HEALTH EVIDENCE REVIEW COMMISSION (HERC)

COVERAGE GUIDANCE: SURGICAL ALTERNATIVES TO TRANSURETHRAL RESECTION OF THE PROSTATE FOR LOWER URINARY TRACT SYMPTOMS IN MEN

DRAFT for 3/12/2015 VbBS/HERC meeting materials

HERC Coverage Guidance

For men with lower urinary tract symptoms (LUTS) due to benign prostate enlargement, coverage of surgical procedures is recommended only if symptoms are severe, and if drug treatment and conservative management options have been unsuccessful or are not appropriate. (*strong recommendation*)

The following are coverage recommendations regarding surgical alternatives to transurethral resection of the prostate (TURP):

Recommended for coverage (*strong recommendation*):

- Bipolar TURP
- Photoselective vaporization of the prostate (PVP)
- Laser enucleation; HoLEP (Holmium Laser Enucleation of Prostate)
- TUIP (Transurethral Incision of the Prostate)

Recommended for coverage (*weak recommendation*):

- TUNA (Transurethral Needle Ablation of Prostate)
- TUMT (Transurethral Microwave Thermotherapy)
- Bipolar TUVP (Transurethral Electrovaporization of Prostate) (Button procedure)
- Thulium laser vaporization/resection of the prostate

Not recommended for coverage (*weak recommendation*):

- Botulinum toxin
- HIFU (High Intensity Focused Ultrasound)
- TEAP (Transurethral Ethanol Ablation of the Prostate)
- Prostatic urethral lifts

Not recommended for coverage (*strong recommendation*):

- Laser coagulation (for example, VLAP/ILC)
- Prostatic artery embolization

Note: Definitions for strength of recommendation are provided in Appendix B GRADE Element Description

RATIONALE FOR GUIDANCE DEVELOPMENT

The HERC selects topics for guideline development or technology assessment based on the following principles:

- Represents a significant burden of disease
- Represents important uncertainty with regard to efficacy or harms
- Represents important variation or controversy in clinical care
- Represents high costs, significant economic impact
- Topic is of high public interest

Coverage guidance development follows to translate the evidence review to a policy decision. Coverage guidance may be based on an evidence-based guideline developed by the Evidence-based Guideline Subcommittee or a health technology assessment developed by the Heath Technology Assessment Subcommittee. In addition, coverage guidance may utilize an existing evidence report produced by one of HERC's trusted sources, generally within the last three years.

EVIDENCE SOURCES

Trusted sources

National Institute for Health and Clinical Excellence (NICE). (2010). *Management of lower urinary tract symptoms in men.* London: NICE. Retrieved from http://publications.nice.org.uk/lower-urinary-tract-symptoms-cg97

NICE. (2013). *Interventional procedure guidance 453: Prostate artery embolisation for benign prostatic hyperplasia.* London: NICE. Retrieved from http://www.nice.org.uk/nicemedia/live/13705/63679/63679.pdf

NICE. (2014). *Interventional procedure guidance 475: Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia*. London: NICE. Retrieved from http://www.nice.org.uk/nicemedia/live/13967/66323/66323.pdf

Additional sources

Ahyai, S. A., Gilling, P., Kaplan, S. A., Kuntz, R. M., Madersbacher, S., Montorsi, F, et al. (2010). Meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement. *European urology*,*58*(3), 384-397. doi:10.1016/j.eururo.2010.06.005. Retrieved from http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0029840/

Bachmann, A.,Tubaro, A., Barber, N., d'Ancona, F., Muir, G., Witzsch, U., et al. (2014). 180-W XPS GreenLight Laser Vaporization Versus Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Obstruction: 6-Month Safety and Efficacy Results of a European Multicentre Randomised Trial – The GOLIATH Study. *European urology*, 65, 931-42. doi: 10.1016/j.eururo.2013.10.040.

Cornu, J. N., Ahyai, S., Bachmann, A., de la Rosette, J., Gilling, P., Gratzke, C., et al. (2014). A systematic review and meta-analysis of functional outcomes and complications following transurethral procedures for lower urinary tract symptoms resulting from benign prostatic obstruction: an update. *European urology*. doi: 10.1016/j.eururo.2014.06.017.

Lee, S. W., Choi, J. B., Lee, K. S., Kim, T. H., Son, H., Jung, T. Y., ... & Kim, J. C. (2013). Transurethral procedures for lower urinary tract symptoms resulting from benign prostatic enlargement: a quality and meta-analysis.*International neurourology journal*, *17*(2), 59-66. doi: 10.5213/inj.2013.17.2.59.Retrieved from http://synapse.koreamed.org/Synapse/Data/PDFData/1092INJ/inj-17-59.pdf

The summary of evidence in this document is derived directly from this evidence source, and portions are extracted verbatim.

EVIDENCE OVERVIEW

Clinical background

Lower urinary tract symptoms (LUTS) comprise storage, voiding and post-micturition symptoms affecting the lower urinary tract. There are many possible causes of LUTS such as abnormalities or abnormal function of the prostate, urethra, bladder or sphincters. In men, the most common cause is benign prostate enlargement (BPE), which obstructs the bladder outlet. BPE happens when the number of cells in the prostate increases, a condition called benign prostatic hyperplasia. Other conditions that can cause LUTS include detrusor muscle weakness or overactivity, prostate inflammation (prostatitis), urinary tract infection, prostate cancer and neurological disease. This guidance document addresses the surgical management of LUTS in men.

LUTS are a major burden for the aging male population. Age is an important risk factor for LUTS and the prevalence of LUTS increases as men get older. Troublesome LUTS can occur in up to 30% of men older than 65 years. There has been an increase in the use of pharmacotherapy for LUTS over the last 25 years, with a considerable decline in surgical rates. However, endoscopic resections of the male bladder outlet remain a common procedure, and although it is often effective in reducing symptoms in men, it is associated with considerable morbidity and a significant overall annual cost. In addition, a significant proportion of men (25–30%) do not benefit from prostatectomy and have poor post-surgical outcome with no improvement of symptoms.

The management options for male LUTS include conservative management, drug therapies and surgery. The decision to opt for a particular type of therapy is dependent on patient choice and clinical considerations, such as severity of symptoms, degree of prostatic enlargement and the response to any preceding treatment. It also takes into account the risk/benefit balance of each therapy.

In general terms the conservative treatments carry the lowest risk but have a lower chance of success and a higher chance of symptom recurrence. Medical therapies with drugs such as alpha blockers and 5 alpha-reductase inhibitors carry a greater risk of interactions and adverse effects but may produce better subjective and objective improvement. Surgical intervention carries the greatest possibility of improvement, particularly in those with severe symptoms but this must be weighed against the risks of surgery, anesthesia and hospitalization.

Transurethral resection of prostate (TURP) has been the mainstay of treatment for symptomatic BPE for many years since it combines high effectiveness with a previously acceptable side effect profile. However, less morbid invasive treatments have been developed. These interventions can be sub-divided into surgical procedures that generally involve removal of prostate tissue requiring general or regional anesthesia and minimally invasive options, which do not require general anesthesia and can be carried out in an outpatient setting.

The interventions considered in this guidance document include the following:

- Holmium:YAG Laser Enucleation of Prostate (HoLEP):
  - Uses Holmium: YAG laser to dissect in the surgical planes and is conceptually the endoscopic equivalent of open prostatectomy.
  - The completely resected prostate lobes are pushed into the bladder, morcellated and removed. The use of the morcellator requires special training.
  - The procedure requires similar operative and anesthetic conditions and post-operative care to TURP, though may take longer.
  - Useful for large prostates which would previously have required an open prostatectomy.
  - Holmium Laser Resection of the Prostate (HoLRP) uses Holmium YAG laser to deliver the energy to the prostate but tissue is removed in a piecemeal fashion similar to undertaking diathermy resection in TURP.
  - Thulium resection uses a Thulium YAG fiber to deliver light of 2000nm wavelength light to vaporize and resect or enucleate tissue. These resection techniques can be undertaken using saline as an irrigating solution, thus reducing the risk of “TURP” syndrome, a rare but serious complication of TURP.
- Laser coagulation techniques:
  - Laser induced necrosis of prostatic tissue is achieved either by surface application of the laser to the prostatic urethra in a technique termed visual laser ablation of the prostate (VLAP) or by inserting specially designed laser fibers into the prostatic tissue via the urethra, termed interstitial laser coagulation (ILC).
  - Typically up to 10 locations can be treated with the procedure lasting 30-60 minutes under local anesthesia.
  - Catheterization is typically required for between three and seven days.
- Laser vaporization techniques:
  - Initially neodinium-yttrium-aluminium-garnet (Nd-YAG – wavelength 1064 nm) was used but this resulted in relatively deep tissue penetration (4mm).
  - Now 532 nm KTP laser is used, generated by passing the Nd-YAG generated beam through a potassium-titanyl-phosphate (KTP) crystal. The light is absorbed by hemoglobin and results in minimal tissue penetration (1mm).
  - Holmium ablation (HoLAP) wavelength 2100nm is a similar technique which results in water absorption of light with tissue penetration of 0.8 mm.
  - Vaporization techniques require similar anesthesia and operating conditions to TURP but with longer operating times.

    - Vaporization technology is rapidly changing (differing wavelengths, power outputs and penetration) and published literature often refers to technology that manufacturers would regard as obsolete.
- Transurethral microwave thermotherapy (TUMT):
    - Microwave energy used to achieve temperatures of 45 - 70°C in the prostate depending on the device and power setting.
    - Treatment lasts 30-60 minutes using local anesthesia and oral analgesia together with sedation for high energy protocols.
    - Requirement for post-operative catheterization varies from 1-12 weeks depending on the protocol used.
- Transurethral vaporization of prostate (TUVP):
    - Utilizes a standard monopolar electro-diathermy device as for TURP.
    - The current is delivered through a grooved ball or modified loop electrode with temperatures up to 300 – 400C. Further modification has allowed the use of bipolar current enabling use of physiological saline as a safer irrigant with tissue effects occurring at lower temperatures (ranging from 40-70C).
    - Electrode rolled over the prostate to vaporize tissue and coagulate surface reducing blood loss.
    - No tissue is available for histological examination.
- Transurethral needle ablation of prostate (TUNA):
    - Radio frequency energy delivered through two adjustable needles which are inserted into the prostate.
    - Localized heating up to 115°C, causing tissue death.
    - Procedure lasts 30 to 60 minutes under local or regional anesthesia.
    - Indwelling catheter placed for up to 3 days.
- Transurethral incision of the prostate (TUIP):
    - Bilateral or unilateral incisions from bladder neck to verumontanum, usually for small prostates.
    - Indwelling catheters usually left in the urethra for less time compared to TURP.
- Botulinum toxin:
    - Injection of botulinum toxin A directly into the prostate.
    - Does not usually require an anesthetic.
    - This treatment is considered investigational.
- Transurethral vaporesection of the prostate (TUVRP):
    - Thick band-like loop electrode at high power used to resect prostate tissue in a similar manner to TURP but combining vaporization and coagulation at the cutting edge.
- High intensity focused ultrasound (HIFU):
    - Ultrasound energy used to achieve temperatures of up to 80–100 C.
    - Treatment lasts about 60 minutes under general anesthetic or sedo-analgesia as an outpatient procedure.
    - Indwelling catheter required for approximately 2 weeks.
- Transurethral ethanol ablation of the prostate (TEAP):
    - Chemical ablation of prostatic tissue using dehydrated ethanol.

  - Delivery of ethanol into the prostate can be achieved either by injecting via a transperineal, transrectal or transurethral (most common) route.
  - Requirement for an indwelling catheter is longer than standard TURP.
- Open prostatectomy (OP):
  - Surgical removal of the prostate through an incision made in the lower abdomen leaving behind only the capsule of the prostate.
  - Hospital stay and recovery period after surgery is usually longer than for TURP.
  - A general or spinal anesthetic is required.
- Transurethral resection of prostate (TURP):
  - Diathermy current for prostate resection via a loop electrode.
  - Continuous flow endoscope passed down the urethra with non-ionic fluid irrigant (usually glycine 1.5%).
  - Coagulative hemostasis achieved with a ball diathermy electrode.
  - Indwelling catheter for 24-48 hours.
  - Hospital stay approximately 1-3 days.
- Bipolar resection of the prostate (bipolar TURP):
  - Uses a continuous flow resectoscope with saline irrigation reducing the risks of fluid absorption.
  - The cutting loop is similar to the monopolar loop in shape but has the active and return electrode on the same axis, separated by a ceramic insulator.
  - The two electrodes form an ionized plasma “pocket” which can be used to resect or vaporize tissues.
- Prostate artery embolization
  - Aim is to reduce the blood supply of the prostate gland, causing some of it to undergo necrosis with subsequent shrinkage.
  - The procedure is usually performed with the patient under local anesthetic and sedation. Using a percutaneous transfemoral approach, super-selective catheterization of small prostatic arteries is done using microcatheters.
  - Embolization involves the introduction of microparticles to block these small prostatic arteries. Embolization agents include polyvinyl alcohol (PVA), gelatin sponge and other synthetic biocompatible materials.
- Prostatic urethral lift implants
  - Aim is to secure the prostatic lobes in retracted positions such that the lumen of the urethra is increased.
  - The procedure is designed to cause less tissue injury than surgical resection or thermal ablation, and it is claimed to reduce the risk of complications such as sexual dysfunction and incontinence.
  - The procedure is undertaken transurethrally with the patient under local or general anesthesia. A pre-loaded delivery device is passed through a rigid sheath under cystoscopic visualization. The delivery device is used to compress one lateral lobe of the prostate in an anterolateral direction towards the prostatic capsule. A needle is then advanced through the lobe and capsule, and a monofilament implant with 2 end pieces is deployed. One end of the implant is

anchored in the urethra and the other on the outer surface of the prostatic capsule, retracting the prostatic lobe away from the urethral lumen.
  - Multiple implants are usually inserted during the same procedure.

EVIDENCE REVIEW

Evidence was identified for the following procedures compared to TURP:

- Bipolar TURP[1]
- Bipolar TUVP
- TUVRP
- TEAP
- TUVP
- TUNA
- Laser
- TUMT
- TUIP
- HOLEP
- Watchful waiting

In addition, evidence was identified for the following comparisons:

- TUVP vs. Laser
- Laser vs. TUMT
- Laser vs. OP
- Laser vaporization vs. laser coagulation
- TUMT vs. sham
- TUIP vs. HOLEP
- OP vs. HOLEP
- Botulinum toxin vs. placebo

HoLEP vs. TURP

There is no statistically significant difference between HoLEP and TURP in improving symptom scores[2] at 3, 6, 12, 24, 36 and 48 months postoperatively [low to moderate strength of evidence (SOE)]. There is no statistically significant difference between HoLEP and TURP in improving quality of life[3] at 3, 6, 12, 24, 36 and 48 months postoperatively (very low to moderate SOE). HoLEP is more effective than TURP in improving urinary flow rate at 3 months and longest follow up (low to moderate SOE). Fewer men treated with HoLEP compared to TURP experienced blood transfusions (moderate SOE). There is no statistically significant difference between HoLEP and TURP in the number of men experiencing strictures, urinary retention,

[1] Monopolar procedure
[2] Symptom scores were reported either using the International Prostate Symptom Score (IPSS) or the American Urological Association's Symptom Score
[3] Quality of life was measured using the IPSS quality of life question

transurethral resection syndrome (TUR), reoperations, incontinence, infection, retrograde ejaculation or mortality (low SOE).

Thulium laser resection vs. TURP

There is no statistically significant difference between thulium laser resection and TURP in improving symptom scores at 6 and 12 months postoperatively (moderate SOE). There is no statistically significant difference between thulium laser resection and TURP in improving maximum urinary flow at long term follow-up (low SOE). There is no statistically significant difference between thulium laser resection and TURP in improving quality of life scores at 6 or 12 months postoperatively (low to moderate SOE). There is no statistically significant difference between thulium laser and TURP in the number of complications for infection, TUR, urinary retention, transfusion, incontinence or retrograde ejaculation (low SOE).

HoLEP vs. TUIP

No studies comparing HOLEP with TUIP were identified in the review. However, one study that compared HoLEP against using holmium laser for bladder neck incision (HoBNI) was found, and it was the opinion of the guideline development group that HoBNI would have outcomes similar to TUIP.

There is no statistically significant difference between HoLEP and HoBNI in improving symptom scores at 3, 6 and 12 months post-operatively. There is no statistically significant difference between HoLEP and HoBNI in improving quality of life scores at 3, 6 and 12 months postoperatively. There is no statistically significant difference between HoLEP and HoBNI in improving the maximum urinary flow at 3 and 12 months post-operatively. There is no statistically significant difference between HoLEP and HoBNI in the number of patients experiencing strictures, incontinence, reoperation, infection, retention or mortality. (Very low SOE for all outcomes.)

HoLEP vs. OP

There is no statistically significant difference between HoLEP and OP in improving symptom scores at 3, 6, 12, 24, 36, 48 or 60 months postoperatively (low to moderate SOE). Open prostatectomy is more effective than HoLEP in improving quality of life scores at 3 months (low SOE). There is no statistically significant difference between HoLEP and OP in improving quality of life scores at 12 and 24 months postoperatively (low SOE). There is no statistically significant difference between HoLEP and OP in improving the maximum urinary flow at 3 months or at long term follow-up (low SOE). Fewer men treated with HoLEP compared to OP experienced blood transfusions (moderate SOE). There is no statistically significant difference between HoLEP and OP with number of patients who experienced mortality, strictures, incontinence, reoperation or retention (low SOE).

Laser coagulation vs. TURP

Laser coagulation techniques are less effective than TURP in improving symptom scores at 12 months and 2 years post-operatively (low SOE). There is no statistically significant difference

between laser coagulation techniques and TURP in improving symptom scores at 3 and 6 months (very low SOE). Laser coagulation techniques are less effective than TURP in improving quality of life at 3, 12 months and at 2 years post-operatively (very low to low SOE). There is no statistically significant difference between laser coagulation techniques and TURP in improving quality of life at 6 months post-operatively (very low SOE). No studies report quality of life at 18 months, 3 years, 4 years and 5 years.

Laser coagulation techniques are less effective than TURP in improving the maximum urinary flow at 3 months or longer follow-up postoperatively (low SOE). There is no statistically significant difference between laser coagulation techniques and TURP in all-cause mortality or number of patients who experienced TUR syndrome and urinary retention (low SOE). More patients treated with laser coagulation techniques compared to TURP experienced urinary tract infection and reoperations (moderate SOE). Fewer patients treated with laser coagulation techniques compared to TURP experienced blood transfusions, strictures, retrograde ejaculation or urinary incontinence (low to moderate SOE).

In acute urinary retention (AUR) patients, there is no statistically significant difference between laser coagulation techniques and TURP in symptom scores or quality of life at 6 months follow up (low SOE). In AUR patients, there is no statistically significant difference between laser coagulation techniques and TURP in all-cause mortality or number of patients who experienced TUR syndrome, blood transfusion and urinary retention, urinary tract infections, urinary incontinence or reoperations (very low to moderate SOE).

Laser vaporization vs. TURP

There is no statistically significant difference between laser vaporization techniques and TURP in improving symptom score at 3 months, 6 months, 2 years and at 5 years or longer follow up (very low SOE). Laser vaporization techniques are less effective than TURP in improving symptom score at 1 year and 3 years follow up (very low to low SOE). There is no statistically significant difference between laser vaporization techniques and TURP in improving the International Prostate Symptom Score (IPSS) QoL score at 3 months, 1 year and 5 years or longer follow up (very low to low SOE). Laser vaporization techniques are less effective than TURP in improving IPSS QoL score at 3 years follow up (very low SOE).

Laser vaporization techniques are less effective than TURP in improving Qmax[4] at 3 months follow up but there is no statistically significant difference at longest available follow up (very low to low SOE). Fewer patients treated with laser vaporization techniques compared to TURP experienced transfusions or strictures (moderate SOE).

More patients treated with laser vaporization techniques compared to TURP experienced urinary retention (moderate SOE). There is no statistically significant difference between laser vaporization techniques and TURP in number of patients with all-cause mortality, UTI, reoperation, incontinence, TUR syndrome or retrograde ejaculation (very low to low SOE).

[4] Maximum urinary flow rate, measured as milliliters of urine passed per second (ml/sec).

Laser vs. OP

There is no statistically significant difference between laser vaporization and OP in improving symptom scores at 3, 6, 12 or 18 months. There is no statistically significant difference between laser vaporization and OP in improving quality of life at 3 months. OP is more effective than laser vaporization in improving quality of life at 6, 12 and 18 months. There is no statistically significant difference between laser vaporization and OP in improving Qmax. Fewer men treated with laser vaporization than OP needed blood transfusions. There is no statistically significant difference between laser vaporization and OP in men experiencing urinary tract infections or reoperation. (Moderate SOE for all outcomes.)

Laser coagulation vs. TUMT

There is no statistically significant difference between TUMT and laser coagulation in improving symptom scores at 6 months postoperatively. There is no statistically significant difference between TUMT and laser coagulation in improving the maximum urinary flow at longer follow-up postoperatively. There is no statistically significant difference between laser coagulation and TUMT with number of patients experiencing urinary retention, strictures, reoperations and retrograde ejaculation. More men treated with laser coagulation compared to TUMT experienced urinary tract infections. (Low SOE for all outcomes.)

Laser vaporization vs. TUVP

TUVP is more effective than laser vaporization in improving symptoms at 6 months, 2 years and 4 years post-operatively (very low SOE). There is no statistically significant difference between TUVP and laser in improving symptom at 12 months, 3 years and 5 years postoperatively (very low SOE). TUVP was more effective than lasers in improving quality of life at 2, 3, and 4 years post-operatively (very low SOE). There is no statistically significant difference between TUVP and laser in improving quality of life at 6 and 12 months postoperatively (very low SOE). There is no statistically significant difference between laser and TUVP in improving the maximum urinary flow at longer follow-up postoperatively (very low SOE). There is no statistically significant difference between laser and TUVP with number of patients who died or experienced strictures, urinary tract infections and incontinence (very low to moderate SOE). More men treated with laser compared to TUVP experienced urinary retention or had reoperation (very low to moderate). Fewer men treated with laser compared to TUVP experienced retrograde ejaculation (moderate SOE).

Laser vaporization vs. laser coagulation

There is no statistically significant difference between laser coagulation techniques and laser vaporization techniques in improving symptom at 3, 6, 12 and 24 months post operatively (very low SOE). There is no statistically significant difference between laser coagulation techniques and laser vaporization techniques in improving Qmax at 3 months or longest available follow up (very low to low SOE). There is no statistically significant difference between laser vaporization techniques and laser coagulation techniques in number of patients who experienced transfusion, urinary retention, urinary tract infections, reoperations or developed erectile dysfunction (very low SOE).

HoLRP vs. visual laser ablation of the prostate (VLAP)

There is no statistically significant difference between HoLRP compared to laser coagulation techniques in number of patients who experienced urinary tract infections or urinary retention (very low SOE).

HoLAP vs. KTP laser vaporization

KTP laser vaporization is more effective than HoLAP in improving symptom scores at 3 months. There is no statistically significant difference between HoLAP and KTP laser vaporization in improving symptom scores at 6 or 12 months. There is no statistically significant difference between HoLAP and KTP laser vaporization in improving quality of life IPSS symptom score at 3, 6 or 12 months. There is no statistically significant difference between HoLAP and KTP laser vaporization in improving Qmax at 3, 6 or 12 months. There is no statistically significant difference between HoLAP and KTP laser vaporization in men experiencing incontinence, re-catheterization, reoperation, strictures or urinary tract infections. (Low SOE for all outcomes.)

Transurethral microwave thermotherapy (TUMT)

TUMT vs. sham

TUMT is more effective than sham in improving symptom scores at 3 and 6 months (low to high SOE). TUMT is more effective than SHAM in improving maximum urinary flow rate at 3 months follow-up (moderate SOE). TUMT is more effective than sham in improving maximum urinary flow rate at longer follow-up (low SOE). Fewer men treated with TUMT compared to SHAM experienced reoperations (low SOE). Fewer men treated with SHAM compared to TUMT experienced urinary retention (moderate SOE).

There is no statistically significant difference between TUMT and sham treatment in number of men experiencing strictures, urinary tract infections, urinary incontinence, retrograde ejaculation and mortality (low SOE).

TUMT vs. TURP

TURP is more effective than TUMT in improving symptom scores at 3, 6, 24 and 36 months postoperatively (very low to moderate SOE). There is no statistically significant difference between TURP and TUMT in improving symptom scores at 12, 48 or 60 months postoperatively (very low to low SOE). TURP is more effective than TUMT in improving maximum urinary flow rates at 3 months and longest follow-up postoperatively (moderate SOE). TURP is more effective than TUMT in improving quality of life scores at 24 months post operatively (low SOE). There is no statistically significant difference between TURP and TUMT in improving quality of life scores at 3, 6, 12, 36, 48 or 60 months (very low to moderate SOE). There is no statistically significant difference between TUMT and TURP in number of patients experiencing infection, blood transfusion, TUR syndrome, incontinence or mortality (very low to low SOE). There is no statistically significant difference between TUMT and TURP in number of men experiencing retrograde ejaculation (very low SOE). Significantly fewer men treated with TURP experienced reoperations compared to TUMT (moderate SOE). Significantly fewer men treated with TURP

experienced acute retention compared to TUMT (low SOE). Significantly fewer men treated with TUMT experienced strictures compared to TURP (low SOE).

Transurethral vaporization of prostate (TUVP)

TUVP vs. TURP

There is no statistically significant difference between TUVP and TURP in improving symptom score at any follow up interval (very low to moderate SOE). TURP is more effective than TUVP in improving quality of life at 6 months (low SOE). TUVP is more effective than TURP in improving quality of life at 3 years (low SOE). There is no statistically significant difference between TUVP and TURP in improving quality of life (IPSS question) at 3 months, 1 year, 2 years and 5 years or longer follow up (low to very low SOE). There is no statistically significant difference between TUVP and TURP in improving Qmax at 3 months or longer follow up (very low to low SOE). Significantly more men treated with TUVP than TURP experience urinary retention (low SOE). Significantly more men treated with TURP than TUVP required blood transfusions (low SOE). There is no statistically significant difference between TUVP and TURP in number of men experiencing UTI, incontinence, retrograde ejaculation, TUR syndrome or strictures (very low to low SOE).

Bipolar TUVP vs. TURP

Bipolar TUVP is more effective than TURP in improving symptom score at 3 months, 6 months and 1 year follow up (very low SOE). Bipolar TUVP is less effective than TURP in improving symptom score at 2 and 3 years follow up (very low SOE). Bipolar TUVP is less effective than TURP in improving Qmax at 3 months and 3 years follow up (very low SOE). There is no statistically significant difference between Bipolar TUVP and TURP in number of men requiring transfusion though the result is borderline in favor of Bipolar TUVP (low SOE). There is no statistically significant difference between Bipolar TUVP and TURP in the number of patients experiencing urinary retention, retrograde ejaculation, TUR syndrome or strictures (very low to low SOE). Catheterization time (days) is significantly shorter for those men treated with Bipolar TUVP compared to TURP (very low SOE). There is no statistically significant difference between Bipolar TUVP and TURP in length of stay (days) though the result is borderline in favor of Bipolar TUVP (very low SOE).

Transurethral needle ablation (TUNA)

TUNA vs. TURP

TUNA is less effective than TURP in improving symptoms scores at 12 months and 2, 3 and 4 years post-operatively (very low to low SOE). There is no statistically significant difference between and TUNA and TURP in improving symptom scores at 3, 18 months and 5 years (very low SOE). There is no statistically significant difference between TUNA and TURP in improving quality of life scores at 3 and 18 months (very low SOE). TUNA is less effective than TURP in improving the maximum urinary flow at 3 months or longer follow-up postoperatively (very low SOE). There is no statistically significant difference between TUNA and TURP in all-cause mortality or number of patients who experienced urinary retention or urinary tract infections

(very low to low SOE). Fewer men treated with TUNA compared to TURP experienced blood transfusion, strictures, retrograde ejaculation or urinary incontinence (very low to moderate SOE). More men treated with TUNA compared to TURP had reoperations (very low SOE).

Transurethral incision of the prostate (TUIP)

TUIP vs. TURP

There is no statistically significant difference between TUIP and TURP in improving symptom scores at 3 and 6 months post operatively (low SOE). TUIP is significantly more effective than TURP in improving symptom scores at 24 months post operatively (low SOE). There is no data for TUIP compared TURP at 12 months, or beyond 24 months post operatively in improving symptom scores. TUIP is less effective than TURP in improving quality of life scores at 24 months post operatively (low SOE). There is no data for TUIP compared to TURP in improving quality of life scores at 3, 6, 12, 36, 48 or 60 months post operatively. There is no significant difference between TUIP and TURP in improving flow rate (Qmax) at 3 months post operatively (low SOE). There is no significant difference between TUIP and TURP in improving peak flow rate (Qmax) at the longest available follow up period reported (low SOE). There is no statistically significant difference between TUIP and TURP in all-cause mortality, number of patients experienced TUR syndrome, urinary retention, urinary incontinence, urinary tract infections or urinary strictures (low SOE). Significantly fewer men treated with TUIP compared to TURP required blood transfusions or experienced retrograde ejaculations (low to moderate SOE). More men treated with TUIP compared to TURP had reoperations (moderate SOE).

TUIP vs. TURP for AUR patients

In men with AUR, there is no statistically significant difference between TUIP and TURP in all-cause mortality, number of men experienced TUR syndrome, urinary retention, urinary incontinence, urinary tract infections or urinary strictures (very low SOE). In men with AUR, significantly fewer men treated with TUIP compared to TURP required blood transfusions (moderate SOE).

Botulinum toxin in the prostate

Botulinum toxin in prostate vs. placebo

Botulinum toxin injection is more effective than placebo in improving symptom scores at 1 and 2 months post injection. Botulinum toxin injection is more effective than placebo in improving peak flow at the longest available follow up (2 months) post injection. There is no data for botulinum toxin compared to placebo in improving symptom scores at 3, 6, 12, 18 or 24 months and beyond in improving peak flow rates (Qmax). There are no events in urinary incontinence for botulinum toxin compared placebo. (Very low SOE for all outcomes.)

Transurethral vaporesection of the prostate (TUVRP)

TUVRP vs. TURP

There is no statistically significant difference between TUVRP and TURP in improving symptom scores at 3 months, 6 months and 2 years (very low to low SOE). TUVRP is more effective than TURP in improving symptom scores at 1 year (moderate SOE). There is no statistically significant difference between TUVRP and TURP in improving Qmax at 3 months and 2 years (very low SOE). There is no statistically significant difference between TUVRP and TURP in improving quality of life IPSS symptom score at 3 months and 2 years (very low SOE). There is no statistically significant difference between TUVRP and TURP in men experiencing incontinence, reoperation, strictures, urinary tract infections, urinary retention, mortality, TUR syndrome or blood transfusions (very low to low SOE).

Bipolar TUVRP vs. TURP

There is no statistically significant difference between Bipolar TUVRP and TURP in improving symptom score from baseline at 3 months. There is no statistically significant difference between Bipolar TUVRP and TURP in improving IPSS QoL score from baseline at 3 months. There is no statistically significant difference between Bipolar TUVRP and TURP in improving Qmax from baseline at 3 months. There is no statistically significant difference between Bipolar TUVRP and TURP in the number of men experiencing urinary retention, UTI and TUR syndrome. (Very low SOE for all outcomes.)

High intensity focused ultrasound (HIFU)

No evidence was identified for this procedure.

Transurethral ethanol ablation of the prostate (TEAP)

TEAP vs. TURP

No studies report symptom score, quality of life or peak flow (Qmax) for TEAP compared to TURP at any time point of follow up. Significantly fewer men had blood transfusions for TEAP compared to TURP. There is no statistically significant difference between TEAP and TURP in number of men who experienced urinary retention, urinary incontinence, urinary tract infections or urinary strictures. (Low SOE for all outcomes.)

Transurethral resection of the prostate (TURP)

TURP vs. watchful waiting (WW)

TURP is more effective than watchful waiting in improving Qmax at 3 years follow up (moderate SOE). Significantly more men were re-catheterized perioperatively for the TURP group compared to watchful waiting; 3.2% of men following TURP were re-catheterized (low SOE). Significantly fewer men had reoperation or received surgery for the TURP group compared to the watchful waiting group during the follow up period (moderate SOE). There is no significant difference between TURP and watchful waiting in the number of all-cause mortality or number of

men who experienced blood transfusions, urinary tract infections and urinary incontinence (low SOE).

Bipolar TURP vs. TURP

There is no statistically significant difference between Bipolar TURP and TURP in improving symptom score at any follow up interval (low to moderate SOE). There is no statistically significant difference between Bipolar TURP and TURP in improving IPSS QoL score at any follow up interval (low to moderate SOE). There is no statistically significant difference between Bipolar TURP and TURP in improving Qmax at 3 months or 1 year follow up (low SOE). There is no statistically significant difference between Bipolar TURP and TURP in number of men requiring transfusion (low SOE). There is no statistically significant difference between Bipolar TURP and TURP in number of men experiencing urinary retention, UTI, incontinence or strictures (low SOE). There is no statistically significant difference between Bipolar TURP and TURP in number of men experiencing TUR syndrome though the result is borderline in favor of Bipolar TURP (low SOE). There is no statistically significant difference between Bipolar TURP and TURP in reoperation rate or mortality rate (very low to low SOE).

Prostatic urethral lifts vs. Sham

In a randomized controlled trial (RCT) of 206 patients comparing 140 patients treated by prostatic urethral lift against 66 patients treated by a sham procedure there was a significant difference in mean change in American Urological Association Symptom Index (AUASI) score (scores range from 0 to 35; higher score indicating greater severity) at 3-month follow-up. The mean score decreased by 11 points at follow-up from a baseline score of 22 in patients treated by prostatic urethral lift and by 6 points at follow-up from a baseline score of 24 in patients treated by the sham procedure (p=0.003 difference between the groups). Patients reported a significant difference in change in AUASI quality-of-life scores (scale 0 to 5; higher score indicating lower quality of life) at 3 months. The mean quality-of-life score decreased from 5 to 2 in patients treated by prostatic urethral lift and from 5 to 4 in patients treated by the sham procedure (p<0.001 difference between the groups). A significant improvement in mean flow rate at 3 months was also found. The mean improvement in flow rate was 4 ml/s in patients treated by prostatic urethral lift and 2 ml/s in patients treated by the sham procedure (from 8 ml/s at baseline for both groups; p=0.005 difference between the groups). Five percent (7/140) of patients treated by prostatic urethral lift were retreated by one year. Urinary tract infections (within 3 months of the procedure) were reported in 3% (4/140) of patients treated by prostatic urethral lift and 2% (1/66) of patients treated by a sham procedure (level of significance not reported).

Prostatic artery embolization (PAE)

No randomized trials of this procedure were identified. One case series of 47 patients reported a 19.4 point improvement in mean IPSS from 24.2 at baseline to 4.8 after prostate artery embolization. Mean prostate volume reduced by 42% from 117 ml to 68 ml. There was an increase in mean Qmax of 97% (from 9.6 ml/s to 18.9 ml/s) after prostate artery embolization

reduction, and the mean post-void residual urine volume decreased from 184 ml to 3 ml (p value not reported for any outcome, follow-up ranged from 7 days to 2 years).

A case series of 15 patients reported a 6.5 point improvement in mean IPSS from 21.0 at baseline to 14.5 after the procedure (n=8, p=0.005). Mean reduction in prostate volume assessed by ultrasound decreased by 27% (from 97 ml to 71 ml, measured in 14 patients, p=0.0001) and by MRI decreased by 28% (from 105 ml to 76 ml, measured in 9 patients, p=0.008). There was an increase in mean Qmax of 54% (from 7.1 ml/s to 10.9 ml/s) after the procedure (n=8, p=0.015), and a mean reduction in post-void residual urine volume from 130.8 ml at baseline to 51.3 ml after the procedure (n=8, p=0.0004). Mean follow-up was eight months.

Recommendations of the NICE Guideline

If offering surgery for managing voiding LUTS presumed secondary to BPE, offer monopolar or bipolar transurethral resection of the prostate (TURP), monopolar transurethral vaporization of the prostate (TUVP) or holmium laser enucleation of the prostate (HoLEP). Perform HoLEP at a center specializing in the technique, or with mentorship arrangements in place.

Offer transurethral incision of the prostate (TUIP) as an alternative to other types of surgery to men with a prostate estimated to be smaller than 30 g. (This recommendation is based on expert opinion of the Guideline Development Group; the majority of studies had an inclusion criteria of prostate size 20 to 40 grams.)

Only offer open prostatectomy as an alternative to TURP, TUVP or HoLEP to men with prostates estimated to be larger than 80 g.(This recommendation is based on expert opinion of the Guideline Development Group; the studies had an inclusion criteria of prostate size 70 to more than 100 grams.)

If offering surgery for managing voiding LUTS presumed secondary to BPE, do not offer minimally invasive treatments (including transurethral needle ablation [TUNA], transurethral microwave thermotherapy [TUMT], high-intensity focused ultrasound [HIFU], transurethral ethanol ablation of the prostate [TEAP] and laser coagulation) as an alternative to TURP, TUVP or HoLEP. (The Guideline Development Group rationale was that, while these minimally invasive techniques offer potentially lower morbidity and shorter lengths of stay than conventional TURP or HoLEP, the current evidence suggests they are less effective and there is little evidence regarding long term outcomes or side effects. They also found that TUNA and TUMT are not cost-effective in the UK setting). If offering surgery for managing voiding LUTS presumed secondary to BPE, only consider offering botulinum toxin injection into the prostate as part of a randomized controlled trial.

If offering surgery for managing voiding LUTS presumed secondary to BPE, only consider offering laser vaporization techniques, bipolar TUVP or monopolar or bipolar transurethral vaporization resection of the prostate (TUVRP) as part of a randomized controlled trial that compares these techniques with TURP. (The Guideline Development Group rationale pertained

to the rapid pace of change with these technologies, and they found that laser vaporization techniques are not cost-effective compared to TURP in the UK setting).

Current evidence on the efficacy and safety of insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. During the consent process clinicians should, in particular, advise patients about the range of possible treatment options and the possible need for further procedures if symptoms recur.

Current evidence on the safety and efficacy of prostate artery embolization for benign prostatic hyperplasia is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research.

For men with voiding symptoms, offer surgery only if voiding symptoms are severe or if drug treatment and conservative management options have been unsuccessful or are not appropriate. Discuss the alternatives to and outcomes from surgery.

Additional Research

At the request of the appointed expert for this topic, additional evidence was sought for the intervention Bipolar TUVP. A MEDLINE ® search using the search terms: “bipolar plasma vaporization”, “bipolar transurethral vaporization of the prostate”, and “TUVP” was conducted from January 1, 2004, to January 1, 2015, limited to SRs and MAs. A total of 91 potential articles were retrieved; after review of title and abstract, 14 were retrieved for full review. Of those, only 4 specifically addressed bipolar TUVP. One of these was limited to the outcome of male sexual function. Of the other three, the most recent was Cornu 2014, with a final search date of September 2013. While it included 8 RCTs of bipolar TUVP, no meta-analysis was undertaken, and the intervention was not discussed in the text. The next most recent review, Lee 2013, included conflicting information on which interventions were evaluated in the included trials. Attempts to contact the author were unsuccessful. Therefore, the third review, Ahyai 2010, will be discussed below. The end search date for this review was 2009 (month not specified), and it was limited to RCTs. Four RCTs were included that compared bipolar TUVP to TURP. A meta-analysis was conducted for functional outcomes, although it was unclear how many studies were combined for each outcome. Results are presented in Table 1.

TABLE 1. FUNCTIONAL OUTCOMES OF BIPOLAR TUVP COMPARED TO TURP

Outcome	Mean Difference	Confidence Interval	P value
IPSS	-0.060	-1.458 to 1.338	0.90
QoL	-0.296	-2.806 to 2.234	0.39
Qmax	-1.696	-3.416 to 0.024	0.05
PVR	-12.886	-226.69 to 200.91	0.58

Harms were categorized by time of onset, and are presented in Table 2.

TABLE 2. HARMS ASSOCIATED WITH BIPOLAR TUVP COMPARED TO TURP

Complication	Odds Ratio	Confidence Interval	P value
Intraoperative	0.189	0.022 to 1.642	0.131
Perioperative	0.525	0.303 to 0.910	0.022
Late	1.483	0.633 to 3.474	0.364
Overall	0.637	0.403 to 1.007	0.054

GOLIATH STUDY

A recent study published after the date of the evidence source was identified by a public commenter that pertains to photoselective vaporization of the prostate, a newer form of laser vaporization. This randomized trial included 281 men and compared this technique, known as "greenlight" laser vaporization to TURP. At six month follow up, laser vaporization was noninferior to TURP for IPSS, Qmax, PVR and percent of patients who were complication free. Length of total time to perform the procedure was significantly longer for the laser procedure, while time until stable health status, length of catheterization, and length of hospital stay were significantly shorter with laser vaporization. Early reintervention rate within 30 days was three times higher after TURP; however, the overall postoperative reintervention rates were not significantly different between treatment arms.

EVIDENCE SUMMARY

The table below summarizes the various comparisons for which evidence was identified.

TABLE 3. EVIDENCE SUMMARY

Procedure	Comparator	Outcome Differences
TURP[5]	HoLEP	HoLEP with significantly better flow rate, fewer transfusions. No significant differences in symptoms, QoL, other AE
	Thulium laser resection	No significant differences in any outcome (symptoms, flow rate, QoL, AE)
	Laser coagulation	TURP with significantly more improvement in symptoms at 12 and 24 mos (but not 3 or 6), better QoL and flow rate.

[5] Monopolar procedure

	techniques	TURP with more transfusions, strictures, retrograde ejaculation, incontinence; laser coag techniques with more UTI, re-operations
	Laser vaporization techniques	TURP with significantly more improvement in symptoms at 1 and 3 yrs (but not other times), better QoL at 3 yrs and flow rate at 3 mos. TURP with more transfusions, strictures; laser vap techniques with more urinary retention.
	Photoselective vaporization of the prostate (PVP/green light)	GOLIATH RCT shows equal effectiveness & retreatment rates at 6 mos, longer op time, shorter post-op duration of catheterization and hospitalization for PVP compared to TURP
	TUMT	TURP with significantly more improvement in symptoms at 3, 6, 24 and 36 mos (but not 12, 48 or 60), better QoL at 24 mos and flow rate. TURP with more strictures, fewer re-operations, less urinary retention
	TUVP	No differences in symptoms or flow rate. TURP with better QoL at 6 mos, but TUVP with better QoL at 3 years. TURP with more transfusions, less urinary retention.
	Bipolar TUVP	TUVP with significantly more improvement in symptoms at 3, 6, 12 mos, but significantly less improvement at 2 and 3 years, worse flow rate. TUVP with significantly shorter catheterization time.
	TUNA	TURP with significantly more improvement in symptoms at 1,2,3 and 4 yrs (but not 3, 18 or 60 mos), better flow rate. TURP with more strictures, transfusions, incontinence, fewer re-operations
	TUIP	TURP with significantly less improvement in symptoms but better QoL at 24 mos. TURP with more transfusions, retrograde ejaculation, fewer re-operations. In patients with AUR, there are no differences in any outcome except there are more transfusions with TURP
	TUVRP	TUVRP with significantly more improvement in symptoms at 12 mos only. No differences in any other outcome.
	Bipolar TUVRP	No difference in any outcome, but longest follow up is 3 mos.
	TEAP	No symptom, QoL or flow rate outcomes reported. No differences in any reported outcome except fewer transfusions with TEAP.
	Watchful waiting	No symptom or QoL outcomes reported. TURP with significantly better flow rate, more recatheterizations but

		fewer repeat or new operations.
	Bipolar TURP	No significant differences for any outcome.
HoLEP	TUIP/ HoBNI	No significant differences for any outcome (single study, very low SOE).
	OP	HoLEP with significantly less improvement in QoL at 3 mos, but not at later times. HoLEP with fewer transfusions.
Laser vaporization	OP	Laser with significantly less improvement in QoL at 6, 12 and 18 mos (but not 3 mos). Laser with fewer transfusions.
Laser coagulation	TUMT	No significant differences in any outcome except laser with more UTIs.
Laser vaporization	TUVP	Laser with significantly less improvement in symptoms at 6, 24 and 48 mos; less improvement in QoL at 2, 3 and 4 yrs. Laser with fewer retrograde ejaculations, more urinary retention and re-operations.
Laser vaporization techniques	Laser coagulation techniques	No differences in any outcome
HoLRP	VLAP	No differences in UTI or urinary retention
HoLAP	KTP laser vaporization	KTP laser with significantly more improvement in symptoms at 3 mos (but not 6 or 12 mos). No other significant differences.
TUMT	Sham	TUMT with significantly more improvement in symptoms at 3 and 6 mos, as well as flow rate. TUMT with fewer re-operations but more urinary retention
Botulinum toxin	Placebo	Botulinum toxin with significantly more improvement in symptoms at 1 and 2 mos as well as flow rate. No outcomes past 2 months.
HIFU	Any comparator	No evidence
Prostatic urethral lifts	Sham	Urethral lifts with significant improvement in symptoms, QoL and flow rate; longest follow up 3 months.
Prostatic artery embolization	None	PAE with improvement in symptoms, flow rate, prostate volume and post-void residual (statistical significance reported in only one small case series).

In general, TURP has significantly better symptomatic outcomes (symptoms, flow rate, QoL) than most of the alternative procedures, at the expense of a higher rate of transfusions, and in some cases, other adverse outcomes. The exceptions to this, where symptomatic outcomes are similar or better, are HoLEP, Thulium laser resection, TUVP, TUVRP and bipolar TURP. TURP comparators for which symptomatic outcomes were not reported or follow up time was 3 months or less are bipolar TUVRP, TEAP, urethral lifts and watchful waiting. Evidence is very low for all outcomes, limiting the ability to draw conclusions, for HoLEP compared to TUIP, HoLRP compared to VLAP, botulinum toxin, HIFU, PAE and bipolar TURVP compared to TURP.

GRADE-INFORMED FRAMEWORK

The HERC develops recommendations by using the concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. GRADE is a transparent and structured process for developing and presenting evidence and for carrying out the steps involved in developing recommendations. There are four elements that determine the strength of a recommendation, as listed in the table below. The HERC reviews the evidence and makes an assessment of each element, which in turn is used to develop the recommendations presented in the coverage guidance box. Balance between desirable and undesirable effects, and quality of evidence, are derived from the evidence presented in this document, while estimated relative costs, values and preferences are assessments of the HERC members.

Indication/ Intervention[6]	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation[7]	Variability in values and preferences	Coverage recommendation	Rationale
HoLEP vs TURP)	Better flow rate, fewer transfusions	Very low to moderate	Moderate	Low	Recommend (strong)	Sufficient evidence; More effective than TURP and similar/less risk.
Thulium laser resection (vs. TURP)	No differences in outcomes	Low to moderate	Moderate	Low	Recommend (strong)	Sufficient evidence; similar effectiveness/risk to TURP; assumed similar/less cost.
Laser vap techniques (vs. TURP)	Less improvement in symptoms, QoL, flow; more UR, fewer transfusions, strictures	Very low to moderate	Low	Low	No recommendation	This treatment has been replaced by PVP, which offers outcomes more comparable to TURP.

[6] When comparator is listed as TURP, this refers to the monopolar procedure unless otherwise specified.
[7] If a procedure is generally undertaken as an outpatient and/or requires only local anesthesia, resource allocation is listed as low; if it generally requires an inpatient stay and/or general or spinal anesthesia, it is listed as moderate.

Indication/ Intervention[6]	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation[7]	Variability in values and preferences	Coverage recommendation	Rationale
Photoselective vaporization of the prostate (PVP, also known as "green light") vs. TURP	RCT shows equal effectiveness & retreatment rates at 6 mos, longer op time, shorter post-op duration of catheterization and hospitalization for laser	Moderate	Moderate	Low	Recommend (strong)	Sufficient evidence, comparable effectiveness to alternatives less risks.
TUMT (vs. TURP)	Less improvement in symptoms, QoL, flow; more re-op, UR, fewer strictures	Very low to moderate	Low	Low	Recommend (weak)	Sufficient evidence; less effective with similar or more risk. Expert opinion said this needs to be covered because some patients can't tolerate more invasive treatment..
TUVP (vs. TURP)	Better QoL at 3 yrs, worse at 6 mos; more UR, fewer transfusions	Very low to moderate	Moderate	Low	Recommend (weak)	Sufficient evidence; similar effectiveness and risk, similar or less cost. HERC's expert indicates this procedure is no longer in use.
Bipolar TUVP (vs. TURP)	More improvement in symptoms early,	Very low to low	Moderate	Low	Recommend (weak)	Sufficient evidence; similar effectiveness and

Indication/ Intervention[6]	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation[7]	Variability in values and preferences	Coverage recommendation	Rationale
	less improvement later (>1 yr), worse flow; shorter cath times					risk, similar or less cost; recommended based on expert input.
TUNA (vs. TURP)	Less improvement in symptoms, flow; more re-op, fewer strictures, RE, incontinence	Very low to moderate	Low	Low	Recommend (weak)	Sufficient evidence; less effective than alternatives with less risk.
TUIP (vs. TURP)	More improvement in symptoms at 24 mos only, worse QoL; more re-op, fewer transfusions, RE	Low to moderate	Moderate	Low	Recommend (strong)	Sufficient evidence; similar effectiveness/risk vs alternatives. Cost assumed similar or less
Botulinum toxin (vs. placebo)	More improvement in symptoms, flow at 1 and 2 mos only	Very low	Low	Low	Do not recommend (weak)	Insufficient evidence; unknown whether available effective alternatives have more or less risk.
HIFU	No evidence	Very low	Low	Low	Do not recommend (weak)	Insufficient evidence; unknown risk vs. available effective alternatives.
TEAP (vs. TURP)	No symptom outcomes; fewer transfusions	Low	Low	Low	Do not recommend (weak)	Insufficient evidence; less risk

Indication/ Intervention[6]	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation[7]	Variability in values and preferences	Coverage recommendation	Rationale
						than effective alternative; similar or more cost.
TURP (vs. watchful waiting)	Better flow; more cath, fewer re-op	Low to moderate	Moderate	Low	Recommend TURP (strong)	Sufficient evidence; More effective than alternatives; similar or less risk.
Bipolar TURP (vs. TURP)	No differences in outcomes	Very low to moderate	Moderate	Low	Recommend (strong)	Sufficient evidence; Similar effectiveness to alternatives with similar risk and similar or less cost.
Prostatic Artery Embolization	Improvement in symptoms, flow, prostate volume, PVR	Very Low	Low	Low	Do not recommend (strong)	Insufficient evidence, unknown risk compared to alternatives. Strength of recommendation increased to strong because it is investigational in the United States.
Urethral Lifts (vs sham)	More improvement in symptoms, QoL, flow at 3 mos and, 2 years	Low	Low	Low	Do not recommend (weak)	Insufficient evidence, unknown risk compared to alternatives.

Indication/ Intervention[6]	Balance between desirable and undesirable effects	Quality of evidence*	Resource allocation[7]	Variability in values and preferences	Coverage recommendation	Rationale
Laser coag techniques (vs. TURP) – general population	Less improvement in symptoms, QoL, flow; more UTI and re-op, fewer transfusions, stricture, RE, incontinence	Very low to moderate	Low	Low	Do not recommend (strong)	Sufficient evidence, less effective than alternatives, similar or more risk.

Coag = coagulation; Vap = vaporization; AUR = acute urinary retention; RE = retrograde ejaculation; UR = urinary retention; re-op = reoperation; cath = catheterization

*The Quality of Evidence rating was assigned by the primary evidence source, not the HERC Subcommittee, with the exception of urethral lifts and PAE.

Note: GRADE framework elements are described in Appendix A

POLICY LANDSCAPE

Quality measures

No pertinent quality measures were identified when searching the National Quality Measures Clearinghouse.

APPENDIX A. GRADE ELEMENT DESCRIPTIONS

Element	Description
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Resource allocation	The higher the costs of an intervention—that is, the greater the resources consumed—the lower the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted

Strong recommendation

In Favor: The subcommittee is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Against: The subcommittee is confident that the undesirable effects of adherence to a recommendation outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences.

Weak recommendation

In Favor: The subcommittee concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Against: The subcommittee concludes that the undesirable effects of adherence to a recommendation probably outweigh the desirable effects, considering the quality of evidence, cost and resource allocation, and values and preferences, but is not confident.

Quality or strength of evidence rating across studies for the treatment/outcome[8]

High: The subcommittee is very confident that the true effect lies close to that of the estimate of the effect. Typical sets of studies are RCTs with few or no limitations and the estimate of effect is likely stable.

Moderate: The subcommittee is moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Typical sets of studies are RCTs with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.

Low: The subcommittee's confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Typical sets of studies are RCTs with serious limitations or nonrandomized studies without special strengths.

Very low: The subcommittee has very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.

[8] Includes risk of bias, precision, directness, consistency and publication bias

APPENDIX C. APPLICABLE CODES

CODES	DESCRIPTION
ICD-9 Diagnosis Codes	
600.01	Hypertrophy (benign) of prostate with urinary obstruction and other lower urinary tract symptoms (LUTS)
600.11	Nodular prostate with urinary obstruction
600.21	Benign localized hyperplasia of prostate with urinary obstruction and other LUTS
600.91	Hyperplasia of prostate, unspecified, with urinary obstruction and other LUTS
ICD-10 Diagnosis Codes	
N40.1	Enlarged prostate with LUTS
N40.3	Nodular prostate with LUTS
ICD-9 Volume 3 (Procedure Codes)	
60.2	Transurethral Prostatectomy
60.3	Suprapubic Prostatectomy
60.4	Retropubic Prostatectomy
60.69	Other
60.92	Injection into prostate
60.96	Transurethral Destruction Of Prostate Tissue By Microwave Thermotherapy
60.97	Other Transurethral Destruction Of Prostate Tissue By Other Thermotherapy
60.99	Other
CPT Codes	
36247	Selective catheter placement, arterial system; initial third order or more selective abdominal, pelvic, or lower extremity artery branch, within a vascular family
36248	Selective catheter placement, arterial system; additional second order, third order, and beyond, abdominal, pelvic, or lower extremity artery branch, within a vascular family (List in addition to code for initial second or third order vessel as appropriate)
37204	Transcatheter therapy, arterial infusion for thrombolysis other than coronary, any method, including radiological supervision and interpretation, initial treatment day
37242	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; arterial, other than hemorrhage or tumor (eg, congenital or acquired arterial malformations, arteriovenous malformations, arteriovenous fistulas, aneurysms, pseudoaneurysms)
37799	Unlisted procedure, vascular surgery
52282	Cystourethroscopy, with insertion of permanent urethral stent
52441	Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; single implant
52442	each additional permanent adjustable transprostatic implant
52450	Transurethral incision of prostate
52500	Transurethral resection of bladder neck (separate procedure)
52601	Transurethral electrosurgical resection of the prostate, including control of

	postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included)
52630	Transurethral resection; of regrowth of obstructive prostate tissue, including control postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included)
52647	Laser coagulation of prostate, including control of postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, and internal urethrotomy are included if performed)
52648	Laser vaporization of prostate, including control of postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, internal urethrotomy, and transurethral resection of prostate are included if performed)
52649	Laser enucleation of the prostate with morcellation, including control of postoperative bleeding, complete (vasectomy, meatotomy, cystourethroscopy, urethral calibration and/or dilation, internal urethrotomy, and transurethral resection of prostate are included if performed)
53850	Transurethral destruction of prostate tissue; by microwave thermotherapy
53852	Transurethral destruction of prostate tissue; by radiofrequency thermotherapy
53855	Insertion of a temporary prostatic urethral stent, including urethral measurement
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation
75898	Angiography through existing catheter for follow-up study for transcatheter therapy, embolization or infusion, other than for thrombolysis
HCPCS Level II Codes	
C9739	Cystourethroscopy, with insertion of transprostatic implant; 1 to 3 implants
C9740	4 or more implants

Note: Inclusion on this list does not guarantee coverage

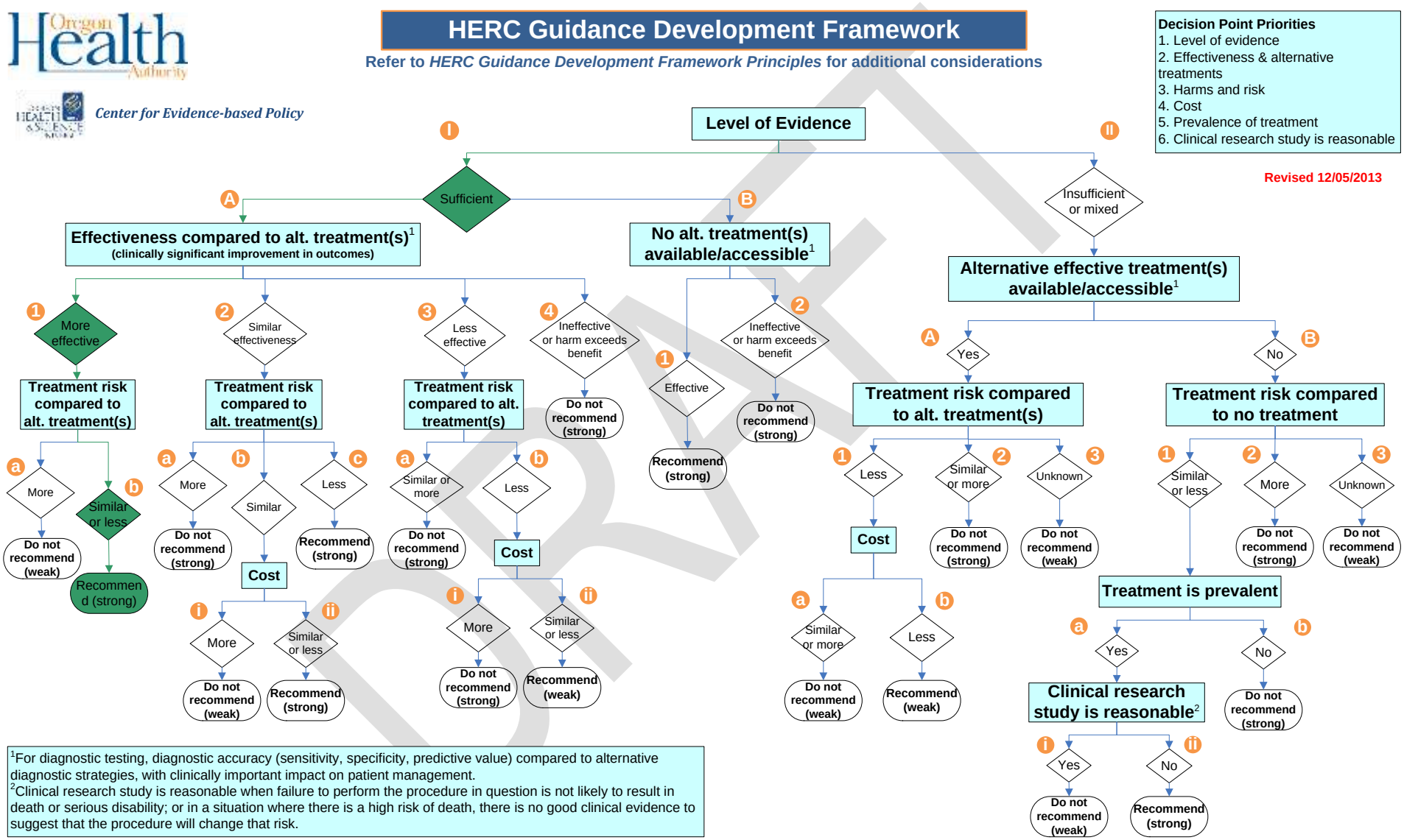
APPENDIX D. HERC GUIDANCE DEVELOPMENT FRAMEWORK

HERC Guidance Development Framework Principles

This framework was developed to assist with the decision making process for the Oregon policy-making body, the HERC and its subcommittees. It is a general guide, and must be used in the context of clinical judgment. It is not possible to include all possible scenarios and factors that may influence a policy decision in a graphic format. While this framework provides a general structure, factors that may influence decisions that are not captured on the framework include but are not limited to the following:

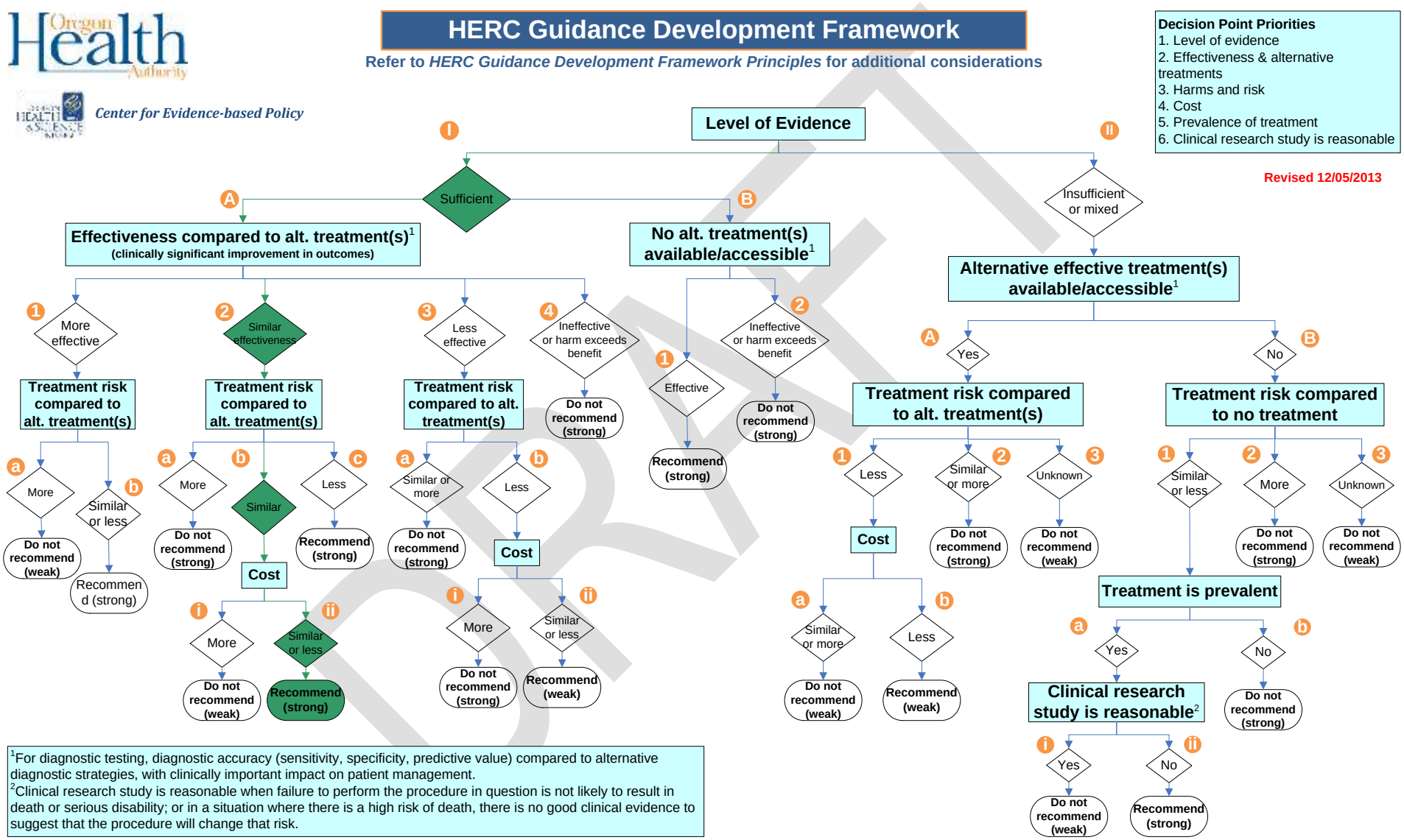
- Estimate of the level of risk associated with the treatment, or any alternatives;
- Which alternatives the treatment should most appropriately be compared to;
- Whether there is a discrete and clear diagnosis;
- The definition of clinical significance for a particular treatment, and the expected margin of benefit compared to alternatives;
- The relative balance of benefit compared to harm;
- The degree of benefit compared to cost; e.g., if the benefit is small and the cost is large, the committee may make a decision different than the algorithm suggests;
- Specific indications and contraindications that may determine appropriateness;
- Expected values and preferences of patients.

HoLEP, TURP (compared to watchful waiting)



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
[2]Clinical research study is reasonable when failure to perform the procedure in question is not likely to result in death or serious disability; or in a situation where there is a high risk of death, there is no good clinical evidence to suggest that the procedure will change that risk.

Thulium laser resection, TUVP, TUIP, and Bipolar TURP; compared to TURP



[1]For diagnostic testing, diagnostic accuracy (sensitivity, specificity, predictive value) compared to alternative diagnostic strategies, with clinically important impact on patient management.
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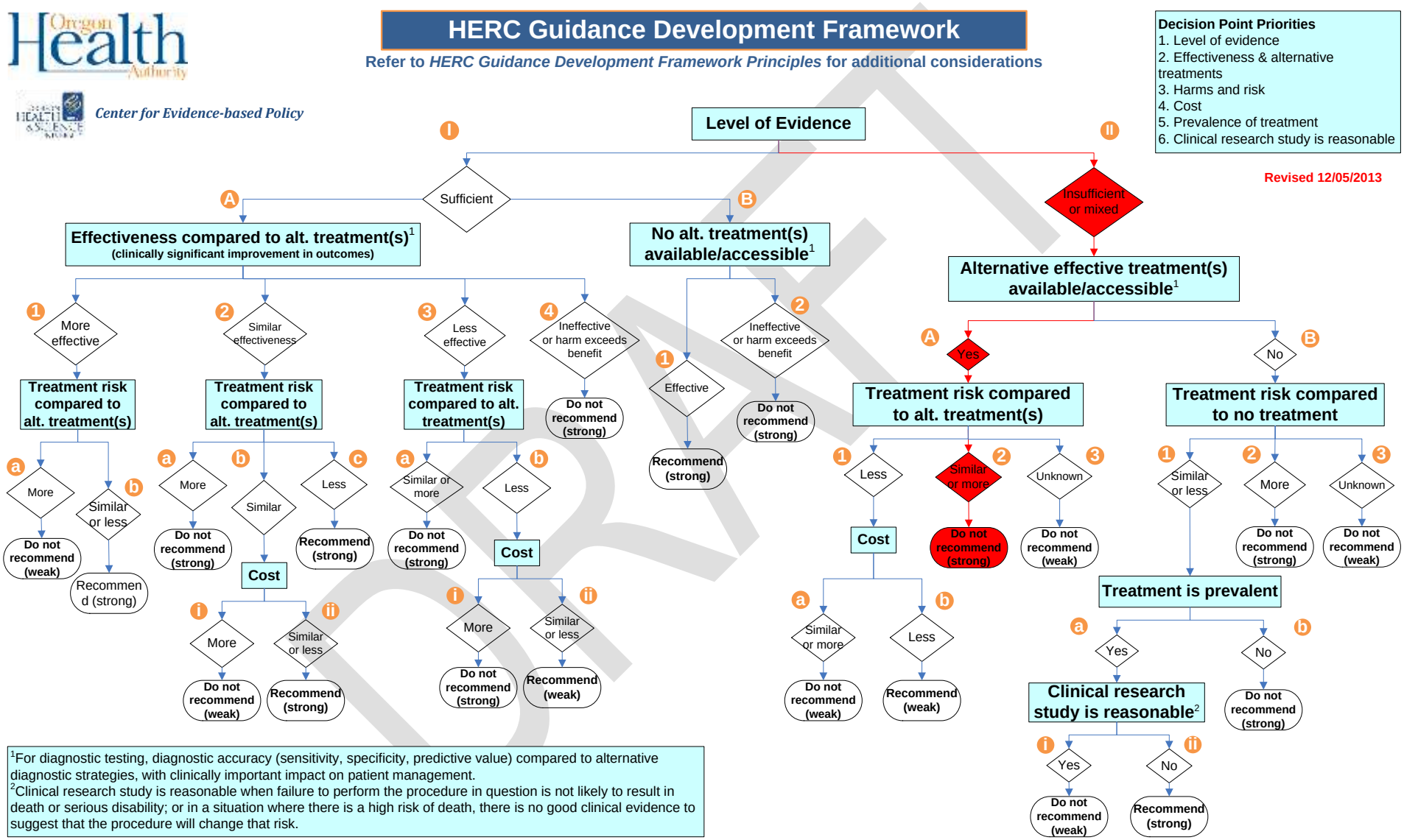
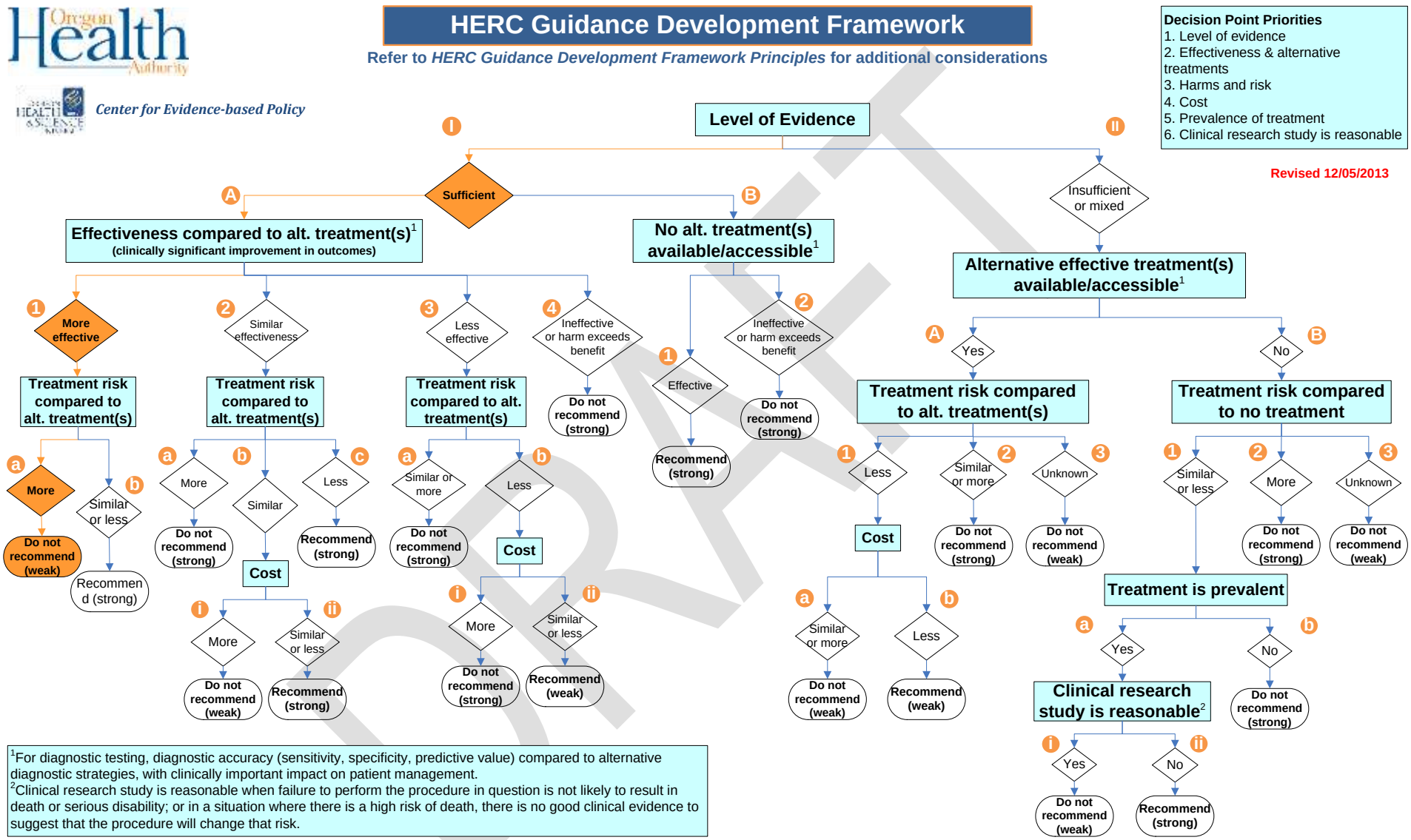
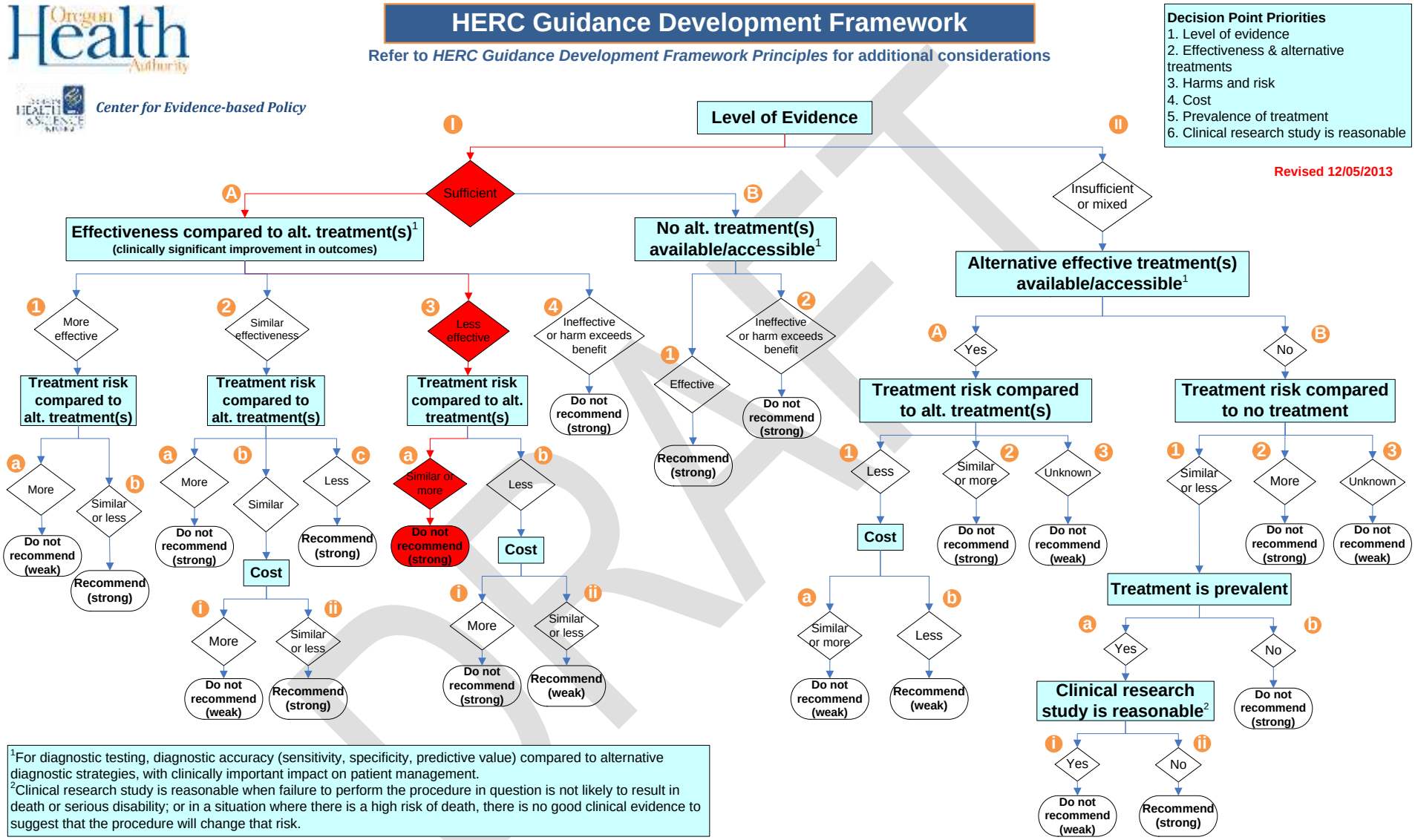
HoLEP (compared to HoBNI); Bipolar TURVP (compared to TURP)



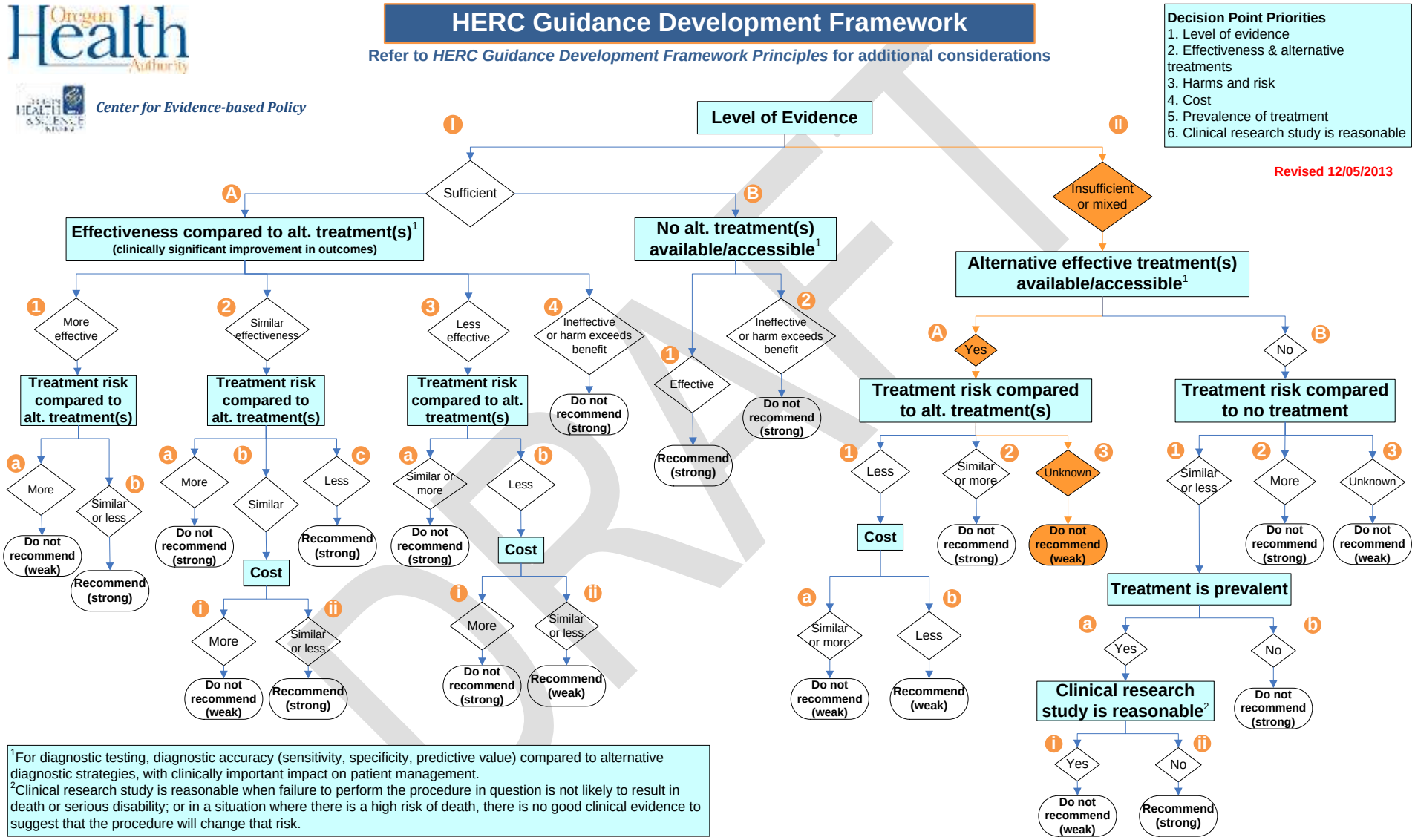
HoLEP; compared to OP



Laser coagulation techniques, and TUMT; compared to TURP



HoLRP (compared to VLAP); Botulinum toxin (compared to placebo); HIFU, prostatic artery embolization, prostatic urethral lifts



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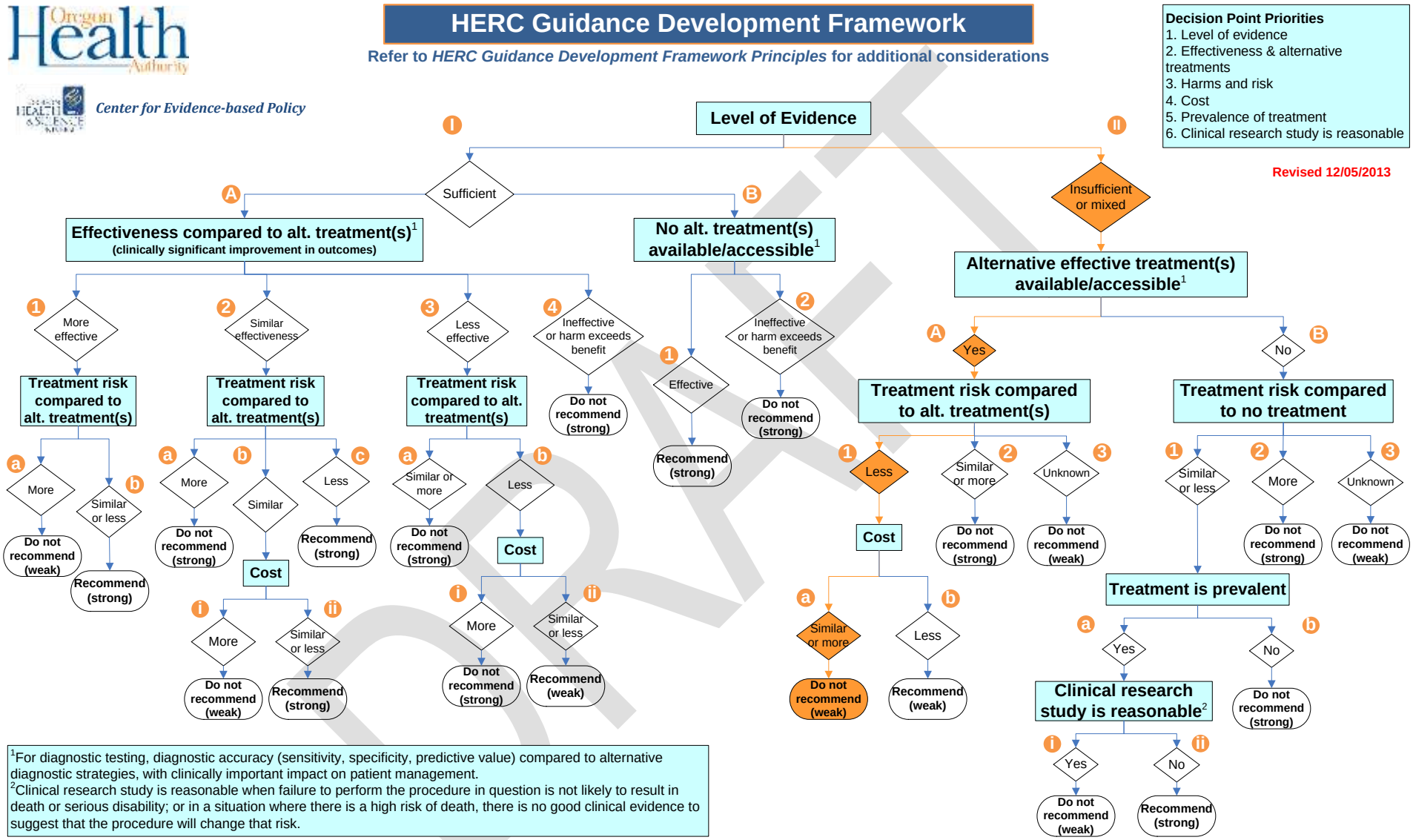
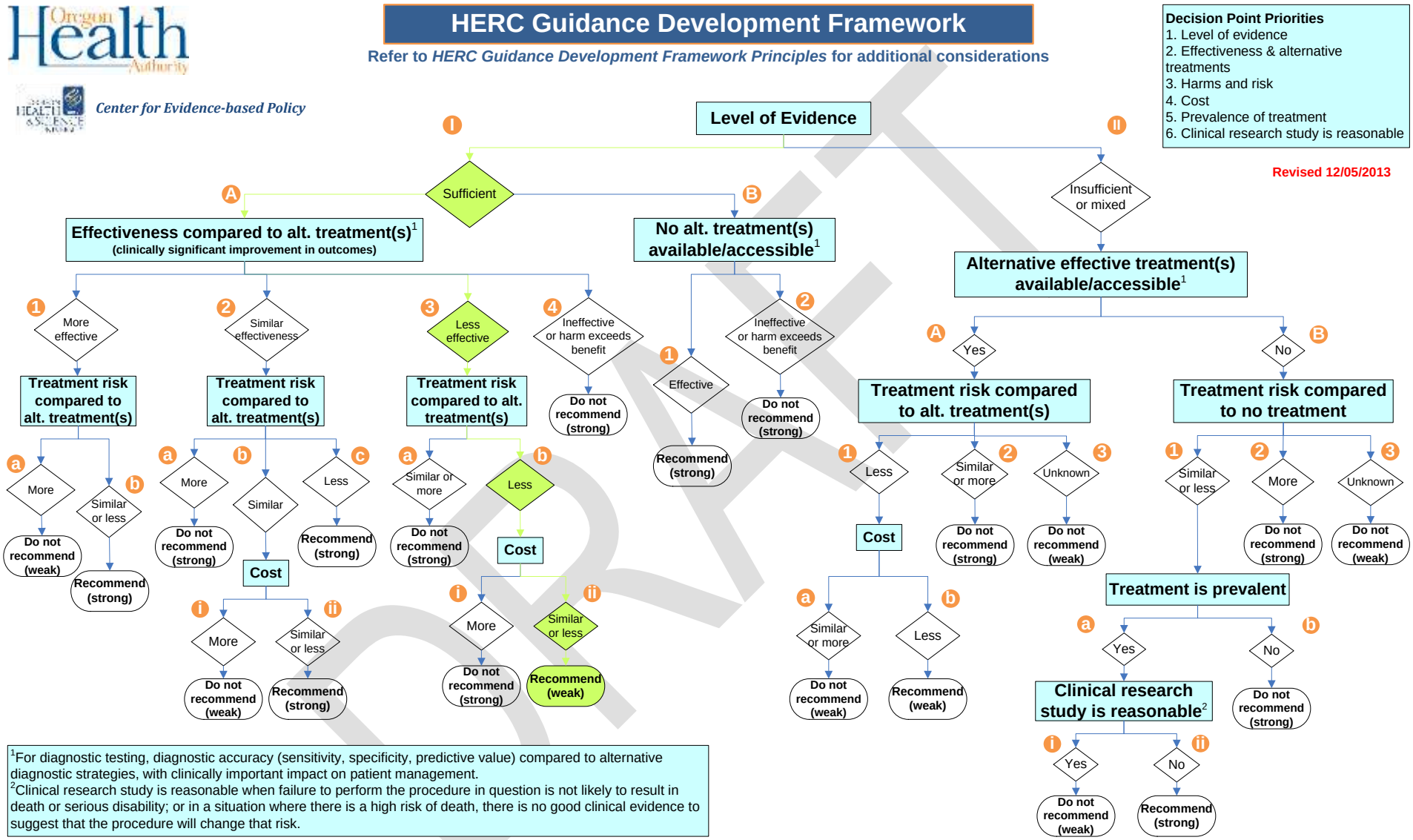
Bipolar TUVP and TEAP; compared to TURP



TUNA; compared to TURP



PVP; compared to TURP

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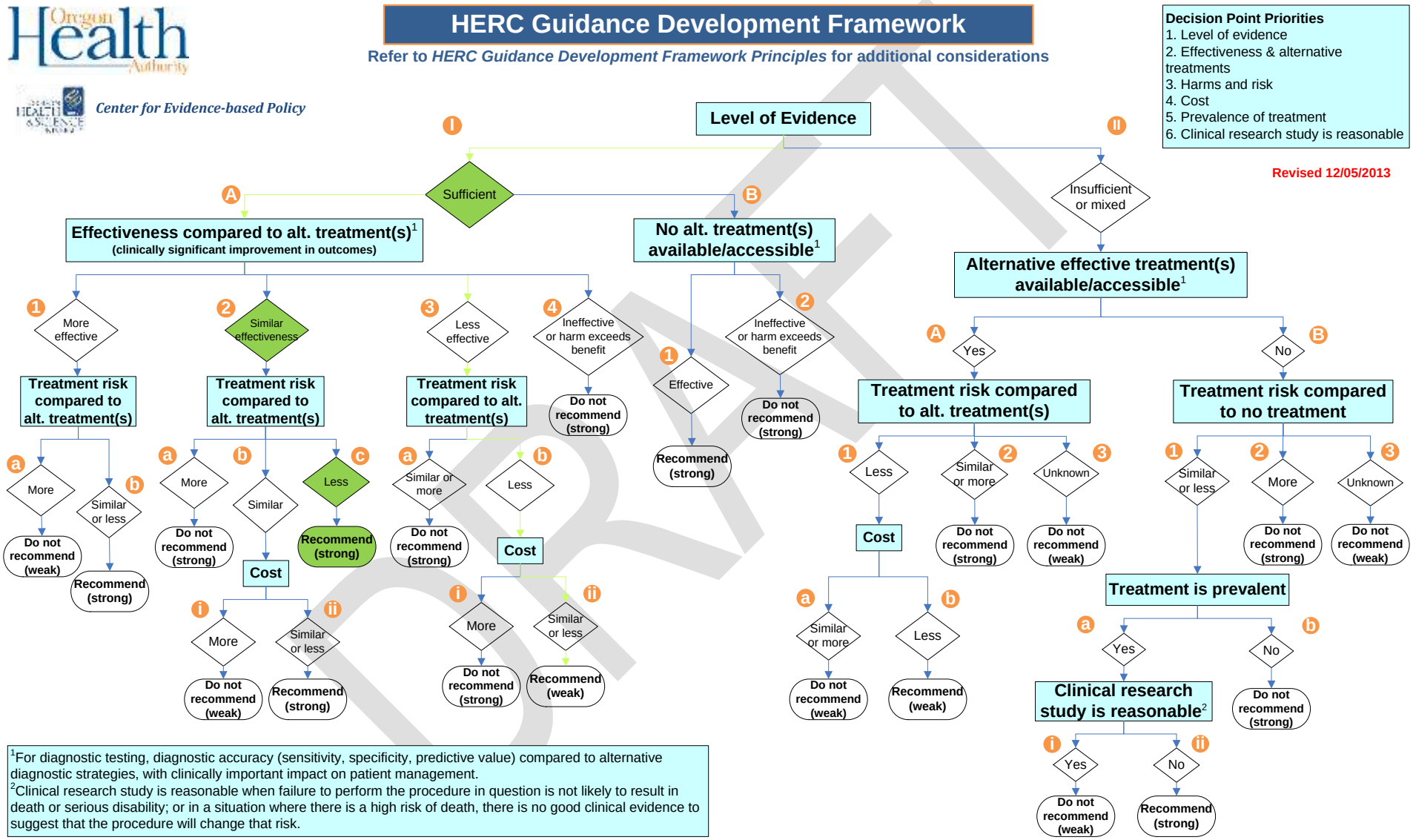

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