# Post op care and topical therapies

Rodney J. Schlosser, MD

Professor and Director of Rhinology
Department of Otolaryngology - HNS
Medical University of South Carolina
Charleston, SC

# Post operative care EBRR

| Treatment | Grade of EBM | Benefit v harm | Recommend | Protocol |
|---|---|---|---|---|
| Saline irrigation | B | Benefit | For | Normal saline within 24-48h |
| Debridement | B | Benefit | For | Sinus debridements post ESS |
| Systemic steroid | N/A | Equal | Option | Single 1b study |
| Abx | B | Equal | Option | Short term benefit |
| INCSpray | A | Benefit | For | Start post ESS |
| Off label topical steroid | D | Equal | Option | Single 3b study, 1b pend |
| Drug eluting spacer/stent | B | Equal | Option | Two level 1b's |

Rudmik L, IFAR 2011

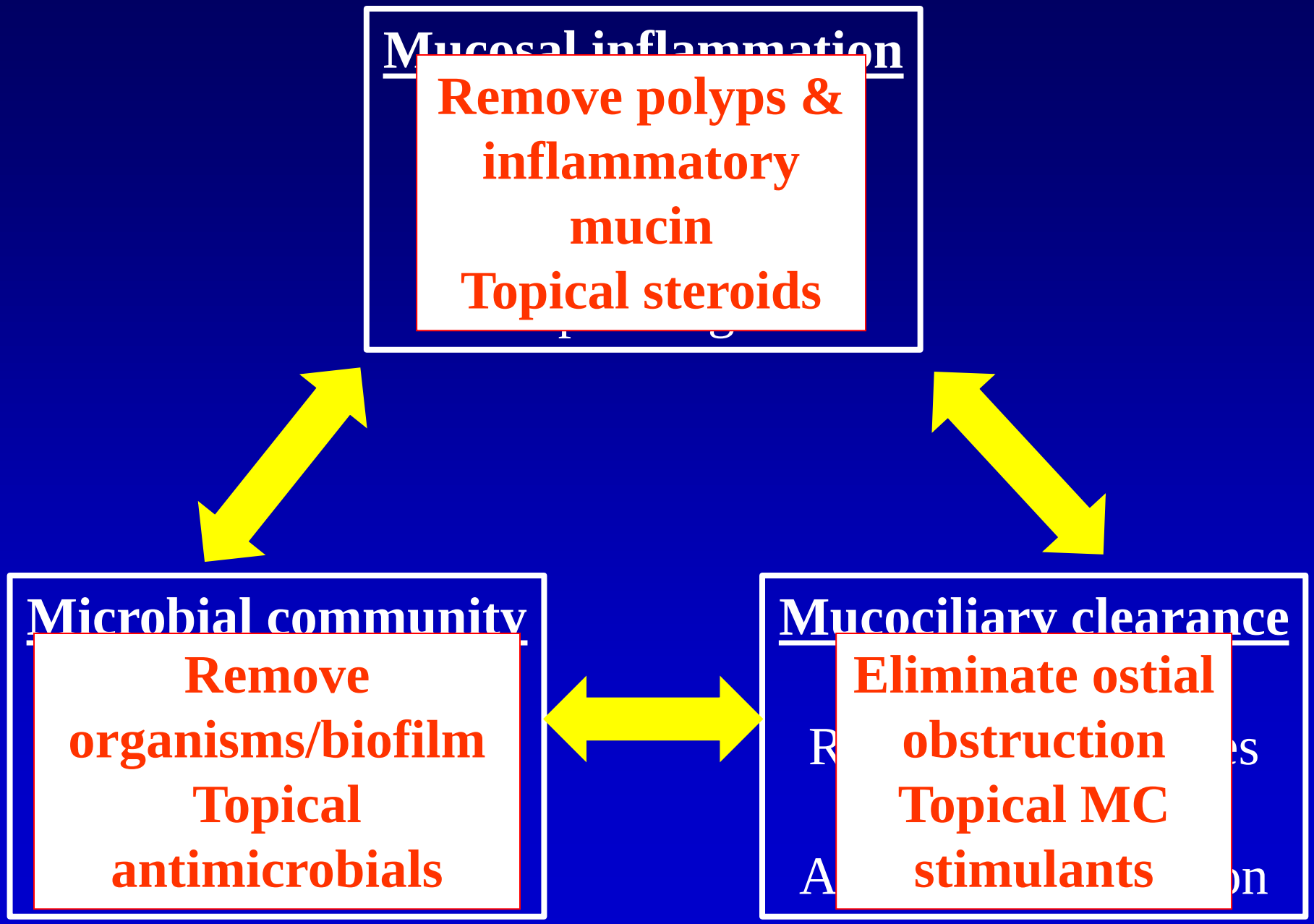
| Middle meatal dressings | | |
|---|---|---|
| **Product** | **Material** | **Improvement v no drsg** |
| Propel implant | Lactide, glycolide copolymers w MMF | |
| Merocel | Polyvinyl alcohol | Synechiae |
| Salman stent | Silicone | |
| Gelfilm/foam | Gelaton (collagen) | |
| Floseal | Gelatin/thrombin | Hemostasis/pain |
| Surgiflo | Gelatin (collagen) | |
| Surgicel | Oxidized cellulose | |
| Merogel | Hyaluronic acid | |
| Sepragel/pack | HA/CMC | Synechiae, pain, congestion |
| Sinufoam | CMC | |
| MPH | Microporous polysacchardie | Hemostasis |
| Chitosan gel | Chitosan/dextran | Synechiae, hemostasis |
| Nasopore | Polyurethane foam | |
| Quixil | Thrombin/fibrinogen | |

# Postop antibiotics

- Cefuroxime x 2 days: no benefit
- Amox/clav x 2 wks: improved endoscopy and sx

Rudmik L, IFAR 2011

# CRS & changing role of surgery?



# Topical therapies

- Delivery to anatomic site (target sinus)
- The proper active agent
- Impact upon lower airway

# Bewildering variety?

# Prescription versions

# What we don't want to become

# Topical drug considerations
## Macro factors

- Surgical state
- Delivery device & volume
- Patient position

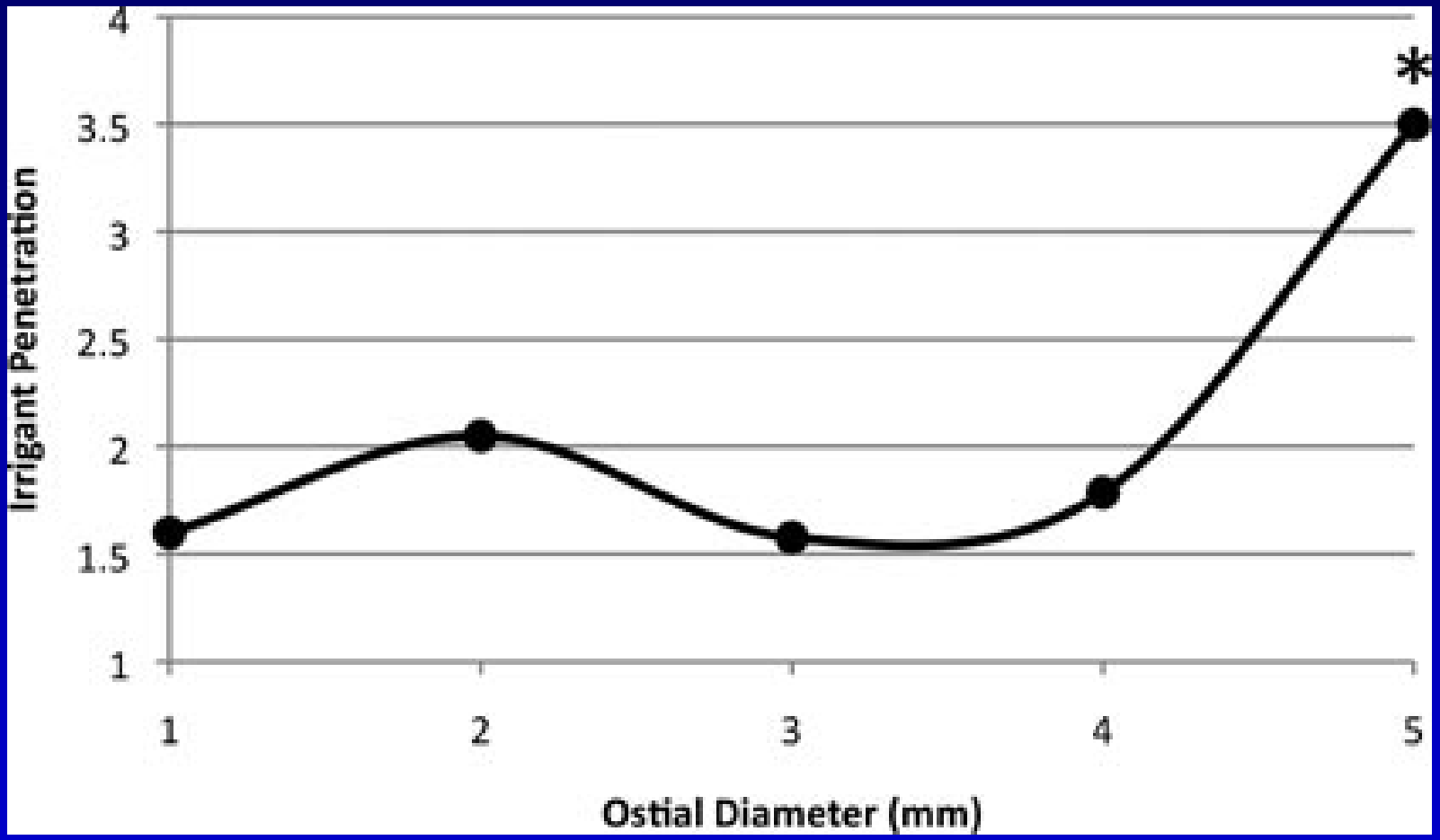
# Impact of surgery

| Surgical State | Findings |
|---|---|
| Unoperated | No consistent delivery regardless of device |
| Balloon | Sphenoid ↑<br>Frontal —<br>Maxillary ↓ |
| ESS | Delivery increases especially with large volume |
| Endoscopic Lothrop or medial maxillectomy | Possible benefit |

- Cadaver (n=5) and human studies (n=3)
- Conclusion: ESS optimal, critical os size 4-5 mm

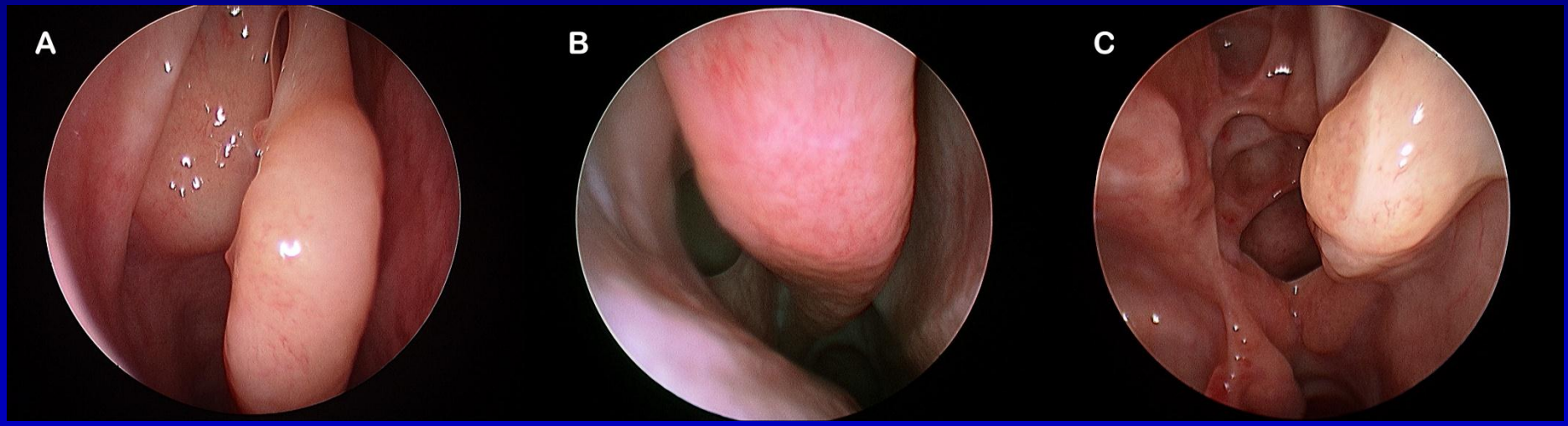
Thomas III, WT et al, IFAR 2013 (in press)

# Critical os size




Brenner etal, IFAR 2012

# What type of surgery is needed for postop topical therapies?

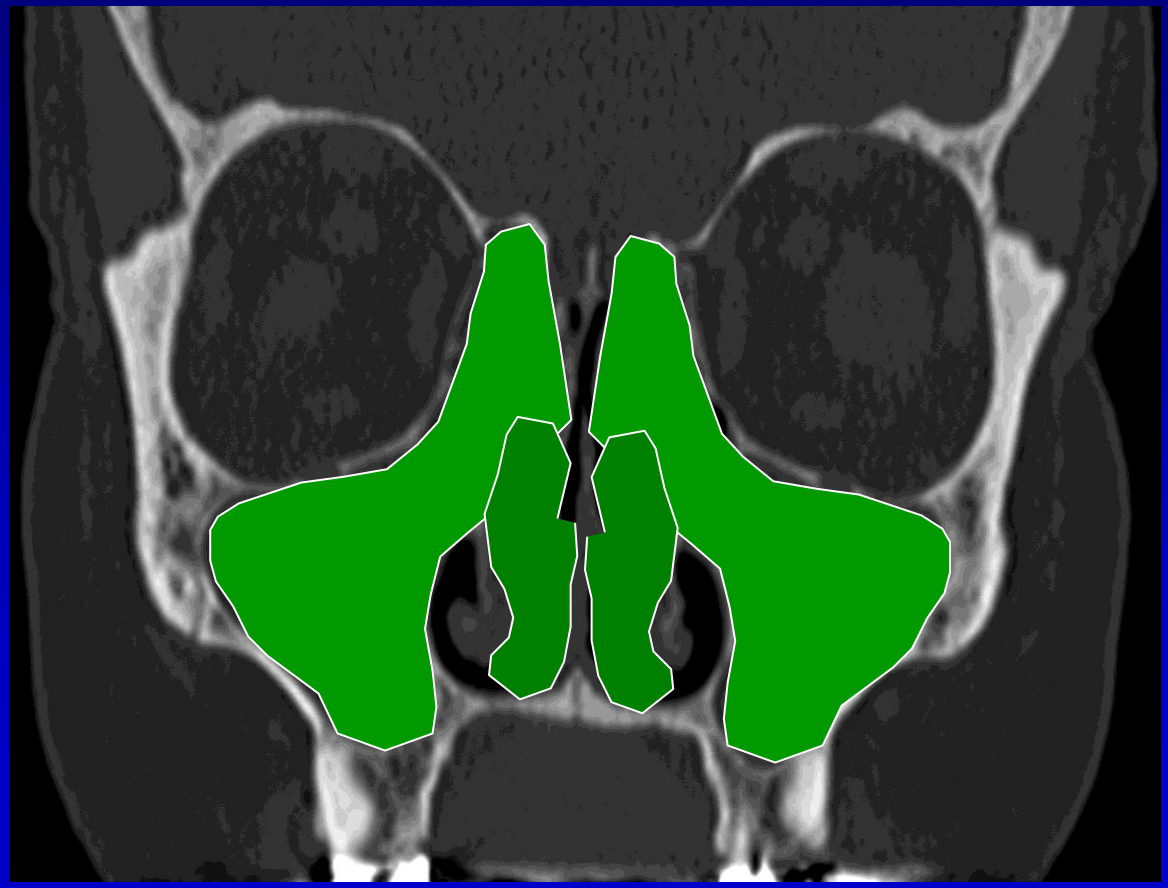



Balloon MIST FESS

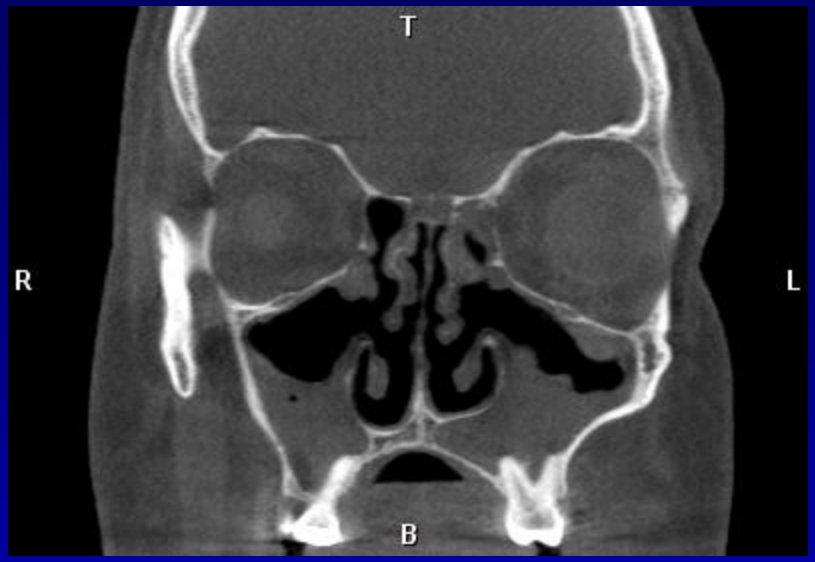
# Ventilation ≠ access for topical treatments

Prior to successful ESS,

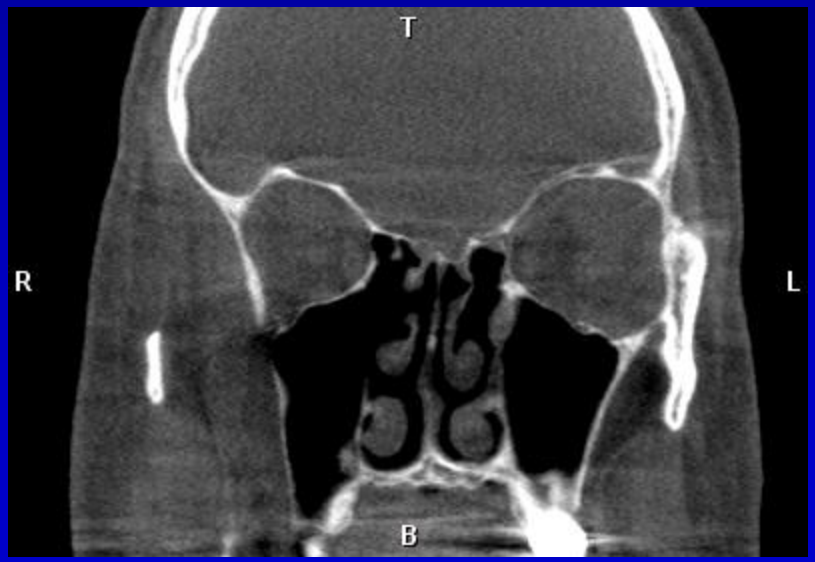
topical therapies are ONLY nasal cavity treatments

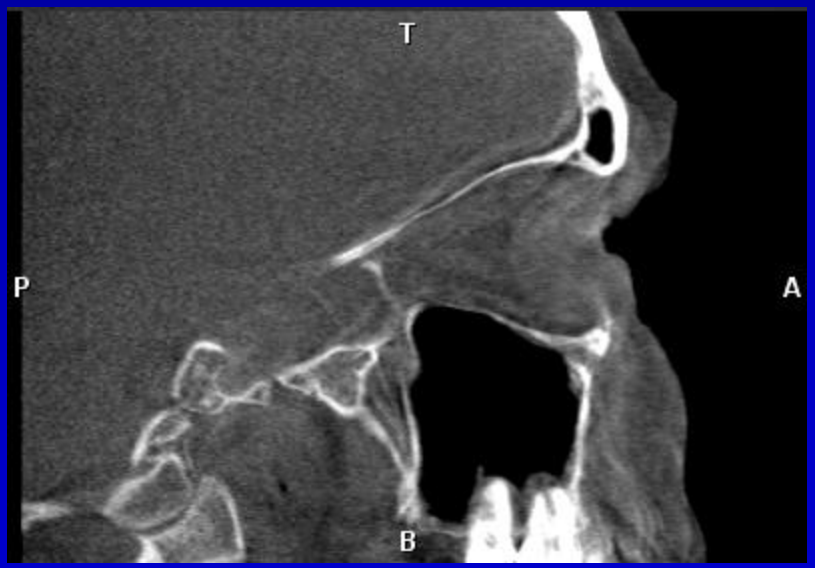


# Access for topical treatments








Harvey RJ, Schlosser RJ. J OHNS, 2009

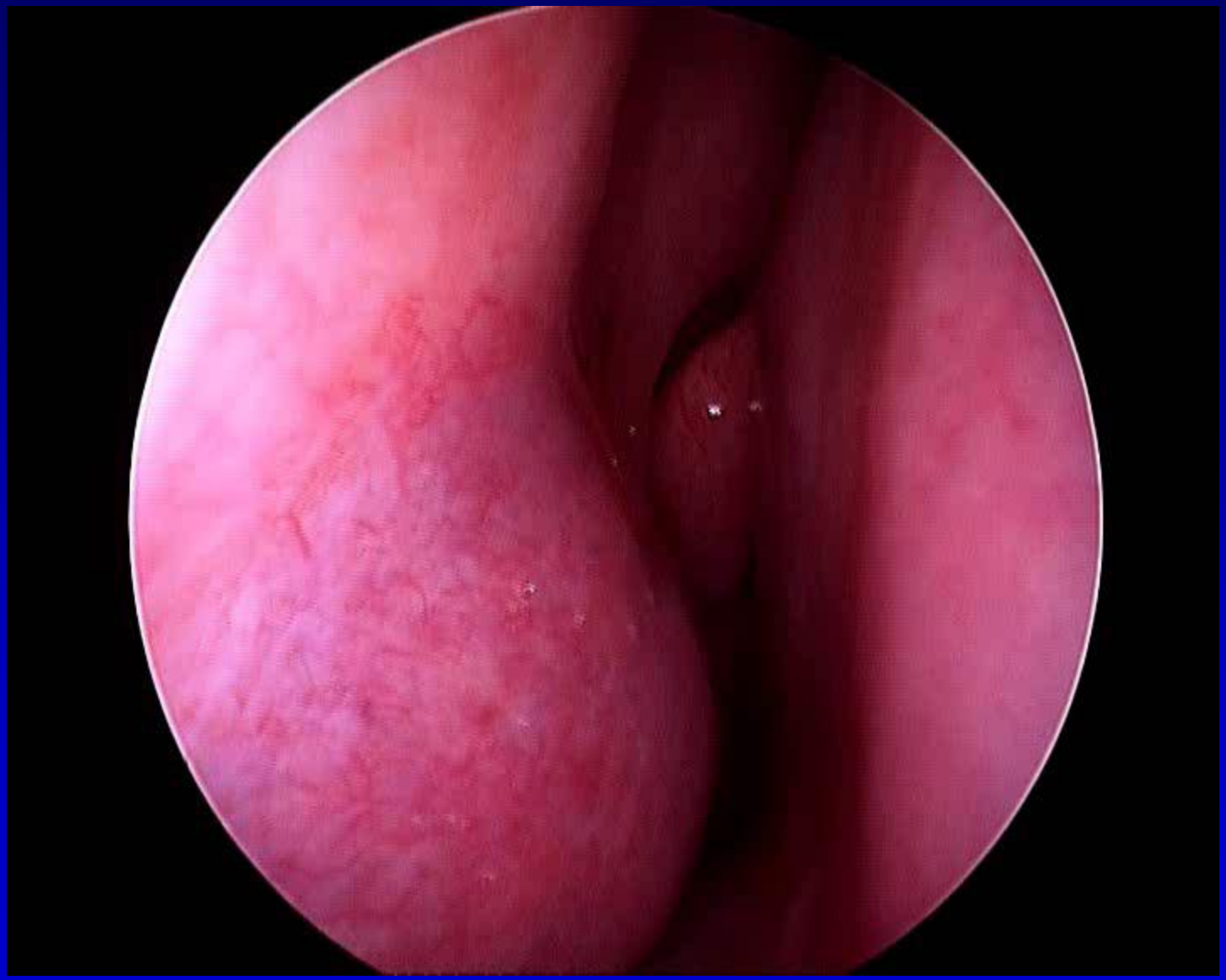
# Impact of device

| Device | Findings |
|---|---|
| Spray/Drops | Little sinus distribution with either technique. Some delivery to olfactory cleft/MT that may be position dependent. |
| Atomizer/ Nebulizer | Pulsating aerosols/nebs with some *limited* distribution to sinuses |
| Squeeze bottle/ Neti Pot | Larger volumes have best distribution |

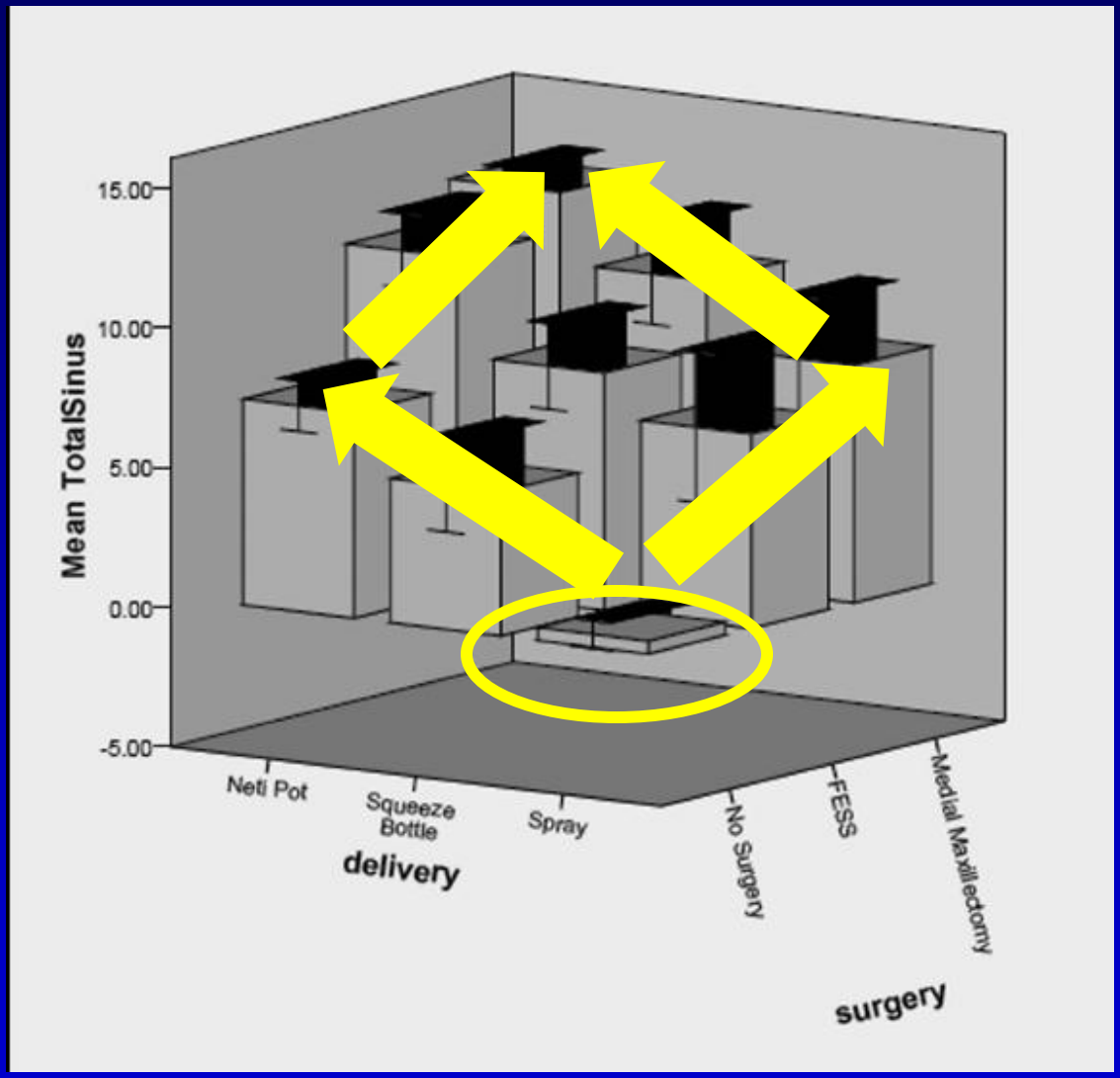
- Cadaver (n=5) and human studies (n=15)
- Recommend for: Large volume devices post ESS
- Recommend against: Low volume devices do not consistently reach sinuses

Thomas III, WT et al, IFAR 2013 (in press)

# Sprays



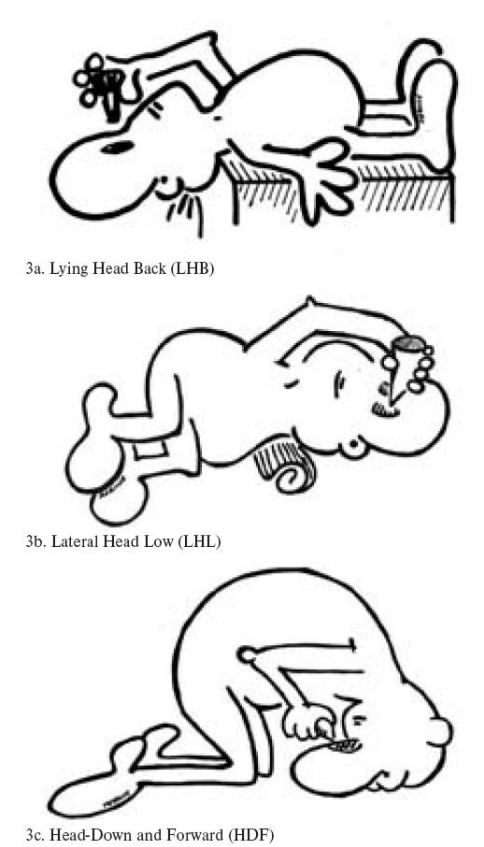
# Combined effects of surgery & volume




Harvey RJ et al, OHNS 2009

# Impact of position

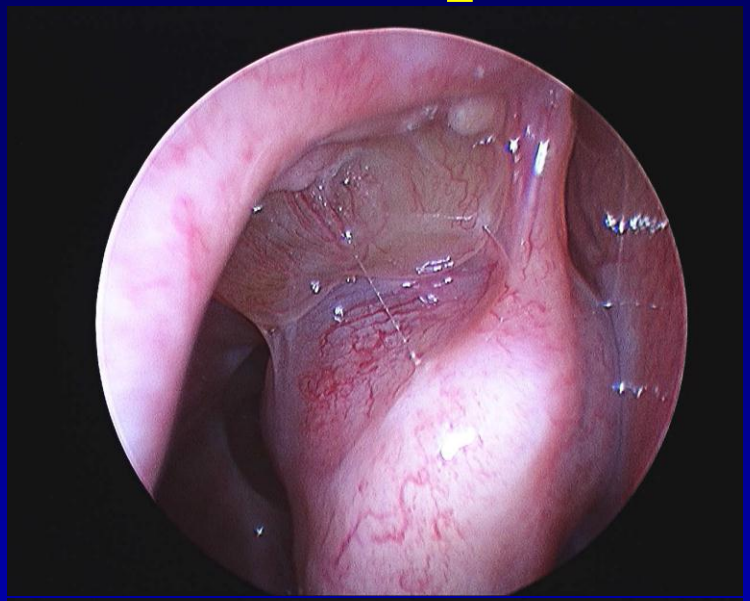
| Position | Findings |
|---|---|
| Head upright | Inferior meatus with gtt |
| LHB (Mygind) | Middle meatus |
| LHL (Ragan) | Middle meatus |
| HDF (Mecca) | Increased superior distribution (Olfactory, limited ethmoid/max) |

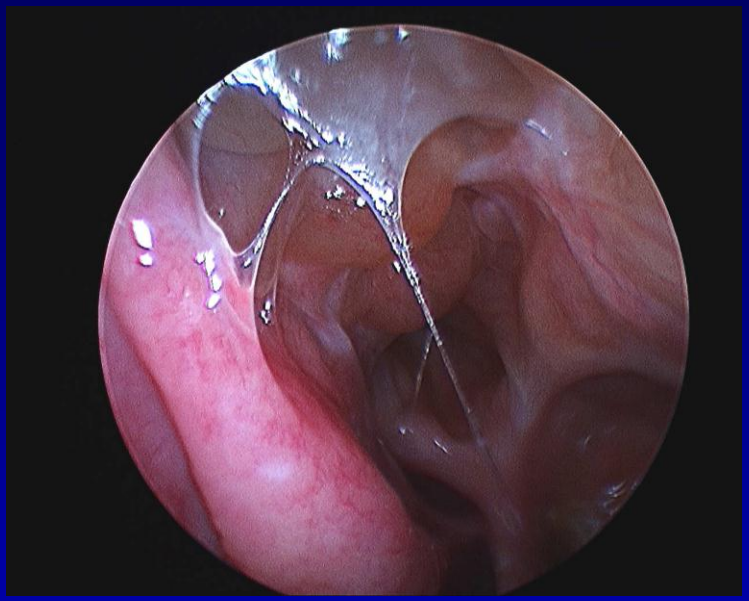


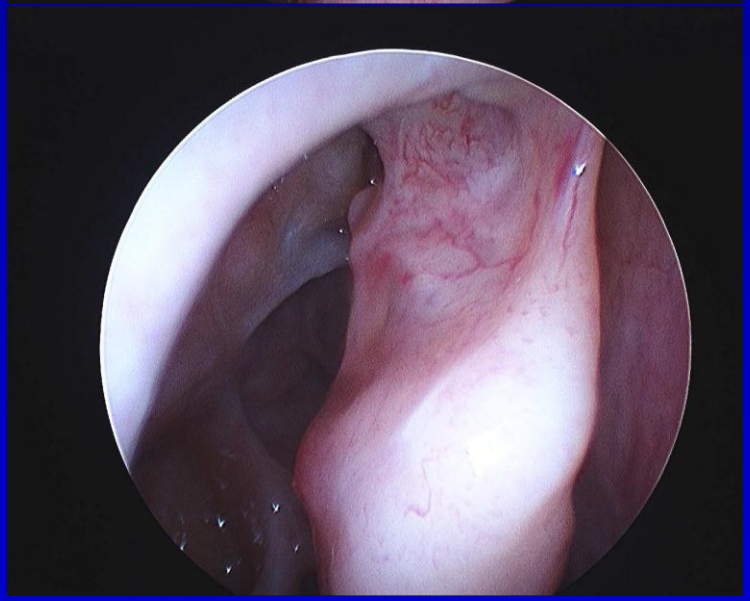

- Cadaver (n=3) & human (n=7) studies
- Recommend for: HDF with high volume devices
- Recommend for: LHB or LHL with drops and sprays

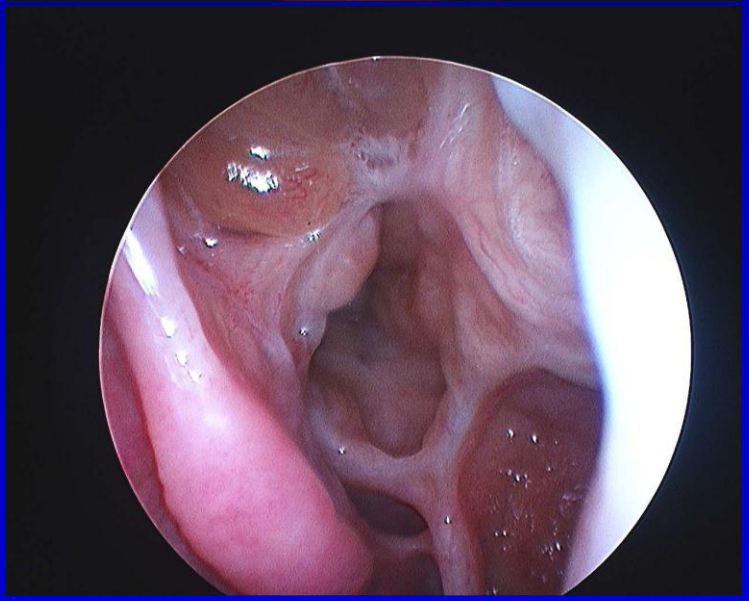
Thomas III, WT et al, IFAR 2013 (in press)

# Drops and LHB Position









# Now that we can reach the sinuses, which active agent ?

- Mechanical
  - Saline
  - Baby Shampoo

- Pharmaceutical
  - Steroids
  - Antibiotic
    - Mupirocin
    - Gentamycin / Tobramycin
    - Ampho B
  - Novel agents
    - Honey
    - Surfactants
    - Dornase Alpha

# What's the goal?

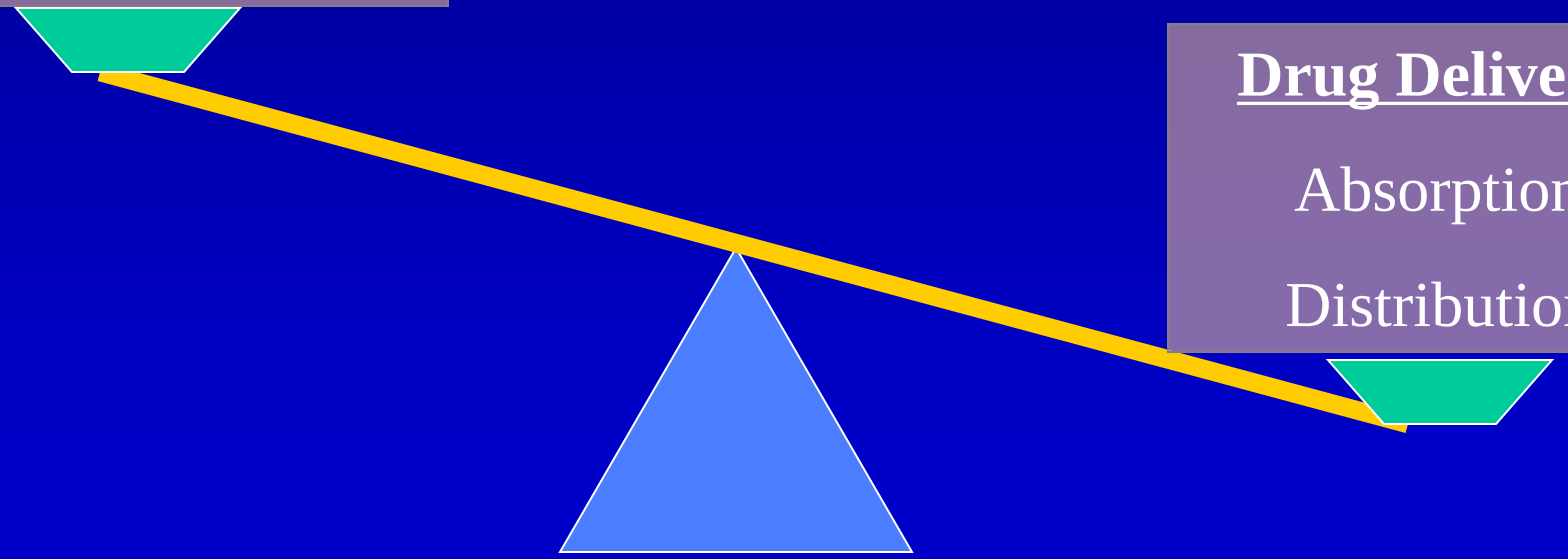
**Mechanical Effects**

MCC

Mucus rheology

Surfactants

Removal of Ag



**Drug Delivery**

Absorption

Distribution

# Summary of active agents

| Agent | Grade of evidence | Benefit vs Harm | Recommendation Level | Protocol |
|---|---|---|---|---|
| Saline | B | Benefit | Recommend | Use saline as adjunct to other topical therapies |
| Standard INCS | A | Benefit | Strong recommendation | Use in CRSsNP and CRSwNP |
| Off label steroid | C | Equal | Option | Irrigation vs drop |

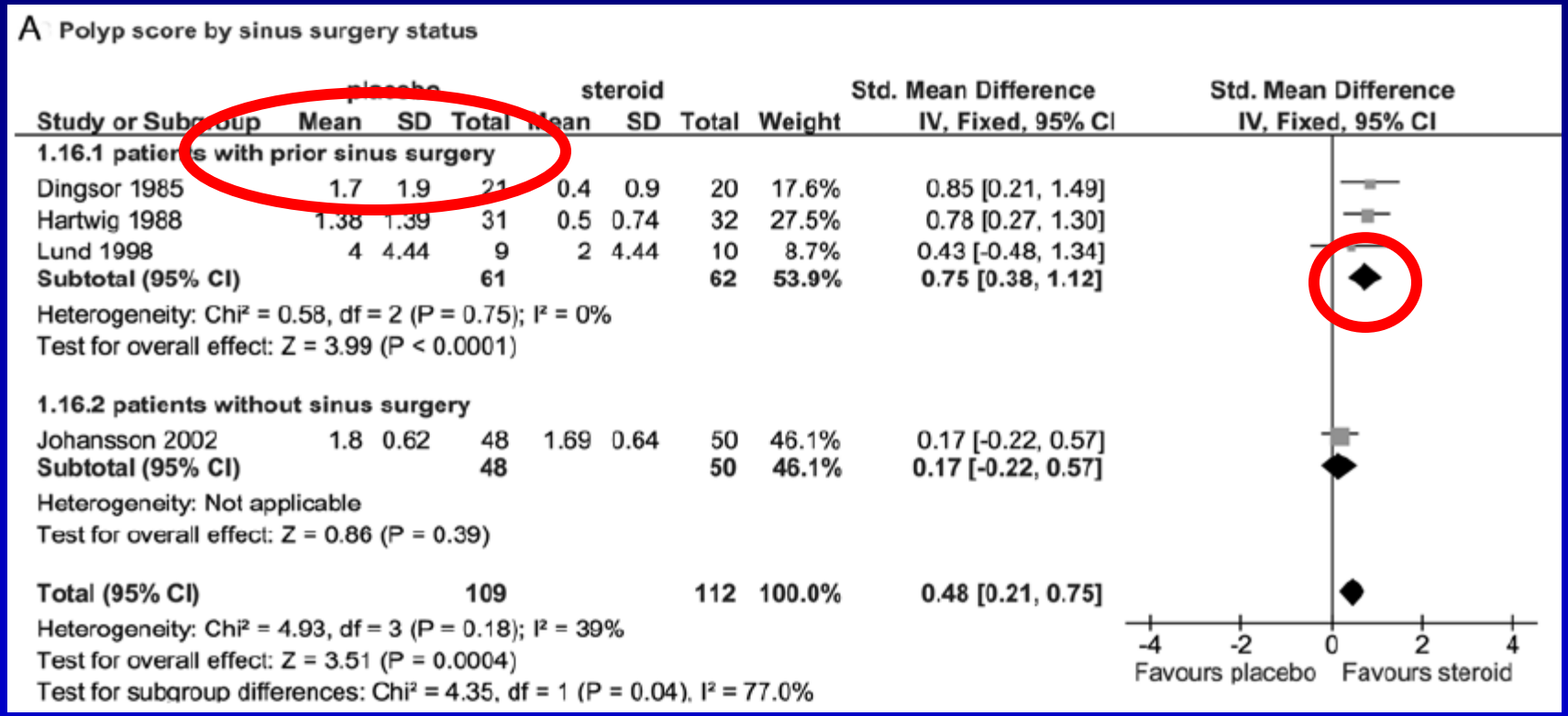
Rudmik L, et al, IFAR 2012

# Topical steroids

- Meta-analyses demonstrate benefit in both CRSwNP and CRSsNP with greatest benefit with direct sinus delivery
- Safety with steroid irrigations

Snidvongs K, etal Cochrane 2011
Rudmik L, etal Laryngoscope 2012
Welch K, etal, AJRA 2010
Steinke JW, etal JACI 2009

# Surgery improves topical steroid delivery




Fokkens W etal EPOS 2012

# Steroid irrigations

- N=111 post ESS pts (56% CRSwNP)
- BUD or BET (1mg qd) via squeeze bottle
- 1 year f/u improved SNOT22, endoscopy
- Most improvement in those with high eosinophilia
- UNC DBPCT no benefit
  - needs further study

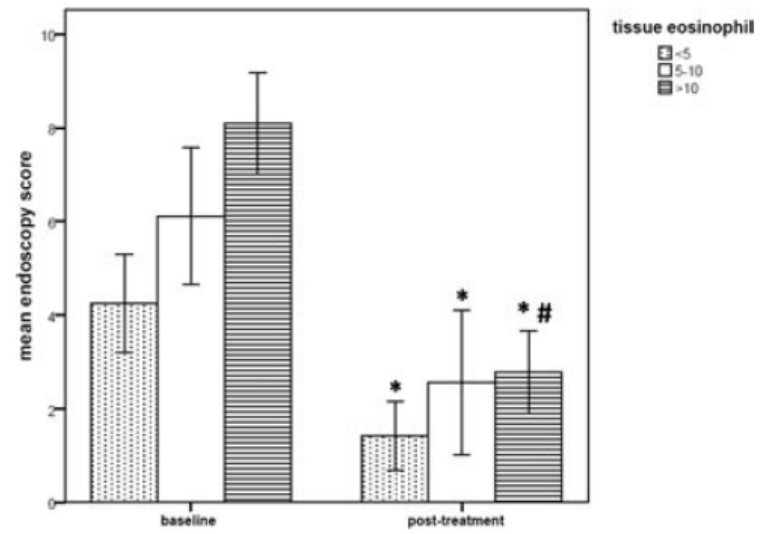



**FIGURE 4.** Endoscopy score improvement by tissue eosinophil (/HPF); asterisk (*) indicates $p < 0.001$ when posttreatment was compared with baseline; number sign (#) indicates $p < 0.05$ when mean change in endoscopy score was compared between patients with high tissue eosinophilia (≥10/HPF) and those without.

Snidvongs K, et al, IFAR 2012

# Safety and drug absorption?

- What % of total irrigation solution remains?
- What is safe dose?

# How much solution remains in the sinuses?

# How much solution remains in the sinuses?

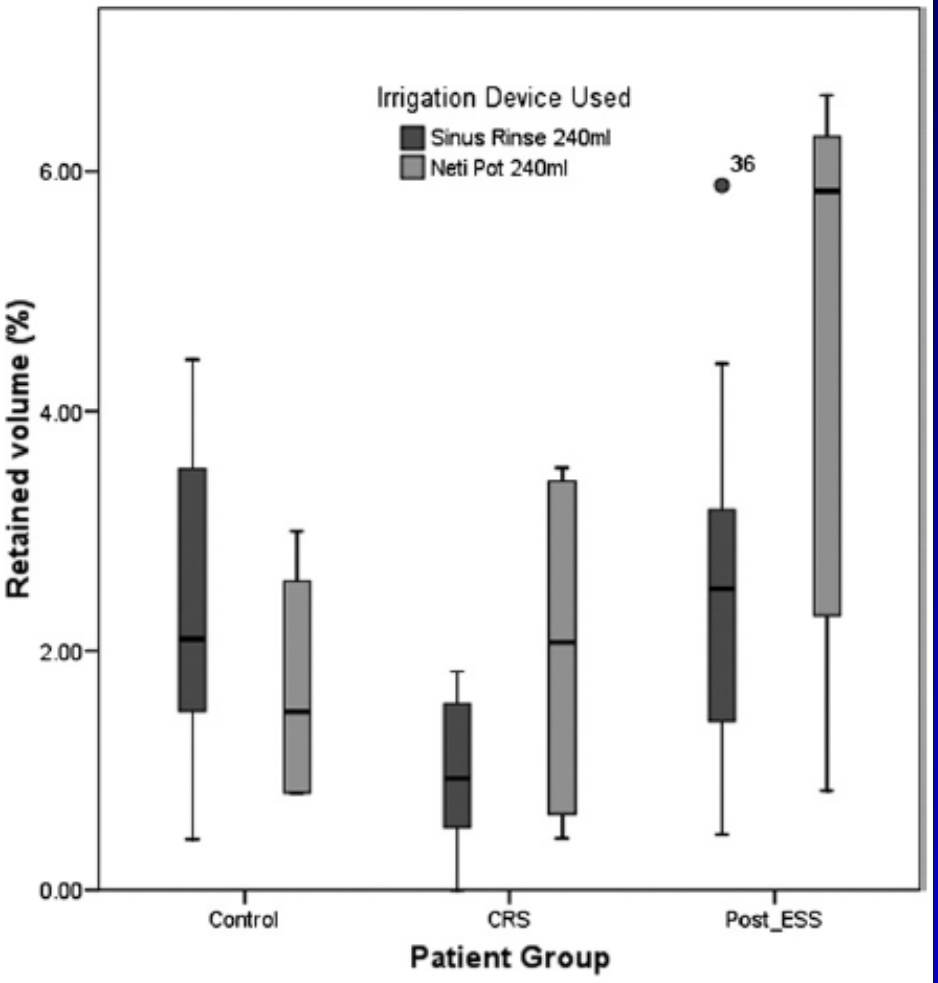



**Figure 3** The effect of the irrigation device was nonsignificant among patient groups.

**2.5±1.5%**

# Benefit to patient


# Safety of budesonide irrigations

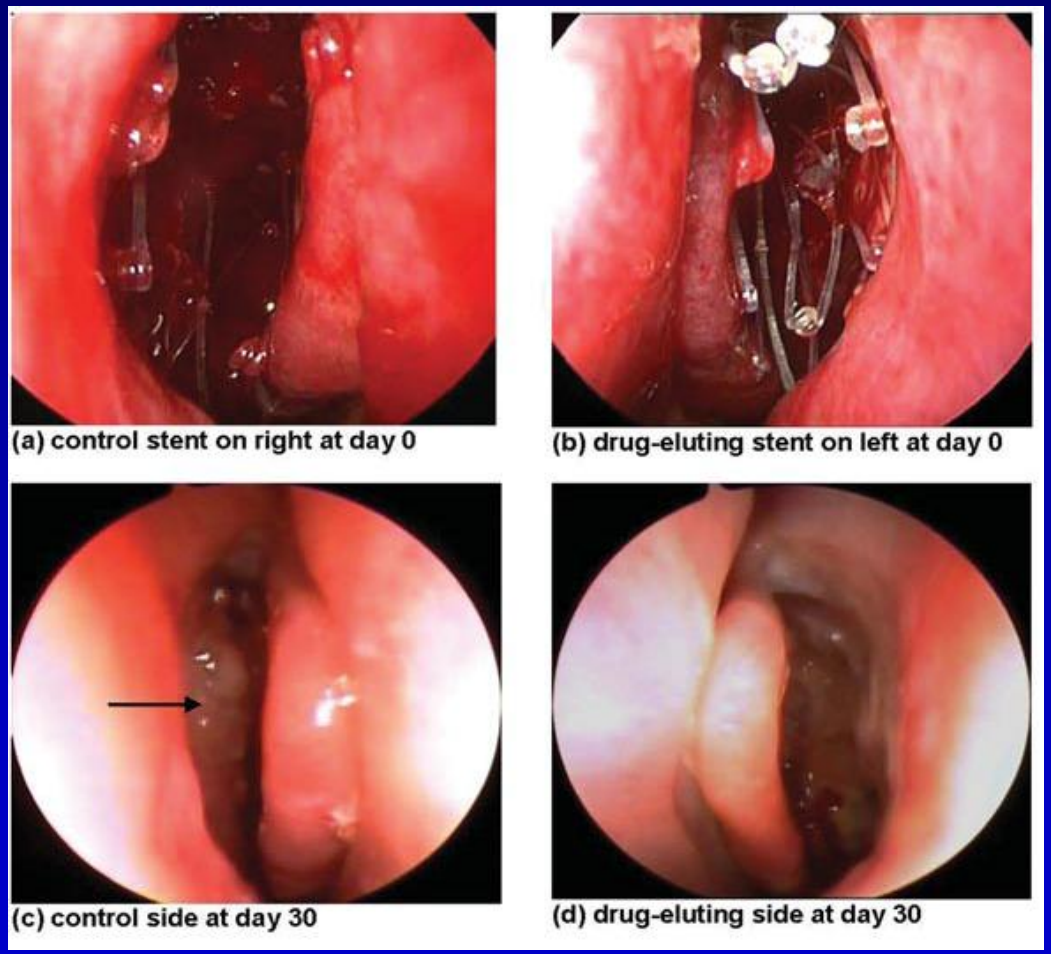
- Respules (0.5mg/2ml) BID = 1 mg/day
- 3% retained volume = 30 mcg drug
- Rhinocort: 32 mcg/spray=128 mcg/day

- Current irrigations are about ¼ dose of topical spray!
- Probably doesn't apply to drops which have higher retention

# Other methods for getting steroid to the sinus cavity

# Mometasone bioresorbable stent

- Meta-analysis, 2 DBRCTs, 143 pts
- Endoscopy, adhesions, oral steroid need improved
- Cost/duration of effect?




Han JK, et al, IFAR 2012

# Summary of active agents

| Agent | Grade of evidence | Benefit vs Harm | Recommendation Level | Protocol |
|---|---|---|---|---|
| Antibiotic | B | Equal | Option vs recommend against | Variable, high volumes appear to be better |
| Antifungal | A- | Harm | Recommend against | |
| Alternative agents | C | N/A | N/A | Surfactants, honey, xylitol |

Rudmik L, etal, IFAR 2012

# The future of topical therapeutics

- Great potential to improve “micro” factors
  - Newer active agents with fewer side effects
  - Modulation of wound healing
  - Better carriers to optimize dosing and concentration protocols
- Better understanding of “macro” factors, such as role of surgery, delivery device, target sinus

# CRS treatments

- Approach based upon pathophysiology & evidence
- Topical therapies likely to make a major impact
- Evidence supports **large volume** delivery of saline and steroids in **post operative** patients
- Other agents and delivery devices have limited evidence to support their use
- May improve lower airway disease

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