GEMs of the Week

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Week of January 20– 24, 2025

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Untangling Preeclampsia Prevention: Comparing Prophylactic Strategies

GEMs GOOD EVIDENCE MATTERS SPOTLIGHT

Comparative Effectiveness of Prophylactic Strategies for Preeclampsia: A Network Meta-Analysis of Randomized Controlled Trials

Liu YH, Zhang YS, Chen JY, et al. Comparative effectiveness of prophylactic strategies for preeclampsia: a network meta-analysis of randomized controlled trials. *Am J Obstet Gynecol*. 2023;228(5):535-546. doi:10.1016/j.ajog.2022.10.014

KEY TAKEAWAY: Low-molecular-weight heparin (LWMH), vitamin D supplementation, exercise, calcium supplementation, and aspirin significantly reduce the risk of preeclampsia and pregnancy-induced hypertension (HTN).

STUDY DESIGN: Meta-analysis of 130 randomized control trials (RCTs) (N=112,916)

LEVEL OF EVIDENCE: STEP 1

BRIEF BACKGROUND INFORMATION: Preeclampsia is an increasingly common disease affecting patients during pregnancy, leading to adverse events for both the fetus and mother. Pregnant patients at risk of preeclampsia or pregnancy-induced HTN have been advised to take prophylactic aspirin to decrease their risk of adverse events. Previous research has confirmed the benefit of aspirin as prophylaxis, but adequate research has not been conducted to compare the efficacy of different prophylactic strategies for preventing preeclampsia.

PATIENTS: Pregnant patients at risk for pre-eclampsia or pregnancy-induced HTN

INTERVENTION: Various prophylactic strategies

CONTROL: No Intervention or placebo

PRIMARY OUTCOME: Pre-eclampsia or pregnancy-induced HTN

METHODS (BRIEF DESCRIPTION):

- PRISM guidelines were used to identify studies in PubMed, Embase, Web of Science, Cochrane Library, and Clinicaltrials.gov with the keywords of preeclampsia and prophylactic strategies.
- The study included pregnant women at risk of pre-eclampsia or pregnancy-induced HTN.
- Inclusion criteria involved RCTs comparing carious prophylactic strategies against each other and compared to negative controls.
- Exclusion criteria disqualified RCTs that included non-pregnant women, combined multiple prophylactic strategies per patient or did not report the incidence of pre-eclampsia or pregnancy-induced HTN.
- Multiple prophylactic strategies were studied including exercise, LWMH (3,800 IU/day–4,000 IU/day), vitamin D supplementation (4,200 IU/week–25,000 IU/week), aspirin (60 mg/day–150 mg/day), and calcium supplement (500 mg/day–2,000 mg/day).
- The interventions were compared to no treatment or placebo.
- The outcome of preeclampsia was proteinuria and HTN diagnosed after 20 weeks gestation or end-organ dysfunction and new HTN.
- The outcome of pregnancy-induced HTN was HTN diagnosed after 20 weeks gestation without proteinuria.

INTERVENTION (# IN THE GROUP):

- Exercise: 1,285
- LWMH: 512
- Vitamin D supplementation: 684
- Aspirin: 26,100
- Calcium supplementations: 8,436
- Other Interventions: 18,630

COMPARISON (# IN THE GROUP): 57,224

FOLLOW-UP PERIOD: Varied (up to 12 months)

RESULTS:

Primary Outcome –

- LWMH, vitamin D supplementation, exercise, calcium supplementation, and aspirin were associated with a significantly reduced risk of pre-eclampsia/pregnancy-induced HTN compared to placebo or no intervention.
  - LWMH (6 studies; n=512; risk ratio [RR] 0.6; 95% CI, 0.42–0.87)
  - Vitamin D (5 studies; n=684; RR 0.65; 95% CI, 0.45–0.95)
  - Exercise (9 studies; n=1,285; RR 0.68; 95% CI, 0.50–0.92)
  - Calcium (15 studies; n=8,436; RR 0.71; 95% CI, 0.62–0.82)

    - Aspirin (50 studies; n=26,100; RR 0.79; 95% CI, 0.72–0.86)
- No significant difference was found in the effectiveness between the prophylactic interventions. Other interventions studied were not associated with significant risk reduction.

LIMITATIONS:

- The meta-analysis used outcomes and statistical methods different from those reported in the PROSPERO registration, raising concerns about selective reporting.
- The inclusion of several small studies may have introduced biases and reduced the reliability of the effect estimates.
- The meta-analysis did not determine appropriate supplemental dosages for prophylaxis, leaving a gap in dosing recommendations.
- Most studies failed to report adverse effects, tolerability, or regimen compliance, limiting the assessment of intervention safety.

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COVID-19 Vaccination During Pregnancy Improved Neonatal Outcomes

COVID-19 Vaccination During the Third Trimester of Pregnancy: Rate of Vaccination and Maternal and Neonatal Outcomes, A Multicentre Retrospective Cohort Study

Rottenstreich M, Sela HY, Rotem R, Kadish E, Wiener-Well Y, Grisaru-Granovsky S. Covid-19 vaccination during the third trimester of pregnancy: rate of vaccination and maternal and neonatal outcomes, a multicentre retrospective cohort study. *BJOG*. 2022;129(2):248-255. doi:10.1111/1471-0528.16941

KEY TAKEAWAY: Receiving the COVID-19 vaccine during the third trimester of pregnancy was not associated with adverse maternal outcomes and was associated with a decreased risk for neonatal outcomes.

STUDY DESIGN: Multicenter, retrospective, computerized cohort database study

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Current evidence states that COVID-19 infections are more severe in pregnant patients compared to their non-pregnant counterparts. Despite this risk, pregnant women were not included in the initial COVID-19 vaccine trials. However, the American College of Obstetrics and Gynecologists (ACOG) and the Society of Maternal-Fetal Medicine (SMFM) recommended that COVID-19 vaccines should be given to pregnant patients. This study aimed to evaluate the impact of vaccination during pregnancy on adverse maternal and neonatal outcomes.

PATIENTS: Women who gave birth at >24 weeks of gestation

INTERVENTION: COVID-19 vaccine

CONTROL: No vaccine

PRIMARY OUTCOME: Composite adverse maternal outcome

Secondary Outcome: Vaccination rate during the third trimester, composite adverse neonatal outcomes

METHODS (BRIEF DESCRIPTION):

- A database study was conducted in two university-affiliated medical centers in Jerusalem, Israel.
- Labor and delivery data were extracted from the medical record database (National Health Plan).
- The study population included all women ≥18 years old, with no documented previous positive COVID-19 PCR test, who delivered >24 weeks gestational age between January 2021 and April 2021.
- Women with current or previous COVID-19 disease were excluded from both study groups.
- The exposure measure of the study was two doses of the Pfizer-BioNTech COVID-19 vaccine during the third trimester (>24 weeks gestation).
- The composite adverse maternal outcome was defined by one or more of the following:
  - Chorioamnionitis, postpartum hemorrhage (>1000 mL blood loss and/or hemoglobin drop of >3 g/dl), endometritis, blood transfusion, a cesarean delivery, intensive care unit (ICU) admission, maternal hospital length of stay >5 days for vaginal delivery and >7 days for cesarean delivery
- The compositive adverse neonatal outcome was defined by one or more of the following:
  - Intrauterine fetal death, Apgar score of <7 at one minute, Apgar score of <7 at five minutes, admission to neonatal intensive care unit (NICU), neonatal asphyxia, intracranial hemorrhage, meconium aspiration, hyperbilirubinemia, neonatal seizures, neonatal hypoglycemia, neonatal sepsis, use of mechanical ventilation
- Categorical variables were presented as percentages and compared using chi-square or Fisher's exact test.
  - Continuous variables with a normal distribution were presented as mean and standard deviation.
  - Comparisons were made using Student's t-test and Mann-Whitney U-test for normally and non-normally distributed data.
  - Maternal and fetal outcomes between the two groups were then compared with univariate analysis and multivariate logistical regression.

INTERVENTION (# IN THE GROUP): 712

COMPARISON (# IN THE GROUP): 1,063

FOLLOW-UP PERIOD: Not available

RESULTS:

Primary Outcome –

- COVID-19 vaccination during pregnancy was not associated with the maternal composite adverse outcome compared to no vaccination (adjusted odds ratio [aOR] 0.8; 95% CI, 0.61–1.03).

Secondary Outcome –

- COVID-19 vaccination during pregnancy was associated with a reduction in the neonatal composite adverse outcomes compared to no vaccination (aOR 0.5; 95% CI, 0.36–0.74).
- 717 women (40%) received either one or two doses of the COVID-19 vaccine, whereas 1,063 women did not.

LIMITATIONS:

- The study design raises the possibility of biases inherent to such investigations.
- There were possible unknown factors present (such as socioeconomic status) that may impact the findings.
- For the duration of the study, the hospital centers did not screen all women who gave birth, so the study may have included asymptomatic COVID-19 carriers.
- There is no information on the interval between vaccination doses and delivery, so the interval might have been too short to reveal adverse outcomes.
- The inclusion criteria significant for 3rd-trimester vaccinations introduce selection bias.
- The current investigation may have lacked sufficient statistical power to detect small but relevant differences in outcome.

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Preventing Teen Substance Use: Are Family Check-Ups the Right Place?

Substance Use Screening and Prevention for Adolescents in Pediatric Primary Care: A Randomized Clinical Trial Using the Family Check-Up

Galán CA, Shaw DS, O'Rourke F, et al. Substance Use Screening and Prevention for Adolescents in Pediatric Primary Care: A Randomized Clinical Trial using the Family Check-Up. *Res Child Adolesc Psychopathol*. 2023;51(2):151-163. doi:10.1007/s10802-022-00978-2

KEY TAKEAWAY: Two years of intensive substance use (SU) intervention in the primary care setting is not associated with a significant risk reduction among typical young adolescents; however, youth with a higher risk of SU at baseline show a reduced risk of initiating a new substance.

STUDY DESIGN: Single-site, randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Adolescent SU, which is known to increase the risk of substance use disorder (SUD) later in life, continues to be highly prevalent despite many years of public health prevention efforts. Well-child checkups (WCCs) targeting young adolescents in primary care present a different prevention opportunity using a family-based intervention, a family check-up (FCU), that may avert harms associated with SUD in later adolescence.

PATIENTS: Youth 10–13 years old

INTERVENTION: FCU

CONTROL: Usual care

PRIMARY OUTCOME: Risk of SU at end of study

METHODS (BRIEF DESCRIPTION):

- The sample was recruited from urban primary care clinics in Pittsburgh, PA.
- Demographics:
  - Parents were primarily female (96%) and Black (82%) with a mean age of 36 years old.
  - Youths were majority female (52%) and Black (75%) with a mean age of 12 years old.
  - Percent who used substances before the study:
    - Zero substances: 68%
    - One substance: 19%
    - Two substances: 7.2%
- Inclusion criteria:
  - Screening measure scores in the elevated risk range
  - Children 10–13 years old
  - Receiving need-based Medicaid or family income ≤150% of the poverty line
- Exclusion criteria:
  - Non-English speakers
  - Moderate-to-severe intellectual disability
- Participants were randomly assigned into three subgroups:
  - Two years of FCU exposure
  - One year of control waitlist then one year followed by FCU
  - True controls
- The FCU consisted of two or more family-based intervention sessions that addressed early adolescent SU risk factors. These sessions included a comprehensive assessment, a feedback session, and optional follow-up treatment sessions involving:
  - Positive behavior support
  - Limit setting and monitoring
  - Relationship quality
  - Parental mental health
  - Housing
- Screening measures included:
  - The Assessment of Liability and Exposure to Substance Use and Antisocial Behavior (ALEXSA). This is a computerized illustration-based self-report measure that identifies risky behavior among youths.
  - The Youth Risk Index (YRI) is a self-report measure similar to ALEXSA and assesses the tendency for SU.
  - The Transmission Liability Index (TLI) is a test that measures a child's heritable risk for SU disorder.

INTERVENTION (# IN THE GROUP): 123

COMPARISON (# IN THE GROUP):

- Year 1 control waitlist: 127
- Year 2 control waitlist: 60
- True control: 51 (combined with control waitlist)

FOLLOW-UP PERIOD: 24 months

RESULTS:

Primary Outcome –

- FCU did not reduce SU compared to usual care among patients with zero or one substance used at baseline (risk ratio [RR] 1.1; 95% CI, 0.95–1.2).
- FCU reduced the risk of new substance initiation by 11% among youth who used more substances at baseline (RR 0.89; 95% CI, 0.83–0.96).
- FCU reduced the frequency of alcohol or tobacco use by 29% among youth who used a greater number of substances at baseline (RR 0.71; 95% CI, 0.56–0.92).
- FCU did not affect the frequency of alcohol or tobacco use in the aggregate.
    - Alcohol (RR 0.73; 95% CI, 0.50–1.1)
    - Tobacco use (RR 0.79; 95% CI, 0.39–1.6)

LIMITATIONS:

- The study was limited to one urban setting.
- The study was limited to very low socioeconomic status (SES) families.
- The study was limited by a two-year follow-up.
- The study used a non-traditional randomization, which included an intervention, control waitlist, and pure control.
- The intervention was very labor intensive, and may not be easily replicated in practice.

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The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the US Army Medical Department, the Army at large, or the Department of Defense.

Head Tremors: Another Use for Botulinum Toxin Injections?

Trial of Botulinum Toxin for Isolated or Essential Head Tremor

Marques A, Pereira B, Simonetta-Moreau M, et al. Trial of Botulinum Toxin for Isolated or Essential Head Tremor. *N Engl J Med*. 2023;389(19):1753-1765. Doi:10.1056/NEJMoa2304192

KEY TAKEAWAY: Botulinum toxin A injection is more effective than placebo in improving isolated or essential head tremors at 18 weeks.

STUDY DESIGN: Multi-site, double-blind, randomized control trial (RCT)

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: Essential tremors affect 4–5% of individuals >65 years old and approximately 1% of the general population. While local injections of botulinum toxin type A are successful in treating essential limb tremors, the efficacy and safety have not been similarly validated for head tremors. This study aimed to evaluate the efficacy of local injections in head tremors.

PATIENTS: Patients with head tremors

INTERVENTION: Botulinum toxin type A injection

CONTROL: Placebo injection

PRIMARY OUTCOME: Improvement of tremor at 18 weeks

Secondary Outcome: Improvement of tremor at six, 12, and 24 weeks, subjective functional effects, social embarrassment effects, severity of head tremors, adverse events

METHODS (BRIEF DESCRIPTION):

- The trial was performed at 17 French hospitals, involving patients recruited through neurologists during clinical follow-ups within movement disorder departments.
- Adults with essential or isolated head tremors were included in the study if the tremor severity was deemed severe enough by having a score of ≥2 on the Fahn-Tolosa-Marin Tremor Rating Scale. The scale ranges from 0–4 with higher scores indicating higher amplitude of tremor.
- Participants had a mean age of 65 years old, 80% were women, and 93% were White.
- Patients with dystonic head tremors, Parkinson's disease, cerebellar syndromes, or botulinum toxin injection within four months were excluded from the study.
- Patients were randomized 1:1 to receive either botulinum toxin injection or placebo injection on day zero and week 12.
  - Day zero botulinum toxin dose was 75 international units (IU) and week 12 was either 75 IU or increased to 100 IU if the initial injection was ineffective at week six.
  - 0.9% sterile saline was used as the placebo.
- Injection into the splenius capitis muscle was done under electromyographic guidance in combination with palpation.
- Patients were able to continue oral treatments and/or deep-brain stimulation if stable and no changes were made during the duration of the trial.
- Improvement of the tremor was defined as an improvement of ≥2 points on the Clinical Global Impression of Change (CGI) scale at week 18.
  - The CGI scale ranges from –3 ("very much worse") to three ("very much improved") based on the patient's assessment of the degree of change.
- Secondary outcomes included the improvement of tremors, subjective functional effects, social embarrassment effects, severity of head tremors, and adverse events.
  - Improvement of tremor was defined as an improvement of ≥2 points on the CHI scale at weeks six, 12, and 24.
  - Subjective functional effects were measured using the Quality of Life in Essential Tremor Questionnaire (QUEST) that covers 30 items. Scores range from 0–120 with lower scores indicating less subjective functional effects.
  - Social embarrassment effects were measured using the Essential Tremor Embarrassment Assessment (ETEA) consisting of a 14-item questionnaire. Scores range from 0–70 with lower scores indicating less social embarrassment effects.

        - The overall ETEA score combined two parts. Part A scored the items as zero (disagree with the item) or one (agree with the item). Part B was scored on a more nuanced six-point scale.
    - Both QUEST and ETEA were expressed as a percentage of the max score (0–100%) with a higher percentage signifying greater impairment.
    - The severity of head tremors was measured using the Tremor Rating Scale (TRS). Scores range from 0–152, with a higher score indicating greater impairment.

INTERVENTION (# IN THE GROUP): 62

COMPARISON (# IN THE GROUP): 55

FOLLOW-UP PERIOD: 24 weeks

RESULTS:

Primary Outcome –

- Botulinum toxin significantly improved head tremors compared to placebo injection at week 18 (relative risk [RR] 3.4; 95% CI, 1.4–8.4).

Secondary Outcome –

- Botulinum toxin significantly improved head tremors more than placebo at:
    - Week six (RR 6.0; 95% CI, 2.2–16)
    - Week 12 (RR 3.2; 95% CI, 1.3–8.0)
- There was no significant difference in head tremors with botulinum toxin compared to placebo at week 24.
- Botulinum toxin decreased the subjective functional effects of head tremors compared to placebo at week 18 (RR –0.31; 95% CI, –0.62 to –0.01).
- Botulinum toxin decreased the social embarrassment effects of head tremors compared to placebo at week 18.
    - Part A of ETEA scale (RR –0.43; 95% CI, –0.76 to –0.10)
    - Part B of ETEA scale (RR –0.48; 95% CI, –0.80 to –0.16)
- Botulinum toxin decreased the severity of head tremors at week 18 (RR –0.16; 95% CI, –0.46 to 0.15).
- The botulinum toxin group was significantly more likely to experience any adverse event compared to placebo (47% vs 16%, respectively; $p<.001$).
    - The most common adverse events included headaches or neck pain (34%), posterior cervical weakness (15%), dysphagia (16%), cervical stiffness (10%), and pain at the injection site (8%).

LIMITATIONS:

- This study had biased analysis due to a high attrition rate in the intervention group.
- Limited generalizability due to the population of patients studied.

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Breathe Easy: Enhanced Respiratory Outcomes in Asthma and COPD Patients Under Pulmonologist Care

Early Diagnosis and Treatment of COPD and Asthma – A Randomized, Controlled Trial

Aaron SD, Vandemheen KL, Whitmore GA, et al. Early Diagnosis and Treatment of COPD and Asthma - A Randomized, Controlled Trial. *N Engl J Med*. 2024;390(22):2061-2073. doi:10.1056/NEJMoa2401389

KEY TAKEAWAY: Guideline-based treatment provided by a pulmonologist and asthma or chronic obstructive pulmonary disease (COPD) educator lowers the rate of healthcare utilization for respiratory illnesses but has no effect on hospitalization, emergency department (ED) visits, or specialty visits among patients newly diagnosed with asthma or COPD, compared to standard care from a primary care physician (PCP).

STUDY DESIGN: Randomized controlled trial

LEVEL OF EVIDENCE: STEP 2

BRIEF BACKGROUND INFORMATION: COPD and asthma, though highly prevalent, remain undiagnosed in many patients. Early detection and treatment can allow for the prevention of acute exacerbations, decreased healthcare utilization, and improved health outcomes. It is not clear if there is a difference in outcomes between patients who are diagnosed and treated by specialized teams including pulmonologists and COPD educators compared to those treated by a PCP.

PATIENTS: Adults with respiratory symptoms and a newly confirmed diagnosis of asthma or COPD on spirometry

INTERVENTION: Pulmonologist-directed treatment + asthma and COPD educator

CONTROL: Primary care-directed treatment

PRIMARY OUTCOME: Frequency of healthcare utilization for respiratory-related illness, hospitalization, ED visits, specialty visits over one year

Secondary Outcome: Repeat spirometry at six and 12 months, disease-specific quality of life, the burden of respiratory symptoms on daily activities, overall quality of life

METHODS (BRIEF DESCRIPTION):

- Recruitment occurred via a telephone survey of randomly selected healthy adults >18 years old with either a landline or cell phone.
- Patients were included if they met the following eligibility criteria:
  - Lived within 90 minutes of trial sites
  - Scored >6 on the Asthma Screening Questionnaire (ASQ). Scores range from 0–20, with a higher score indicating worse respiratory symptoms.
  - Scored >20 on the COPD Diagnostic Questionnaire. Scores range from 0–38, with a higher score indicating greater COPD risk.
- Patients who screened positive based on the questionnaire underwent spirometry to confirm asthma or COPD diagnosis; only those with confirmed asthma or COPD were included in the trial.
- Exclusion criteria included patients with previous diagnoses of respiratory disease by a physician, current use of inhalers except for short-acting beta-agonists, and contraindications to the use of spirometry.
- Patients had a mean age of 63 years old, mostly male (64% and 58% in intervention and control groups, respectively).
- Spirometry was used to confirm diagnosis of asthma or COPD (pre- and post-bronchodilator)
  - Diagnosis of asthma: At least 12% and 200 ml increase in forced expiratory volume in one second (FEV_1) after 400 ng of salbutamol
  - Diagnosis of COPD: < 5^{th} percentile for FEV1/FVC following bronchodilator use
  - If patients met the criteria for both, were considered to have COPD.
  - Spirometry results were sent to PCP regardless of group assignment.
- Randomization was computer-generated.
- Patients in the intervention group received treatment from a pulmonologist as well as an asthma-COPD educator to provide care per GINA 2017 guidelines.
  - Scheduled visits occurred on the first day of the trial, with the second visit four months later.
- Patients in the control group received usual care from a PCP who was given GINA guidelines as well.
  - The control group did not have scheduled visits or access to an asthma-COPD educator.

- The annual rate of respiratory-related visits (any type of visit, any kind of provider, or health settings) was monitored using monthly phone calls to patients in both groups.
- Repeat spirometry was performed at six and 12 months for both groups.
- Disease-specific quality of life was measured using the St George Respiratory Questionnaire (SGRQ). Scores range from 0–100, with lower scores indicating better health status.
- Respiratory symptoms burden on activities of daily life was measured using the COPD Assessment Test (CAT). Scores range from 0–40, with lower scores indicating better health status.

INTERVENTION (# IN THE GROUP): 253

COMPARISON (# IN THE GROUP): 253

FOLLOW-UP PERIOD: 12 months

RESULTS:

Primary Outcome –

- Care from a pulmonologist and COPD educator reduced the annualized rate of healthcare utilization for respiratory illnesses compared to PCP-only care (incidence rate ratio [IRR] 0.48; 95% CI, 0.36–0.63).
- The care provided by a pulmonologist and COPD caregiver compared to PCP-only care was similar for the following:
  - Hospitalization rate (IRR 0.71; 95% CI, 0.17–3.0)
  - ED visit rate (IRR 0.92; 95% CI, 0.46–1.9)
  - Specialist visit rate (IRR 0.89; 95% CI, 0.45–1.8)

Secondary Outcome –

- Care from a pulmonologist and COPD educator improved disease-specific quality of life compared to PCP-only care (SGRQ mean difference [MD] –3.5; 95% CI, –6.0 to –0.9).
- Care from a pulmonologist and COPD educator improved COPD symptoms compared to PCP-only care (CAT score MD –1.3; 95% CI, –2.4 to –0.1).
- Care from a pulmonologist and COPD educator increased FEV_1 more than PCP-only care (difference 94 mL; 95% CI, 50–138).

LIMITATIONS:

- There was insufficient power to detect differences in subgroups or secondary outcomes.
- The study was restricted to a Canadian healthcare system, so findings may not be generalizable to other populations.
- Participants needed to have cell phones or landlines.
- Older people were more willing to volunteer.
- Pulmonologists and PCPs were not monitored for the use of guideline-directed care.
- Intervention and control groups differed in multiple ways other than pulmonologist care vs PCP care, making it difficult to draw causal inferences about what aspect of the intervention was most helpful.

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How Safe and Efficient Are MASPORT and DYSPORT at Ironing Away Your Wrinkles?

A Phase III Clinical Study of the Efficacy and Safety of Botulinum Toxin Type A (MASPORT) with DYSPORT for the Treatment of Glabellar Lines

Hedayat K, Ehsani AH. A Phase III Clinical Study of the Efficacy and Safety of Botulinum Toxin Type A (MASPORT) with DYSPORT for the Treatment of Glabellar Lines. *Aesthetic Plast Surg*. 2024;48(3):324-332. doi:10.1007/s00266-023-03766-5

KEY TAKEAWAY: Abobotulinum toxin A (MASPORT) is equally safe and effective as a commercial product (DYSPORT) for the treatment of glabellar lines with a dose of 50 units, with effects up to 120 days.

STUDY DESIGN: Double-blinded, randomized comparative phase III clinical trial

LEVEL OF EVIDENCE: STEP 3 (downgraded due to small effect size)

BRIEF BACKGROUND INFORMATION: There is demand for safe and effective anti-aging treatments due to increased lifespan and society's proclivity for youthful appearance. Botulinum toxin type A is widely utilized to treat facial wrinkles. No large studies have compared MASPORT with DYSPORT in their effectiveness at reducing glabellar lines.

PATIENTS: Adults

INTERVENTION: MASPORT

CONTROL: DYSPORT

PRIMARY OUTCOME: Glabellar line improvement

Secondary Outcome: Adverse side effects

METHODS (BRIEF DESCRIPTION):

- The Iranian Registry of Clinical Trials reviewed and approved the study protocols by the Ethics Committee of Tehran University of Medical Science.
- Included participants were adults 18–60 years old (81% female) with moderate to severe glabellar lines.
- Excluded were those with medical conditions exacerbated by botulinum toxin, had allergies to ingredients, had botulinum toxin injection in the past six months, or were pregnant or lactating.
- On day zero, participants received a total dose of 50 units of MASPORT or DYSPORT. Both were evenly distributed into five injections of 0.05 mL utilizing a 27 gauge needle in the midline procerus, inferomedial, and superior middle aspect of the corrugator muscle of the glabellar area.
- The efficacy endpoints utilized investigator evaluations and patient-reported outcomes at 14, 30, 60, 90, and 120 days.
- Investigators completed a four-point glabellar line assessment at frown/rest on a scale of 0–3, with zero indicating no glabellar lines and three indicating severe glabellar bulging with deep frown lines bulging at rest.
- The participant-reported outcomes included improvement as either complete, significant, partial, or none.
- Investigators evaluated possible side effects including headache, drowsiness, drooping eyelids, rhinorrhea, headache associated with rhinorrhea, and headache associated with drooping eyelids.

INTERVENTION (# IN THE GROUP): 127

COMPARISON (# IN THE GROUP): 135

FOLLOW-UP PERIOD: 120 days

RESULTS:

Primary Outcome –

- MASPORT was non-inferior to DYSPORT in terms of glabellar line improvement based on the following measures:
  - There was no difference in severity at max frown at 120 days (N=209; 90% vs 86%, respectively; *P*>.99).
  - There was no difference in severity at rest at 120 days (N=209; 66% vs 69%, respectively; *P*>.99).
  - There was no difference in the subject's global assessment of change at 120 days (N=209; 80% vs 82%, respectively; *P*=.97).

Secondary Outcome –

- There was no difference in reported adverse side effects between MASPORT and DYSPORT (N=209; 18% vs 17%, respectively; *P*=.91).

LIMITATIONS:

- The study included short follow-up periods precluding researchers from assessing the full effect of the BoNT-A MASPORT.
- The study relied on patient-reported outcomes which are subjective and less reliable.

- The study had a loss of follow-up of 53 patients in total.
- This study had limited generalizability due to ethnicity (only Caucasian Iranians) and a small sample size of 262 subjects.

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