Logbook

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May 30, 2024

Ideas

- Research:
    - Meta-analysis?
        - Statistics
        - CMA? Which software
        - What topic?
        - Focus on endo - common but not well known

- Experiment
    - Psychological experiment?
        - Need a large sample size
- Innovation:
    - Using household materials to create cheaper version of smth?
    - Pap smears are uncomfortable, women are often reluctant to get one, make more comfortable?
    - Make certain treatments/tests more accessible? (Cost, comfortable, etc.)
        - home materials

Jul 8, 2024, Jul 9, 2024, Jul 10, 2024, Jul 12, 2024

- Sticking to Endometriosis? (working with Dr. Belland more + already know a lot so easier)
- Perhaps innovating smth to make diagnosis easier?
- Diagnosis of endo:
    - Ultrasound - if i can find some way to make this cheaper/more accessible
    - Pelvic Exam - can't really make something to help with this right
    - Laparoscopy - can't do much here, it's surgical
    - MRI -
    - Treatments of endo:
    - Pain Management (OTCs, NSAIDs, etc.) ----
    - Hormone Therapy ----
        - Contraceptives
        - GnRH agonists and antagonists
        - Progestin Therapy
        - Aromatase inhibitors

    - Conservative Surgery ----
    - Fertility Treatment ----
    - Hysterectomy -----

- Ultrasound gels?
- Ultrasound gels mainly H2O, glycerin/propelyene glycol, carbomer
- Homemade alternatives = cheaper, more eco-friendly?
- How to test? - buy a machine? Bit expensive… and buying commercially avail ultrasound is maybe a bit inaccruate
- Changing levels of a specific material for efficacy?
- Comparing it to commercially available ultrasound gels?

Jul 9, 2024

- I should learn statistics
- Either way, research or innovation or experiment, I probably need stats
- Learn from Brilliant or Khan Academy + Josh Starmer

Jul 10, 2024

- Using AI/machine learning to use ultrasound images to help diagnose endometriosis?
- CNN - convolution neural network
- Coding would prob be involved
- I can't find any datasets

Jul 15, 2024 , Jul 16, 2024 , Jul 17, 2024 , Jul 18, 2024 , Jul 19, 2024 , Jul 20, 2024 , Jul 22, 2024 , Jul 23, 2024 , Jul 24, 2024 , Jul 25, 2024 , Jul 26, 2024 , Jul 27, 2024 , Jul 28, 2024 , Jul 29, 2024 , Jul 30, 2024 , Aug 1, 2024 , Aug 2, 2024 , Aug 3, 2024 , Aug 5, 2024 , Aug 6, 2024 , Aug 7, 2024 , Aug 8, 2024

- Comparison or researching the feasibility of a specific treatment?
- Dichloroacetate - new drug that's a non-hormonal, non-surgical treatment to endo
- Immunotherapy - hard to find studies on
- "No new treatments for endometriosis in 40 years."
- Statins - there's some info, not very much though
- Aromatose inhibitors - can get more sources? Compare with other hormonal therapies like GNRH (like elagolix.)
- Would be interesting
- Need to choose outcomes, right?
    - Efficacy/pain relief
    - Adverse effects
    - Lesion size
    - Quality of life, patient satisfaction?

        - Very heterogeneous
    - Elagolix is actually very new (2017 approved). Could compare with some older, more well-established treatments?
        - Outcomes: Dysmennorhea (, Non-menstrual pelvic pain (NRS), Endometriosis-related pain (NRS), Adverse effects
        - Compare to Linzagolix?
        - Compare to relugolix?
    - Compare danazol to leuprolide? - 8 studies so far
        - Outcomes?
        - Not consistent in the studies i've found
- Maybe I need to consider other conditions?
- Endometriosis
- Perturbation with lidocaine (EHP-30)
- 150 QD elagolix (NRS and 0-3 scale for DYS)
- Dienogest (VAS)
- Excision vs Ablation? (VAS - 3 two-arm studies)
- Depot Leuprolide (VAS)
- Nafarelin and Danazol (lots of studies inaccessibly even with U of A account, also not consistent measures)
- Endometrial cancer?
- Maybe do depot leuprolide vs. dienogest
    - 1 article with two-arms
    - 4 articles that contains dienogest
    - 3 articles with leuprolide
    - All full-text yay except for 1 leuprolide article
    - https://link.springer.com/article/10.1007/s43032-019-00094-5
    - https://www-sciencedirect-com.login.ezproxy.library.ualberta.ca/science/article/pii/S0301211510001715
    - https://academic.oup.com/humrep/article/25/3/633/2915724?login=false
    - https://www-sciencedirect-com.login.ezproxy.library.ualberta.ca/science/article/pii/S0301211521005261
    - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9092804/
    - https://pubmed.ncbi.nlm.nih.gov/9252932/ (Not Full-Text Uh oh)
    - https://www-sciencedirect-com.login.ezproxy.library.ualberta.ca/science/article/pii/S0015028220307160
    - https://www-sciencedirect-com.login.ezproxy.library.ualberta.ca/science/article/pii/S0015028221022147
    - file:///C:/Users/andre/Downloads/4061-Article%20Text-9736-10237-10-20220101.pdf

Leuprolide:

- 1st study: Relugolix dose-ranging
    - 3.75mg/month subcutaneous injection

    - VAS scale
    - Outcomes assessed: pelvic pain, dysmenorrhea pain and dyspareunia - going to use MEAN VAS change, NOT maximum VAS change
    - 12 week treatment period (3 months)
    - Pre-treatment period of 4-12 weeks (double-dummy placebo run-in period), 4-week follow up period
    - 487 patients
    - Also used B&B as well EHP-30
- 2nd study:
    - 3.75mg/month, some patients <50kg could get 1.88mg at visit 3 (exclude)
    - VAS scale
    - Outcomes assessed: pelvic pain, NMPP, Dymenorrhea, Dyspareunia (endpoints)
    - 24 weeks treatment period (6 months)
    - Pre-treatment period: 3-6 weeks
    - 4 week follow-up period
    - 454 patients
    - Also used B&B and EHP-30
- 3rd study:
    - 3.75 mg/month for 6 months intramuscularly
    - VAS scale
    - Outcomes assessed:

- They measure VAS at EOT but the EOT times differ (3 months vs 6 months)

- Screening Dienogest
- Dienogest definitely has good amount of studies that are full-text with VAS and 24 weeks TP (5)
    - If I can find another that would be perfect

- Levonorgestrel: 5 studies with VAS and 24 weeks

Studies - DG

Randomized study on the effectiveness of nomegestrol acetate plus 17β-estradiol oral contraceptive versus dienogest oral pill in women with suspected endometriosis-associated chronic pelvic pain

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9092804/

- Compared nomegestrol acetate plus 17β-estradiol oral contraceptive vs **dienogest**
- RCT

PICO:
P: women with suspected endometriosis-associated chronic pelvic pain
I: nomegestrol acetate plus 17β-estradiol oral contraceptive
C: dienogest 2mg
O: endometriosis-associated chronic pelvic pain (EACPP) and on the quality of life (QoL) and sexual function

- Other outcomes include adverse events, dysmenorrhea, and dyspareunia
- VAS scale to assess CPP, dysmenorrhea, and dyspareunia

Safety and Effectiveness of Dienogest (Visanne®) for Treatment of Endometriosis: A Large Prospective Cohort Study

https://link.springer.com/article/10.1007/s43032-019-00094-5

- Prospective study to evaluate safety and effectiveness of Dienogest

PICO:
P: Women with endometriosis in Korea
I: Dienogest 2mg
C: N/A
O: Adverse events, Serious Adverse Events, Adverse Drug Events, Menstrual bleeding pattern, EAPP

- VAS scale to assess EAPP

Dienogest is as effective as leuprolide acetate in treating the painful symptoms of endometriosis: a 24-week, randomized, multicentre, open-label trial

https://academic.oup.com/humrep/article/25/3/633/2915724?login=false

- A non-inferiority clinical trial comparing leuprolide acetate to dienogest

PICO:
P: Patient with confirmed endometriosis
I: Dienogest (2mg)
C: Leuprolide acetate
O: Pelvic Pain, Adverse event profile, laboratory parameters, bone mineral density (BMD), bone markers and bleeding patterns

- Pelvic Pain measured using VAS

Efficacy of dienogest vs combined oral contraceptive on pain associated with endometriosis: Randomized clinical trial

https://www-sciencedirect-com.login.ezproxy.library.ualberta.ca/science/article/pii/S0301211521005261

- RCT comparing dienogest to COC (Yasmin, 0.03 mg ethinyl estradiol and 3 mg drospirenone)

PICO:
P: Endometriosis-associated chronic pelvic pain, dysmenorrhoea or both for >6 months
I: Dienogest (2mg)
C: COC
O: EAPP, CPP, dysmenorrhoea, dyspareunia, HRQoL

- EAPP measured using VAS
- CPP, dysmenorrhea and dyspareunia measured using B&B
- HRQoL measured suing EHP-30

Dienogest versus continuous oral levonorgestrel/EE in patients with endometriosis: what's the best choice?

https://www.tandfonline.com/doi/full/10.1080/09513590.2021.1892632#d1e233

- Prospective cohort study comparing Dienogest versus continuous oral levonorgestrel/EE in patients with endometriosis

PICO:
P: Patients with endo
I: Dienogest (2mg)
C: continuous oral levonorgestrel with ethinyl estradiol
O:Ovarian endometrioma size, DIE size, chronic pelvic pain (CPP), dyspareunia, analgesic use, quality of life (QoL), compliance and side effects.

- Dyspareunia and CPP was measured with VAS

Studies - LNG-IUS

Randomized clinical trial of a levonorgestrel-releasing intrauterine system and a depot GnRH analogue for the treatment of chronic pelvic pain in women with endometriosis
https://academic.oup.com/humrep/article/20/7/1993/2356569?login=false

- Multicentre RCT to compare the efficacy of a levonorgestrel-releasing intrauterine system (LNG-IUS) and a depot-GnRH-analogue in the control of endometriosis-related pain

PICO:
P: Women with endometriosis with CPP and/or dysmenorrhea
I: LNG-IUS
C: depot GnRH analogue
O: Endometriosis-associated CPP and quality of life, bleeding score
- EACPP is measured using VAS

Control of endometriosis-associated pain with etonogestrel-releasing contraceptive implant and 52-mg levonorgestrel-releasing intrauterine system: randomized clinical trial

https://www.fertstert.org/article/S0015-0282(18)30568-5/fulltext
- RCT comparing etonogestrel (ENG)-releasing contraceptive implant with the 52-mg levonorgestrel-releasing intrauterine system (LNG-IUS) in the control of endometriosis-associated pelvic pain.

PICO:
P: Women with endometriosis
I: ENG implant
C: LNG-IUS
O: Daily scores of noncyclic pelvic pain, dysmenorrhea, HRQoL, bleeding pattern
- Noncyclic/Non-menstrual pelvic pain and dysmenorrhea measured using VAS
- HRQoL measured using EHP-30

Endometriosis-associated pain scores and biomarkers in users of the etonogestrel-releasing subdermal implant or the 52-mg levonorgestrel-releasing intrauterine system for up to 24 months

https://www.tandfonline.com/doi/epdf/10.1080/13625187.2020.1725461?needAccess=true

- Randomized trial comparing the ENG implant or the 52-mg LNG-releasing intrauterine sys-tem (52 mg LNG-IUS for endometriosis-associated pain and biomarkers

PICO:
P: Patients with endometriosis having EAPP and/or dysmenorrhea for more than 6 months
I: ENG implant
C: LNG-IUS
O: CCP, Dymenorrhea, serum levels of CA-125, and soluble CD23
- CCP and Dysmenorrhea measure using VAS

The evaluation of the effectiveness of an intrauterine-administered progestogen (levonorgestrel) in the symptomatic treatment of endometriosis and in the staging of the disease
https://academic.oup.com/humrep/article/19/1/179/690050
- Prospective non-comparative observational study to evaluate the effectiveness of an intrauterine-administered progestogen (levonorgestrel) in the symptomatic treatment of endometriosis and in the staging of the disease

PICO:
P: Women with known or suspected symptomatic endometriosis
I: LNG-IUS
C: None
O: Severity and frequency of pain, dysmenorrhoea, non-cyclical pelvic pain, amount and frequency of bleeding, and American Fertility Society staging and score of the disease.
- Severity and frequency of pain measured using VAS

The levonorgestrel-releasing intrauterine system and endometriosis staging

https://www.fertstert.org/action/showPdf?pii=S0015-0282%2806%2904483-9
RCT to investigate the efficacy of 6 months of LNG-IUS treatment in the symptomatic relief of endometriosis, and compare the results to those obtained after 6 months of treatment with a GnRH agonist (GnRHa).

PICO:
P: Women with endometriosis
I: LNG-IUS
C: GNrHa
O: Pain relief, laparoscopic staging of the disease
- Pain relief measured using VAS

Meta-Analysis:

P: Women with endometriosis
I: Dienogest
C: LNG-IUS
O: Pelvic Pain, Adverse events, Dysmenorrhea, Dyspareunia, SF-36

Aug 13, 2024 , Aug 14, 2024 , Aug 15, 2024 , Aug 16, 2024 , Aug 17, 2024
Aug 18, 2024 , Aug 19, 2024

- Inputting data into a spreadsheet.

- Comprehensive overview with a mix of post-surgical and non post surgical?
- Or stick to non-post surgical?
- Subgroup analyses to reduce heterogenity?
- Depends on how many studies i can get for lng-ius

- Need to rescreen for studies that only talk about ovarian endometriomas, still a form of endo, were prev. excluded

- Do ITT-analyses, not per protocol
    - Fix spreadsheet

Aug 20, 2024 Aug 21, 2024 , Aug 22, 2024

- Do more bg research on dienogest and the levonorgestrel releasing intrauterine system

RESEARCH:

Dienogest - what is it, and how does it work?

A synthetic oral progestin (synthetic progesterone)

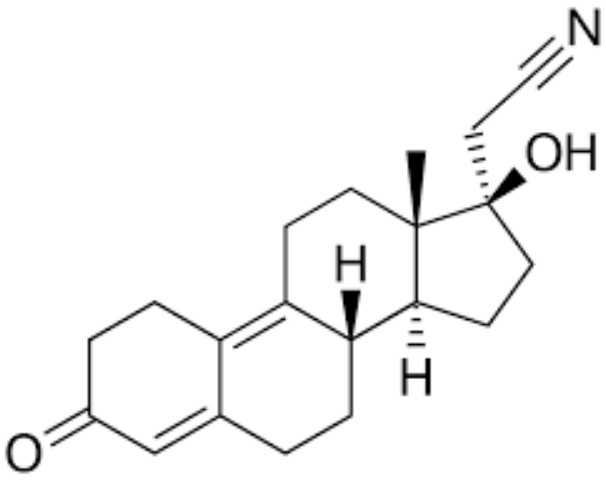
- Prevents ovulation
    - Exerts negative feedback on hypothalamus, reducing GnRH secretion
        - Reduction of GnRH = decrease of LH and FSH
        - LH and FSH is needed for final maturation and release of an egg, thus less LH and FSH= less ovulation
- Lowers estrogen levels
    - Decrease in FSH inhibits growth of ovarian follicles, which produce estrogen
    - Less ovarian follicle growth = less estrogen production = less endometrial tissue growth

- Decreases uterine blood flow & uterine volume

Selective progestin that binds with specific progesterone receptors in the body - mimics the effect of progesterone but is even more targeted

Similar structure to 19-Norprogestin - progetsins with increased affinity to bind to progesterone receptors, 19th carbon atome is removed

- Has minimal androgenic activity (male-hormone)
- Has no estrogenic, glucocorticoid, or anti-mineralocorticoid activity.



Levonorgestrel-releasing intrauterine system - what is it and how does it work

A T-shaped device that releases small doses of progestin/day.

- Contains 52 mg of levonorgestrel total
- Releases approx. 20 µg/day

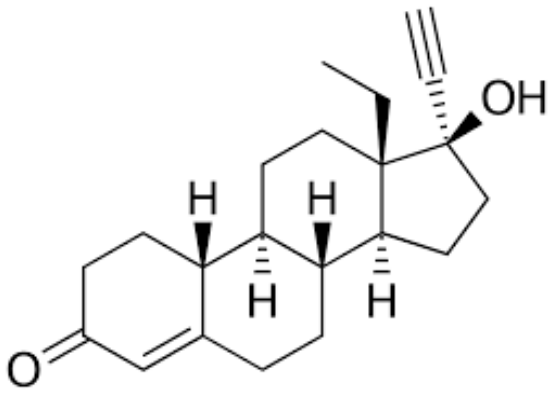
Levonorgestrel:

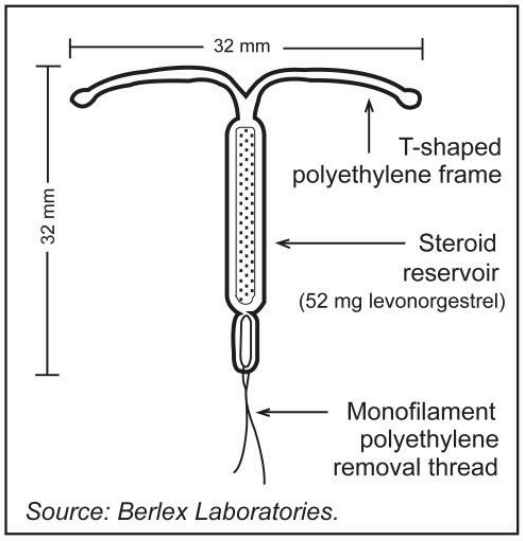
- Bind to progesterone receptors and slows GNrH production
    - Reduces LH & ovulation
- Thins endometrium and reduces endometrial growth
    - Suppresses cell proliferation in endometrium

- Anti-inflammatory effects

Derived from 19-Nortestosterone

- Derived from synthetic testosterone





Source: Berlex Laboratories.

Research Question: What is the comparative effectiveness of dienogest and the levonorgestrel-releasing intrauterine system in the treatment of endometriosis?

Primary Outcomes: Pelvic Pain, Adverse Events
Secondary Outcomes: Dysmenorrhea, Dyspareunia

Inclusion Criteria:

- Endometriosis specifically
- Dienogest or LNG-IUS or both
    - 2mg dienogest, 52mg LNGIUS
- Data on 24 weeks of treatment
- One of more of the selected outcomes with the measures specifcied (VAS for pelvic pain, DYS, and DYSP, SF-36 for QoL, etc.)
- Clear reporting
- English
- Full-text
- RCTs, prospective, retrospective

Exclusion Criteria;

- Adenymosis or other non-endometriosis patients
- Combined dienogest/LNG-IUS with other medications
    - Not the right dosage
- Didn't report 24 weeks
- Reported on adolescents or seniors, or those considered obese
- Unclear data (eg. graphs w/o specific numbers)
- Did not include any of the selected outcomes
- Not in English
- No full-text access
- Conference papers, case studies

Aug 23, 2024
Databases:

PubMed, Medline, Embase,
Keywords:

"Endometriosis" AND "dienogest"
"Endometriosis" AND "levonorgestrel"
"Endometriosis" AND "levonoregestrel-releasing"

Limits:

Limited to trials & studies only

Selection Process:

PubMed (D) - 42
Pubmed (L) - 44
Medline (D) - 308
Medline (L) - 60
Embase (D) - 156
Embase (L) - 212
Aug 24, 2024 , Aug 25, 2024 , Aug 26, 2024 , Aug 27, 2024
Total: 822
Duplicates removed with EndNote: 89
Duplicates manually removed: 111
Articles Left: 622
Removed (Title screening): 467
Articles Left: 155
Aug 28, 2024 , Aug 29, 2024
Removed (Abstract screening): 105
Aug 30, 2024 , Aug 31, 2024 , Sep 2, 2024
Articles Left (Full-Texts Retrieved): 50
Removed (Full Text Screening): 24
Articles Left: 26 (18 DNG and 8 LNG-IUS)
Records excluded for other reasons: 9 (focus on one type of endo - ovarian endometriomas)
ARTICLES INCLUDED: 17 (9 in DNG and 8 in LNG-IUS)

REMOVE K.H. LEE FOR GNRH-A USE AND ALSO ADD PORTO INTO DIENOGEST

- [x] ~~Fix DNG AE analysis~~

```
Number of studies: k = 7
Number of observations: o = 4252
Number of events: e = 1325

                         rate            95%-CI
Common effect model   1.0444 [0.7353;  1.3535]
Random effects model 31.4042 [1.1836; 61.6248]

Quantifying heterogeneity:
 tau^2 = 1658.9758 [684.6474; 8125.8484]; tau = 40.7305 [26.1658; 90.1435]
 I^2 = 99.5% [99.4%; 99.6%]; H = 14.61 [13.08; 16.33]

Test of heterogeneity:
       Q d.f.  p-value
 1281.14    6 < 0.0001
```

```
Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed rates
```

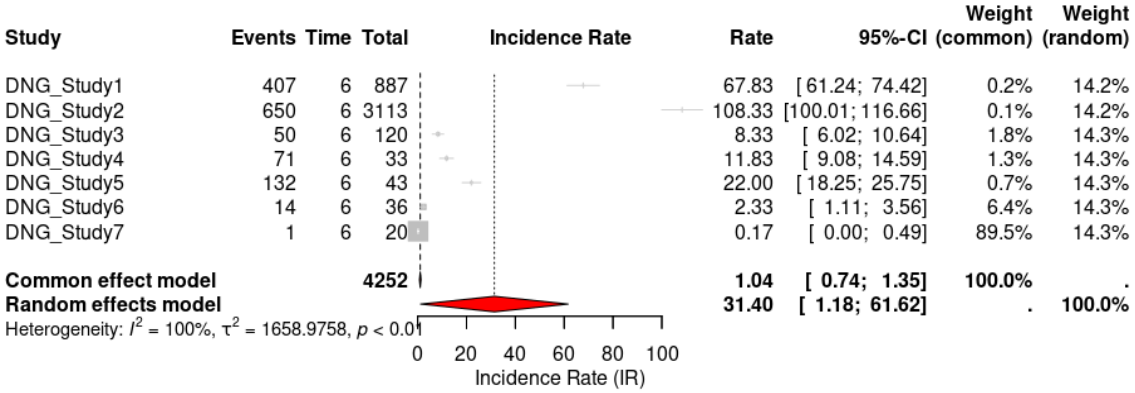
☑ ~~Fix LNG PP~~

```
Number of studies: k = 3
Number of observations: o = 95

                          mean              95%-CI
Common effect model  -50.3133 [-54.2749; -46.3516]
Random effects model -47.6935 [-64.4795; -30.9074]

Quantifying heterogeneity:
 tau^2 = 195.0569 [36.3740; >1950.5686]; tau = 13.9663 [6.0311; >44.1652]
 I^2 = 91.5% [78.3%; 96.7%]; H = 3.44 [2.15; 5.50]

Test of heterogeneity:
     Q d.f.  p-value
 23.63    2 < 0.0001

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed (raw) means
```

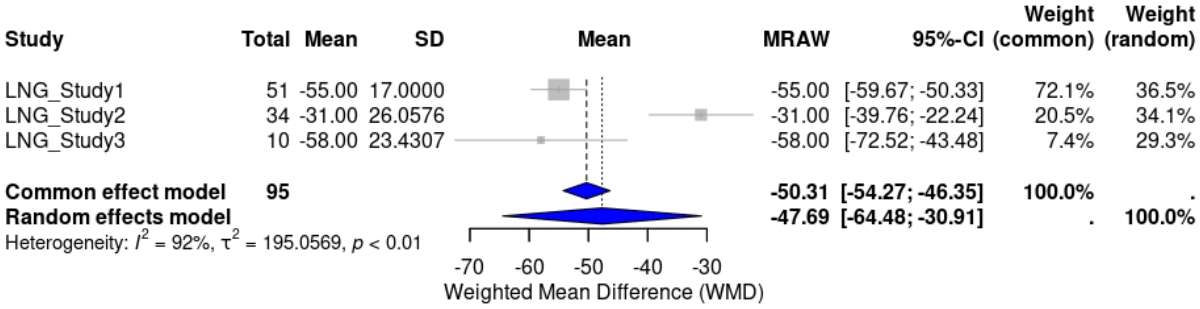
☑ ~~LNG AE~~

```
Number of studies: k = 3
Number of observations: o = 80
Number of events: e = 38

                         rate           95%-CI
Common effect model  0.4312 [0.1279; 0.7346]
Random effects model 1.9965 [0.0000; 4.6571]

Quantifying heterogeneity:
 tau^2 = 5.1955 [1.0916; >100.0000]; tau = 2.2794 [1.0448; >10.0000]
 I^2 = 93.4% [84.0%; 97.3%]; H = 3.89 [2.50; 6.04]

Test of heterogeneity:
     Q d.f.  p-value
 30.24    2 < 0.0001

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed rates
```

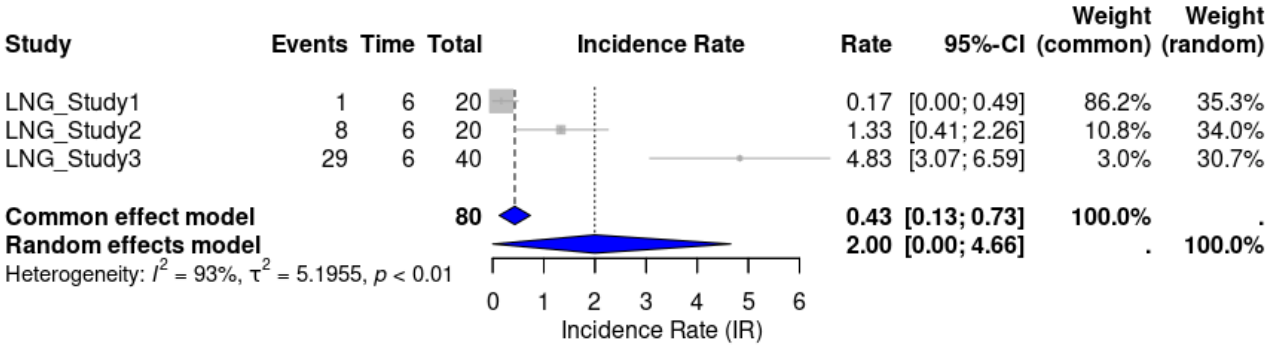
- [x] ~~DNG AE FOREST PLOT~~



- [x] ~~LNG PP FOREST PLOT~~



- [x] ~~LNG AE FOREST PLOT~~



- [x] ~~Fix PRISMA flow and methods~~
- [x] ~~Fix results and discussion~~

Sep 4, 2024 , Sep 5, 2024 , Sep 6, 2024

- Data extraction from studies into spreadsheet: Data Extraction

Sep 9, 2024 , Sep 10, 2024 , Sep 11, 2024 , Sep 12, 2024 , Sep 13, 2024 , Sep 14, 2024 , Sep 15, 2024

WMD Calcs? Research

Mean Differences:

Mean change in VAS scores (mean follow-up score minus mean baseline score).

Calculate Standard Deviations:

Get standard deviations of these mean changes for each study.

Weight:

The weight is typically the inverse of the variance of the mean difference. Variance is calculated from the standard deviation and sample size:

$$\text{Variance} = \frac{SD^2}{n}$$

The weight for each study is then:

$$\text{Weight} = \frac{1}{\text{Variance}}$$

Weighted Mean Difference (WMD):

Use the weights to combine the mean differences across studies:

$$\text{WMD} = \frac{\sum(\text{Weight}_i \times \text{Mean Difference}_i)}{\sum \text{Weight}_i}$$

Gives pooled mean difference, which represents the overall effect of the treatment on VAS scores.

Heterogeneity:

After calculating the WMD, assess heterogeneity (variability) across studies using statistical tests like I^2 or Cochran's Q to understand how much the results vary between studies.

Sep 21, 2024 , Sep 22, 2024 , Sep 23, 2024 , Sep 24, 2024 , Sep 25, 2024

Pelvic Pain
Input:

```
# PELVIC PAIN LNG
lnd_data <- data.frame(
  study = c("LNG_Study1", "LNG_Study2", "LNG_Study3", "LNG_Study4"),
  baseline.mean = c(74, 77, 79, 46),   # Baseline means
  followup.mean = c(19, 46, 21, 10),   # Follow-up means (6 months)
  baseline.sd = c(17, 13, 12, 30),     # SD for baseline
  followup.sd = c(17, 30, 27, 10),     # SD for follow-up          # Standard deviation
  n.e = c(51, 34, 10, 72)              # Sample size
)

# Calculate mean change
lnd_data$mean.change <- lnd_data$followup.mean - lnd_data$baseline.mean
lnd_data$sd.change <- sqrt(lnd_data$baseline.sd^2 + lnd_data$followup.sd^2 - 2 *
lnd_data$baseline.sd * lnd_data$followup.sd * 0.5)  # Assuming r = 0.5

lnd_analysis <- metamean(
  n = lnd_data$n.e,               # Sample size
  mean = lnd_data$mean.change,     # Mean change
  sd = lnd_data$sd.change,         # Standard deviation of the mean change
  studlab = lnd_data$study,        # Study labels
  sm = "MRAW"                      # Summary measure: Raw Mean Difference
)

print(lnd_analysis)



# PELVIC PAIN DNG
dng_data <- data.frame(
  study = c("DNG_Study1", "DNG_Study2", "DNG_Study3", "DNG_Study4", "DNG_Study5", "DNG_Study6",
"DNG_Study7", "DNG_Study8"),
  baseline.mean = c(56, 40.22, 60.2, 84, 78, 61, 85.9, 17.5),  # Baseline means
  followup.mean = c(10, 16.33, 12.7, 24.4, 51, 40, 32, 3),  # Follow-up means (6 months)
  baseline.sd = c(28, 31.1, 24.2, 13, 18, 9, 22.5, 3.7),  # SD for baseline
  followup.sd = c(14, 17.95, 20.3, 21, 20, 13, 17.7, 4.57),  # SD for follow-up
  n.e = c(887, 3113, 120, 33, 43, 83, 36, 40)  # Sample size
)

# Calculate Mean Change
dng_data$mean.change <- dng_data$followup.mean - dng_data$baseline.mean

# Calculate Standard Deviation of Mean Change
dng_data$sd.change <- sqrt(dng_data$baseline.sd^2 + dng_data$followup.sd^2 - 2 *
dng_data$baseline.sd * dng_data$followup.sd * 0.5)  # Assuming r = 0.5
```

```
dng_analysis <- metamean(
  n = dng_data$n.e,              # Sample size
  mean = dng_data$mean.change,    # Mean change
  sd = dng_data$sd.change,        # Standard deviation of the mean change
  studlab = dng_data$study,       # Study labels
  sm = "MRAW"                    # Summary measure: Raw Mean Difference
)

# Print Analysis Results
  print(dng_analysis)
```

Output (lng first):

```
Number of studies: k = 4
Number of observations: o = 167

                           mean                 95%-CI
Common effect model   -46.0781 [-49.4024; -42.7538]
Random effects model -44.5401 [-57.5286; -31.5515]

Quantifying heterogeneity:
 tau^2 = 155.0280 [36.7381; >1550.2798]; tau = 12.4510 [6.0612; >39.3736]
 I^2 = 92.2% [83.2%; 96.4%]; H = 3.58 [2.44; 5.25]

Test of heterogeneity:
     Q d.f.  p-value
 38.47    3 < 0.0001

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed (raw) means
```

Sep 28, 2024 , Sep 29, 2024

- Made PRISMA flowchart: PRISMA Diagram

Oct 2, 2024

FINAL CONSOLE OUTPUT:

```
library(meta)

#LNG PELVIC PAIN
lnd_data <- data.frame(
+    study = c("LNG_Study1", "LNG_Study2", "LNG_Study3", "LNG_Study4"),
+    baseline.mean = c(74, 77, 79, 46),    # Baseline means
+    followup.mean = c(19, 46, 21, 10),    # Follow-up means (6 months)
+    baseline.sd = c(17, 13, 12, 30),      # SD for baseline
+    followup.sd = c(17, 30, 27, 10),      # SD for follow-up          #
Standard deviation
+    n.e = c(51, 34, 10, 72)               # Sample size
+ )

> # Calculate mean change
> lnd_data$mean.change <- lnd_data$followup.mean - lnd_data$baseline.mean
> lnd_data$sd.change <- sqrt(lnd_data$baseline.sd^2 +
lnd_data$followup.sd^2 - 2 * lnd_data$baseline.sd * lnd_data$followup.sd *
0.5)  # Assuming r = 0.5
> > lnd_analysis <- metamean(
+    n = lnd_data$n.e,                 # Sample size
+    mean = lnd_data$mean.change,      # Mean change
+    sd = lnd_data$sd.change,          # Standard deviation of the mean
change
+    studlab = lnd_data$study,         # Study labels
+    sm = "MRAW"                       # Summary measure: Raw Mean
Difference
+ )
> > print(lnd_analysis)

Number of studies: k = 4
Number of observations: o = 167

                          mean                 95%-CI
Common effect model  -46.0781 [-49.4024; -42.7538]
Random effects model -44.5401 [-57.5286; -31.5515]

Quantifying heterogeneity:
 tau^2 = 155.0280 [36.7381; >1550.2798]; tau = 12.4510 [6.0612; >39.3736]
 I^2 = 92.2% [83.2%; 96.4%]; H = 3.58 [2.44; 5.25]

Test of heterogeneity:
     Q d.f.  p-value
 38.47    3 < 0.0001
```

```
Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed (raw) means

> > # DNG PELVIC PAIN
> dng_data <- data.frame(
+     study = c("DNG_Study1", "DNG_Study2", "DNG_Study3", "DNG_Study4",
"DNG_Study5", "DNG_Study6", "DNG_Study7", "DNG_Study8"),
+     baseline.mean = c(56, 40.22, 60.2, 84, 78, 61, 85.9, 17.5),  #
Baseline means
+     followup.mean = c(10, 16.33, 12.7, 24.4, 51, 40, 32, 3),  # Follow-up
means (6 months)
+     baseline.sd = c(28, 31.1, 24.2, 13, 18, 9, 22.5, 3.7),  # SD for
baseline
+     followup.sd = c(14, 17.95, 20.3, 21, 20, 13, 17.7, 4.57),  # SD for
follow-up
+     n.e = c(887, 3113, 120, 33, 43, 83, 36, 40)  # Sample size
+ )

> > # Calculate Mean Change
> dng_data$mean.change <- dng_data$followup.mean - dng_data$baseline.mean
> > # Calculate Standard Deviation of Mean Change
> dng_data$sd.change <- sqrt(dng_data$baseline.sd^2 +
dng_data$followup.sd^2 - 2 * dng_data$baseline.sd * dng_data$followup.sd *
0.5)  # Assuming r = 0.5
> > dng_analysis <- metamean(
+     n = dng_data$n.e,                # Sample size
+     mean = dng_data$mean.change,     # Mean change
+     sd = dng_data$sd.change,         # Standard deviation of the mean
change
+     studlab = dng_data$study,        # Study labels
+     sm = "MRAW"                      # Summary measure: Raw Mean
Difference
+ )
> > # Print Analysis Results
> print(dng_analysis)

Number of studies: k = 8
Number of observations: o = 4355

                          mean                 95%-CI
Common effect model  -26.3170 [-26.9634; -25.6705]
Random effects model -36.5149 [-48.2622; -24.7676]
```

```
Quantifying heterogeneity:
 tau^2 = 282.7642 [120.9617; 1190.5373]; tau = 16.8156 [10.9983; 34.5042]
 I^2 = 99.4% [99.3%; 99.5%]; H = 13.22 [11.84; 14.76]

Test of heterogeneity:
       Q d.f.  p-value
 1223.19    7 < 0.0001

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed (raw) means
```

```
> # AE LNG
> lnd_adverse_data <- data.frame(
+     study = c("LNG_Study1", "LNG_Study2", "LNG_Study3", "LNG_Study4"),
+     events = c(29, 1, 8, 29),
+     n = c(72, 20, 20, 40),
+     time = c(6, 6, 6, 6)
+ )

> # Analysis for LNG adverse events
> lnd_adverse_analysis <- metarate(
+     event = lnd_adverse_data$events,
+     n = lnd_adverse_data$n,
+     time = lnd_adverse_data$time,
+     studlab = lnd_adverse_data$study,
+     sm = "IR"
+ )
> > print(lnd_adverse_analysis)

Number of studies: k = 4
Number of observations: o = 152
Number of events: e = 67

                         rate            95%-CI
Common effect model  0.5584 [0.2594; 0.8573]
Random effects model 2.6674 [0.2993; 5.0355]

Quantifying heterogeneity:
 tau^2 = 5.3947 [1.4415; 79.9945]; tau = 2.3227 [1.2006; 8.9440]
 I^2 = 94.4% [88.8%; 97.2%]; H = 4.23 [2.98; 5.99]

Test of heterogeneity:
     Q d.f.  p-value
 53.60    3 < 0.0001
```

```
Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed rates

> # AE DNG
> dng_adverse_data <- data.frame(
+     study = c("DNG_Study1", "DNG_Study2", "DNG_Study3", "DNG_Study4",
"DNG_Study5", "DNG_Study6"),
+     events = c(407, 650, 50, 71, 132, 14),
+     n = c(887, 3113, 120, 33, 43, 36),
+     time = c(6, 6, 6, 6, 6, 6)
+ )
> > # Meta-analysis for DNG adverse events
> dng_adverse_analysis <- metarate(
+     event = dng_adverse_data$events,
+     n = dng_adverse_data$n,
+     time = dng_adverse_data$time,
+     studlab = dng_adverse_data$study,
+     sm = "IR"
+ )
> > print(dng_adverse_analysis)

Number of studies: k = 6
Number of observations: o = 4232
Number of events: e = 1324

                         rate             95%-CI
Common effect model    8.5409 [7.5862;  9.4955]
Random effects model 36.6384 [2.9522; 70.3247]

Quantifying heterogeneity:
 tau^2 = 1766.2905 [683.2026; 10720.2471]; tau = 42.0273 [26.1381;
103.5386]
 I^2 = 99.5% [99.4%; 99.6%]; H = 14.26 [12.60; 16.14]

Test of heterogeneity:
       Q d.f.  p-value
 1016.53    5 < 0.0001

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed rates
```

```
> # LNG DYS
> lng_dysmenorrhea_data <- data.frame(
+    study = c("LNG_Study1", "LNG_Study2"),
+    baseline.mean = c(73, 61.3),
+    followup.mean = c(19, 35.3),
+    baseline.sd = c(17, 11.5),
+    followup.sd = c(22, 10.1),
+    n.e = c(51,45)
+ )

> # Calculate mean changes and SDs of change for LNG
> lng_dysmenorrhea_data$mean.change <- lng_dysmenorrhea_data$followup.mean
- lng_dysmenorrhea_data$baseline.mean
> lng_dysmenorrhea_data$sd.change <-
sqrt(lng_dysmenorrhea_data$baseline.sd^2 +
lng_dysmenorrhea_data$followup.sd^2 - 2 *
lng_dysmenorrhea_data$baseline.sd * lng_dysmenorrhea_data$followup.sd *
0.5)  # Assuming r = 0.5
> > # Run meta-analysis for LNG
> lng_dysmenorrhea_analysis <- metamean(
+    n = lng_dysmenorrhea_data$n.e,
+    mean = lng_dysmenorrhea_data$mean.change,
+    sd = lng_dysmenorrhea_data$sd.change,
+    studlab = lng_dysmenorrhea_data$study,
+    sm = "MRAW"
+ )
> print(lng_dysmenorrhea_analysis)

Number of studies: k = 2
Number of observations: o = 96

                          mean                95%-CI
Common effect model  -33.0338 [-35.7815; -30.2861]
Random effects model -39.9072 [-67.3461; -12.4683]

Quantifying heterogeneity:
 tau^2 = 386.7759; tau = 19.6666; I^2 = 98.7% [97.2%; 99.4%]; H = 8.66
[5.95; 12.62]

Test of heterogeneity:
     Q d.f.  p-value
 75.04    1 < 0.0001

Details on meta-analytical method:
- Inverse variance method
```

```
- Restricted maximum-likelihood estimator for tau^2
- Untransformed (raw) means
> # DYS DNG
> dng_dysmenorrhea_data <- data.frame(
+    study = c("DNG_Study1", "DNG_Study2"),
+    baseline.mean = c(69, 70),
+    followup.mean = c(38, 55),
+    baseline.sd = c(26, 12),
+    followup.sd = c(27,14),
+    n.e = c(64,83)
+ )

> # Calculate mean changes and SDs of change for DNG
> dng_dysmenorrhea_data$mean.change <- dng_dysmenorrhea_data$followup.mean
- dng_dysmenorrhea_data$baseline.mean
> dng_dysmenorrhea_data$sd.change <-
sqrt(dng_dysmenorrhea_data$baseline.sd^2 +
dng_dysmenorrhea_data$followup.sd^2 - 2 *
dng_dysmenorrhea_data$baseline.sd * dng_dysmenorrhea_data$followup.sd *
0.5)  # Assuming r = 0.5
> > # Run meta-analysis for DNG
> dng_dysmenorrhea_analysis <- metamean(
+    n = dng_dysmenorrhea_data$n.e,
+    mean = dng_dysmenorrhea_data$mean.change,
+    sd = dng_dysmenorrhea_data$sd.change,
+    studlab = dng_dysmenorrhea_data$study,
+    sm = "MRAW"
+ )
> > print(dng_dysmenorrhea_analysis)

Number of studies: k = 2
Number of observations: o = 147

                          mean                95%-CI
Common effect model  -17.5394 [-20.1273; -14.9516]
Random effects model -22.7215 [-38.3917;  -7.0513]

Quantifying heterogeneity:
 tau^2 = 121.4717; tau = 11.0214; I^2 = 94.9% [84.5%; 98.3%]; H = 4.43
[2.54; 7.71]

Test of heterogeneity:
     Q d.f.  p-value
 19.61    1 < 0.0001

Details on meta-analytical method:
- Inverse variance method
```

```
- Restricted maximum-likelihood estimator for tau^2
- Untransformed (raw) means
> # DYSP LNG
> lng_dyspareunia_data <- data.frame(
+    study = c("DNG_Study1"),
+    baseline.mean = c(60.4),
+    followup.mean = c(31.1),
+    baseline.sd = c(9.5),
+    followup.sd = c(9.5),
+    n.e = c(45)
+ )

> # Calculate mean changes and SDs of change for LNG
> lng_dyspareunia_data$mean.change <- lng_dyspareunia_data$followup.mean -
lng_dyspareunia_data$baseline.mean
> lng_dyspareunia_data$sd.change <-
sqrt(lng_dyspareunia_data$baseline.sd^2 +
lng_dyspareunia_data$followup.sd^2 - 2 *lng_dyspareunia_data$baseline.sd *
lng_dyspareunia_data$followup.sd * 0.5)  # Assuming r = 0.5
> > # Run meta-analysis for LNG
> lng_dyspareunia_analysis <- metamean(
+    n = lng_dyspareunia_data$n.e,
+    mean = lng_dyspareunia_data$mean.change,
+    sd = lng_dyspareunia_data$sd.change,
+    studlab = lng_dyspareunia_data$study,
+    sm = "MRAW"
+ )
> > print(lng_dyspareunia_analysis)

Number of observations: o = 45

                mean                 95%-CI
lng_Study1 -29.3000 [-32.0757; -26.5243]

Details:
- Untransformed (raw) means

> # DYSP DNG
> dng_dyspareunia_data <- data.frame(
+    study = c("DNG_Study1", "DNG_Study2", "DNG_Study3", "DNG_Study4"),
+    baseline.mean = c(74, 52, 57, 48.1),
+    followup.mean = c(56, 37, 43, 26.7),
+    baseline.sd = c(22, 38, 19, 8.9),
+    followup.sd = c(25, 31, 22, 18.3),
+    n.e = c(43, 64, 83, 36)
+ )
```

```
> > # Calculate mean changes and SDs of change for DNG
> dng_dyspareunia_data$mean.change <- dng_dyspareunia_data$followup.mean -
dng_dyspareunia_data$baseline.mean
> dng_dyspareunia_data$sd.change <-
sqrt(dng_dyspareunia_data$baseline.sd^2 +
dng_dyspareunia_data$followup.sd^2 - 2 * dng_dyspareunia_data$baseline.sd
* dng_dyspareunia_data$followup.sd * 0.5)  # Assuming r = 0.5
> > # Run meta-analysis for DNG
> dng_dyspareunia_analysis <- metamean(
+    n = dng_dyspareunia_data$n.e,
+    mean = dng_dyspareunia_data$mean.change,
+    sd = dng_dyspareunia_data$sd.change,
+    studlab = dng_dyspareunia_data$study,
+    sm = "MRAW"
+ )
> > print(dng_dyspareunia_analysis)

Number of studies: k = 4
Number of observations: o = 226

                          mean                 95%-CI
Common effect model  -17.0428 [-19.9116; -14.1740]
Random effects model -17.1683 [-21.0800; -13.2567]

Quantifying heterogeneity:
 tau^2 = 6.4556 [0.0000; >100.0000]; tau = 2.5408 [0.0000; >10.0000]
 I^2 = 37.6% [0.0%; 78.6%]; H = 1.27 [1.00; 2.16]

Test of heterogeneity:
    Q d.f. p-value
 4.81    3  0.1864

Details on meta-analytical method:
- Inverse variance method
- Restricted maximum-likelihood estimator for tau^2
- Q-Profile method for confidence interval of tau^2 and tau
- Untransformed (raw) means

> # Define 95% confidence intervals (CI) for DNG and LNG
> CI_lower_DNG <- -48.2622  # Replace with your actual lower CI for DNG
> CI_upper_DNG <- -24.7676 # Replace with your actual upper CI for DNG
> > CI_lower_LNG <- -57.5286  # Replace with your actual lower CI for LNG
> CI_upper_LNG <- -31.5515   # Replace with your actual upper CI for LNG
> > # Step 1: Calculate SE for DNG
> SE_DNG <- (CI_upper_DNG - CI_lower_DNG) / (2 * 1.96)
```

```
> > # Step 2: Calculate SE for LNG
> SE_LNG <- (CI_upper_LNG - CI_lower_LNG) / (2 * 1.96)
> > # Output the results
> cat("Standard Error for DNG WMD:", SE_DNG, "\n")
Standard Error for DNG WMD: 5.99352
> cat("Standard Error for LNG WMD:", SE_LNG, "\n")
Standard Error for LNG WMD: 6.626811

> # Define WMDs and Standard Errors (SE) for DNG and LNG
> WMD_DNG <- -36.5149
> SE_DNG <- 5.99352
> > WMD_LNG <- -44.5401
> SE_LNG <- 6.626811
> # Calculate the Difference in WMDs
> difference_WMD <- WMD_DNG - WMD_LNG
> Calculate the Standard Error of the Difference
> SE_difference <- sqrt(SE_DNG^2 + SE_LNG^2)
> # Calculate the Z-score
> Z <- difference_WMD / SE_difference
> # Calculate the P-value for two-tailed test
> p_value <- 2 * (1 - pnorm(abs(Z)))

> # Output the results
> cat("Difference in WMDs:", difference_WMD, "\n")
Difference in WMDs: 8.0252
> cat("Standard Error of the Difference:", SE_difference, "\n")
Standard Error of the Difference: 8.93515
> cat("Z-score:", Z, "\n")
Z-score: 0.8981606
> cat("P-value:", p_value, "\n")
P-value: 0.3690999
> # Interpretation: If p-value < 0.05, the difference is statistically
significant
> if (p_value < 0.05) {
+    cat("The difference between DNG and LNG is statistically
significant.\n")
+ } else {
+    cat("The difference between DNG and LNG is not statistically
significant.\n")
+ }
The difference between DNG and LNG is not statistically significant.

> # Define 95% confidence intervals (CI) for DNG and LNG DYSMENORRHEA
> CI_lower_DYSDNG <- -38.3917  # Replace with your actual lower CI for DNG
> CI_upper_DYSDNG <- -7.0513  # Replace with your actual upper CI for DNG
> > CI_lower_DYSLNG <- -67.3461  # Replace with your actual lower CI for
LNG
```

```
> CI_upper_DYSLNG <- -12.4683   # Replace with your actual upper CI for
LNG
>  #Calculate SE for DNG
> SE_DYSDNG <- (CI_upper_DYSDNG - CI_lower_DYSDNG) / (2 * 1.96)
> # Calculate SE for LNG
> SE_DYSLNG <- (CI_upper_DYSLNG - CI_lower_DYSLNG) / (2 * 1.96)

> # Output the results
> cat("Standard Error for DNG WMD:", SE_DYSDNG, "\n")
Standard Error for DNG WMD: 7.995
> cat("Standard Error for LNG WMD:", SE_DYSLNG, "\n")
Standard Error for LNG WMD: 13.99944

> # Define WMDs and Standard Errors (SE) for DNG and LNG
> WMD_DYSDNG <- -22.7215
> SE_DYSDNG <- 7.995
> > WMD_DYSLNG <- -39.9072
> SE_DYSLNG <- 13.99944
> # Calculate the Difference in WMDs
> difference_DYSWMD <- WMD_DYSDNG - WMD_DYSLNG
> # Calculate the Standard Error of the Difference
> DYSSE_difference <- sqrt(SE_DYSDNG^2 + SE_DYSLNG^2)
> # Calculate the Z-score
> DYSZ <- difference_DYSWMD / DYSSE_difference
> # Calculate the P-value for two-tailed test
> DYSp_value <- 2 * (1 - pnorm(abs(DYSZ)))

> # Output the results
> cat("Difference in WMDs:", difference_DYSWMD, "\n")
Difference in WMDs: 17.1857
> cat("Standard Error of the Difference:", DYSSE_difference, "\n")
Standard Error of the Difference: 16.12155
> cat("Z-score:", DYSZ, "\n")
Z-score: 1.066008
> cat("P-value:", DYSp_value, "\n")
P-value: 0.28642

> # Interpretation: If p-value < 0.05, the difference is statistically
significant
> if (DYSp_value < 0.05) {
+    cat("The difference between DNG and LNG is statistically
significant.\n")
+ } else {
+    cat("The difference between DNG and LNG is not statistically
significant.\n")
+ }
The difference between DNG and LNG is not statistically significant.
```

```
> # Define 95% confidence intervals (CI) for DNG and LNG DYSPAREUNIA
> CI_lower_DYSPDNG <- -21.0800  # Replace with your actual lower CI for
DNG
> CI_upper_DYSPDNG <- -13.2567  # Replace with your actual upper CI for
DNG
>
> CI_lower_DYSPLNG <- -32.0757
> CI_upper_DYSPLNG <- -26.5243
>
> # Calculate SE for DNG
> SE_DYSPDNG <- (CI_upper_DYSPDNG - CI_lower_DYSPDNG) / (2 * 1.96)
>
> # Calculate SE for LNG
> SE_DYSPLNG <- (CI_upper_DYSPLNG - CI_lower_DYSPLNG) / (2 * 1.96)
>
> # Output the results
> cat("Standard Error for DNG WMD:", SE_DYSPDNG, "\n")
Standard Error for DNG WMD: 1.99574
> cat("Standard Error for LNG WMD:", SE_DYSPLNG, "\n")
Standard Error for LNG WMD: 1.416173

> # Define WMDs and Standard Errors (SE) for DNG and LNG
> WMD_DYSPDNG <- -17.1683
> SE_DYSPDNG <- 1.99574
>
> WMD_DYSPLNG <- -29.3000
> SE_DYSPLNG <- 1.416173
>
> # Calculate the Difference in WMDs
> difference_DYSPWMD <- WMD_DYSPDNG - WMD_DYSPLNG
>
> # Calculate the Standard Error of the Difference
> DYSPSE_difference <- sqrt(SE_DYSPDNG^2 + SE_DYSPLNG^2)
>
> # Calculate the Z-score
> DYSPZ <- difference_DYSPWMD / DYSPSE_difference
>
> # Calculate the P-value for two-tailed test
> DYSPp_value <- 2 * (1 - pnorm(abs(DYSPZ)))

> # Output the results
> cat("Difference in WMDs:", difference_DYSPWMD, "\n")
Difference in WMDs: 12.1317
> cat("Standard Error of the Difference:", DYSPSE_difference, "\n")
Standard Error of the Difference: 2.447146
```

```
> cat("Z-score:", DYSPZ, "\n")
Z-score: 4.957489
> cat("P-value:", DYSPp_value, "\n")
P-value: 7.141008e-07

> # Interpretation: If p-value < 0.05, the difference is statistically
significant
> if (DYSPp_value < 0.05) {
+    cat("The difference between DNG and LNG is statistically
significant.\n")
+ } else {
+    cat("The difference between DNG and LNG is not statistically
significant.\n")
+ }
The difference between DNG and LNG is statistically significant.

> # AE: Extracting IR and SE for LNG
> lng_ir <- lnd_adverse_analysis$TE.random
> lng_se <- lnd_adverse_analysis$seTE.random

# Print the results
> print(lng_ir)  # IR for LNG
[1] 2.66736
> print(lng_se)  # SE for LNG
[1] 1.208233

> # Extract the incidence rates (IR) and their standard errors (SE) from
the result
> dng_ir <- dng_adverse_analysis$TE.random    # Incidence rate (IR) from
the random effects model
> dng_se <- dng_adverse_analysis$seTE.random  # Standard error (SE) for
the IR
> print(dng_ir)
[1] 36.63843
> print(dng_se)
[1] 17.18719


> # Analyze
> dng_ir <- 36.63843  # DNG incidence rate
> lng_ir <- 2.66736   # LNG incidence rate
> dng_se <- 17.18719  # DNG standard error
> lng_se <- 1.208233  # LNG standard error
>
> # Calculate the Z-score for the difference in incidence rates
> AEz_score <- (dng_ir - lng_ir) / sqrt(dng_se^2 + lng_se^2)
>
```

```
> #: Calculate the p-value for a two-tailed test
> AEp_value <- 2 * (1 - pnorm(abs(AEz_score)))
> print(paste("Z-score:", z_score))
[1] "Z-score: 1.97166840389705"
> print(paste("P-value:", AEp_value))
[1] "P-value: 0.0486474728085711"

> if (AEp_value < 0.05) {
+    cat("The difference between DNG and LNG is statistically
significant.\n")
+ } else {
+    cat("The difference between DNG and LNG is not statistically
significant.\n")
+ }
The difference between DNG and LNG is statistically significant.
```

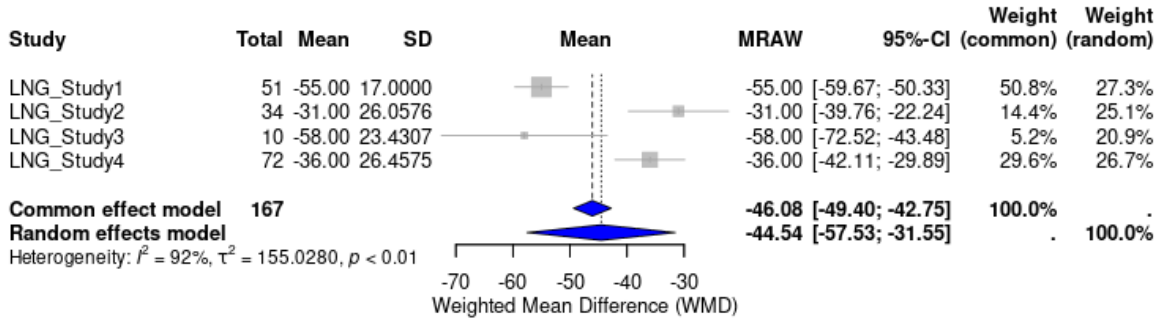
Oct 7, 2024 , Oct 8, 2024

Forest Plots:

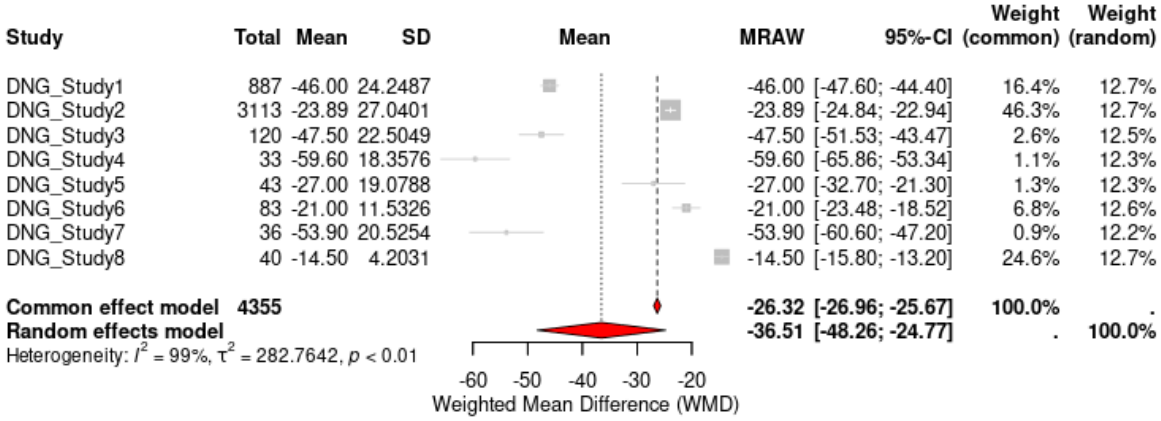
```
#Forest Plots
  forest(lnd_analysis,
         main = "Pelvic Pain Reduction (WMD)",
         xlab = "Weighted Mean Difference (WMD)",
         col.diamond = "blue",
         col.study = "darkgray")
  forest(dng_analysis,
         main = "Pelvic Pain Reduction (WMD)",
         xlab = "Weighted Mean Difference (WMD)",
         col.diamond = "red",
         col.study = "lightgray")
  forest(lng_dysmenorrhea_analysis,
         main = "Pelvic Pain Reduction (WMD)",
         xlab = "Weighted Mean Difference (WMD)",
         col.diamond = "blue",
         col.study = "darkgray")
  forest(dng_dysmenorrhea_analysis,
         main = "Pelvic Pain Reduction (WMD)",
         xlab = "Weighted Mean Difference (WMD)",
         col.diamond = "red",
         col.study = "lightgray")
  forest(lng_dyspareunia_analysis,
         main = "Pelvic Pain Reduction (WMD)",
         xlab = "Weighted Mean Difference (WMD)",
         col.diamond = "blue",
```

```
        col.study = "darkgray")
forest(dng_dyspareunia_analysis,
        main = "Pelvic Pain Reduction (WMD)",
        xlab = "Weighted Mean Difference (WMD)",
        col.diamond = "red",
        col.study = "lightgray")
```

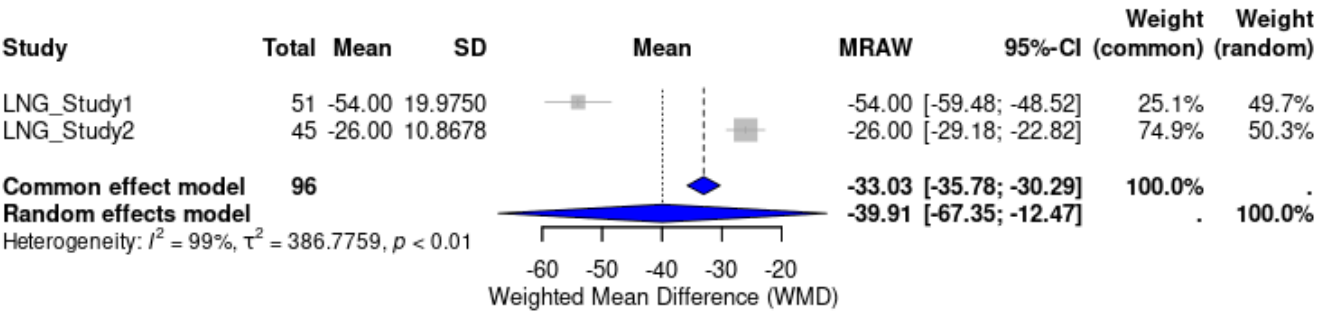
LNG PP:



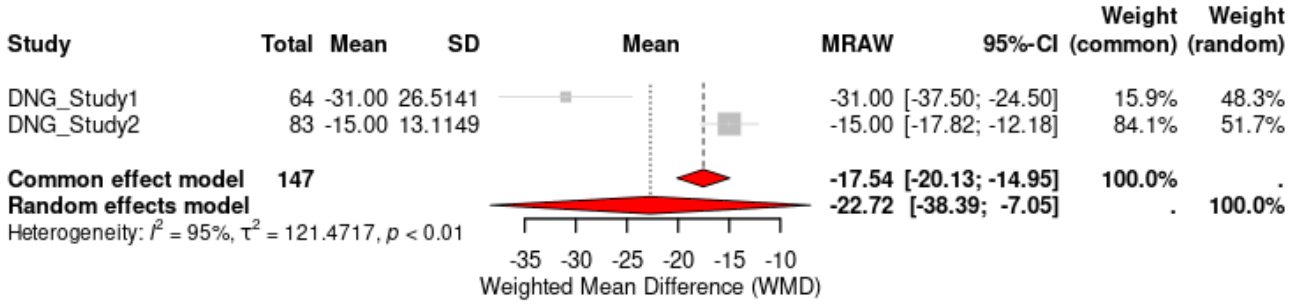
DNG PP:



LNG DYS:

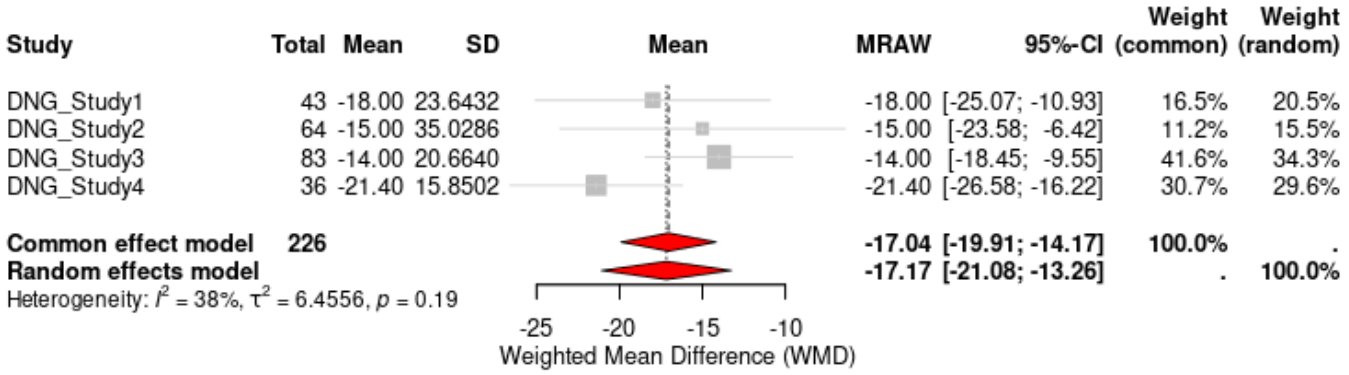


DNG DYS:



LNG DYSP:
N/A - ONLY 1 STUDY

DNG DYSP:



Oct 10, 2024

- Beginning to write my review

Oct 11, 2024 , Oct 14, 2024

- Introduction

Oct 16, 2024 , Oct 17, 2024 , Oct 19, 2024

- Methods

Oct 18, 2024 , Oct 22, 2024

- Results - Study Selection

Oct 24, 2024 , Oct 28, 2024

- Results of Meta-Analyses

Oct 20, 2024

- Results - Patient Characteristics + Study Characteristics tables created, PRISMA flowchart

Nov 2, 2024, Nov 7, 2024

- Discussion

Nov 9, 2024

- Abstract

Nov 12, 2024, Nov 13, 2024, Nov 17, 2024, Dec 3, 2024

- Editing

Dec 20, 2024, Dec 23, 2024

- Citations/Bibliography

Dec 27, 2024

- Added figure labels to review

Dec 31, 2024

- Created LaTex table (scientific standard)
- Replaced old table and combined 2 tables into one

Jan 1, 2025

- Naive direct comparison to comparative analysis

Jan 3, 2025

- Edited by u of a resident

Jan 4, 2025, Jan 5, 2025, Jan 6, 2025, Jan 7, 2025, Jan 8, 2025, Jan 9, 2025

- Fixed paper based on feedback
- Updated references

Jan 13, 2025, Jan 14, 2025, Jan 15, 2025, Jan 16, 2025, Jan 17, 2025

- Wrote presentation notes
- Questions for Dr. Belland:

1. In your experience, what are the most common and most effective medical and hormonal therapies for treating endometriosis? Which factors are most important in determining what you prescribe?
2. Have you used oral dienogest and/or the levonorgestrel-releasing intrauterine system before? If so, how do you find them in terms of effectiveness and patient satisfaction? Are there specific situations where you'd be more inclined to use one of these?
3. Are there any patient-reported outcomes or quality-of-life measures that you feel are underrepresented in research but are crucial in clinical practice?
4. Do you find that patients often come with misconceptions about hormonal therapies for endometriosis? How do you address those, and is there a way research can better support patient education?

5. Are there any other emerging treatments for endo that you're particularly excited about
6. (For funsies) Have there been any particular cases in your career that changed how you think about managing endometriosis or inspired your work in this field?

Jan 18, 2025, Jan 19, 2025, Jan 20, 2025, Jan 21, 2025

- Trifold formatting

Jan 23, 2025, Jan 24, 2025, Jan 25, 2025, Jan 26, 2025, Jan 28, 2025

- Trifold cutting and pasting
- Speech practicing

Jan 30, 2025

- Presented at Louis fair

Feb 4, 2025

- Got into CYSF!

Feb 13, 2025, Feb 14, 2025

- Used judges feedback
- Uploading to CYSF platform

Mar 6, 2025

- Made slideshow
- Updated CYSF platform
-

Mar 8, 2025, Mar 9, 2025, Mar 11, 2025, Mar 12, 2025, Mar 14, 2025

- Made video
- Updated CYSF platform