, and those of diverse racial/ethnic backgrounds)
  - Efficacy of the various interventions
  - Need for patient-specific outcome measures by subgroup
  - Evidence of differential adherence to specific interventions

Interventions

- Trials of mirabegron use in women with UI.

Study Design

- More data to determine what adverse events concern patients the most, and to what degree patients balance potential benefits and harms.
- To allow better interpretation of the evidence the following are recommended for future studies:
  - Studies need to more clearly describe prior treatments used by study participants.
  - A set of core outcome measures needs to be adopted for effectiveness and for safety outcomes.
  - The core outcome measures should include standardized definitions for patient-centered outcomes.

Outcomes

- More studies that clearly define and report UI outcomes (cure, improvement, satisfaction).
- Differential effects/outcomes of interventions in women by subgroups such as specific type of UI (stress, urgency, mixed), degree of UI severity (e.g., frequency or volume), or past treatment history.

Breastfeeding Programs and Policies, Breastfeeding Uptake, and Maternal Health Outcomes in Developed Countries

July 18, 2018

https://effectivehealthcare.ahrq.gov/products/breastfeeding/research

Purpose

The purpose of this review was to summarize the effectiveness of community, workplace, and healthcare system–based programs and policies aimed at supporting and promoting breastfeeding, and to present an analysis of the recent studies that evaluated the association between breastfeeding and maternal health.

Key Messages

- Baby-Friendly Hospital Initiative (BFHI) is associated with improved rates of breastfeeding initiation and duration.
- Healthcare staff education combined with postpartum home visits may be effective for increasing breastfeeding duration.
- Healthcare staff education alone (with no additional breastfeeding support services) may not be effective for increasing breastfeeding initiation rates.
- For women enrolled in the WIC Program, peer-support interventions offered by WIC agencies may improve rates of breastfeeding initiation and duration.
- Breastfeeding is associated with reduced maternal risk of breast and ovarian cancer, hypertension, and type 2 diabetes.
- Workplace, school-based, and community-based interventions and underlying socioeconomic factors need further research.

Evidence Gaps

Interventions

- Studies exploring the benefits of workplace, school-based, and other community-based interventions for improving rates of breastfeeding.
- Interventional studies exploring effectiveness of maternal support strategies for groups of women who differ demographically.

Study Design

- Comparative studies on the various types of support, such as manual versus electric pumps or interventions delivered by international board-certified lactation consultants versus certified lactation consultants.
- Observational studies on the association between breastfeeding and maternal health.

Outcomes

- Potential harms related to breastfeeding interventions.
- Studies to inform types of professional and material support (e.g., double-electric vs. manual breast pumps) that enable women to achieve their infant feeding goals.

Management of Uterine Fibroids
December 14, 2017
https://effectivehealthcare.ahrq.gov/products/uterine-fibroids/research-2017

Purpose

To review treatment effectiveness and the risk of leiomyosarcoma (LMS) in women with fibroids.

Key Findings

- Gonadotropin-releasing hormone (GnRH) agonists, mifepristone, ulipristal, and uterine artery embolism (UAE) reduce fibroid size, and improve symptoms and quality of life. High-intensity focused ultrasound reduces fibroid size, but impact on quality of life was not measured. Myomectomy and hysterectomy also improve quality of life. Direct comparisons of interventions provide little evidence.
- For women in their 30s, the chance of needing retreatment for fibroids within the next 2 years was 6–7 percent after medical treatment or myomectomy and 44 percent after UAE. For older women, the chance was 9–19 percent after medical treatment or UAE and 0 percent after myomectomy.
- Using data from 160 studies, risk of unexpected LMS ranged from less than 1 to 13 of 10,000 surgeries.
- Survival time appears shorter with power morcellation; however, confidence intervals are wide and overlap with other surgical approaches.

Evidence Gaps

Study Populations

- When possible, women without or with mild symptoms should be included in a delayed treatment arm or expectant management group in order to better understand the natural history of fibroids and to examine the degree to which symptoms may wax and wane.

Interventions

- Comparative effectiveness trials to compare surgery to medication and to procedures.

Study Design

- Randomized clinical trials evaluating treatment goals of women with fibroids, followed by larger effectiveness and comparison studies

Outcomes

- Studies of adequate size to answer questions about priorities for patient centered outcomes, minimal important differences on standard measures, resolution of symptoms, satisfaction with outcomes, recurrence or growth of fibroids, and further care needs at time horizons of a year and longer.
- Longitudinal studies investigating time to return to work, maintenance of symptom control, recurrence of fibroids, subsequent surgery, and fertility and pregnancy outcomes.