Update in Outpatient Medicine
Medical Grand Rounds
ACP Scientific Session
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Disclosures

• Stock Holdings
  • Abbott Labs
  • Abbvie
  • Bristol Myers Squibb
  • Proctor and Gamble
  • Walgreens
Topics

- Herpes Zoster vaccination
- Osteoporosis/Osteopenia Treatment
- Arthroscopy for meniscal tears
- Carpal Tunnel
- Insulin cost and effectiveness
- Hypothyroidism and thyroid replacement
- Risk of colon cancer based on colonoscopy findings
- Aspirin use in primary prevention
- Statins to prevent cardiovascular disease
- Cardiac procedures in patients with CHF

Efficacy of an Adjuvanted HZV Subunit Vaccine

- 15,411 immunocompetent, previously unvaccinated patients age ≥ 50 randomized to receive 2 doses HZ/su 2 months apart
  - 95% patients received both doses
- Mean follow up 3.2 years
- Vaccine efficacy 97.2%
- Injection site reaction 81.5%
- Systemic reaction 66.1% (mostly myalgia, fatigue, headache)
  - 11.4% Grade 3 (10 cm injection site reaction, temp 39, unable to engage in normal activity)
  - Transient, most patients received 2nd dose

NEJM 2015;372:2087-96
Cost-effectiveness of the Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults

- Markov decision model for immunocompetent patients age ≥ 60
- Compared no vaccine, single dose live attenuated vaccine, HZ/su
- Outcomes total cost and QALYs
- HZ/su cost $280 per series
  - Zostavax price $213 per dose
- Accounted for differences in efficacy, rate of post-herpetic neuralgia, ophthalmic complications, hearing loss, hospitalization, death
- Assumed only 56.2% adherence for receiving 2nd dose
- HZ/su less expensive than Zostavax and ICE $20,038-30,084 per QALY compared to placebo

JAMA IM 2018; 178:248-258

Association of Osteoporosis Medication Use After Hip Fracture.

- Observational cohort study using data from Truven Market Scan claims between 01/01/2004 and 9/30/2015
- 97,169 patients 50 and older who were not taking osteoporosis medications at the time of hip fracture
  - 15-25% of patients with osteoporotic fx. experience a second fracture within 10 years
- Assessed initiation of treatment within 180 days of hip fracture
- Primary outcome was non-vertebral fractures
- Treatment initiated in 6.9% of patients within 180 days

JAMA Network Open 2018; 1(3):e180826
Hospital variation from 2% to 25%

Rate of subsequent fracture was 4.2 events per 100 patient years lower in treated group

Treatment rates could increase if orders written to start treatment 2 weeks post discharge or at first TCM visit

Fracture Prevention with Zoledronate in Older Women with Osteopenia

- 2000 women age ≥ 65 with T score -1.0 to -2.5 at either the hip or femoral neck.
  - 35% of enrollees had >3% risk of hip fracture or > 20% risk of osteoporotic fracture
  - Excluded patients with vertebral T score < -3.0, eGFR < 30 ml/min, recent cancer, major systemic disease, use of bone active drugs within 1 year
  - Randomized to an 5 mg zoledronate IV every 18 months vs. placebo
    - Patients not taking vitamin D given 1 dose of 100,000 IU followed by 50,000 monthly
    - Calcium intake 1 g/day advised, supplements not given
  - 6 year follow up

NEJM 2018 published online 10/1/2018
Fragility fracture defined excluding fingers, metacarpals, toes, skull, face and jaw

Risk lower for non-vertebral fractures, symptomatic vertebral Fractures.

HR for hip fracture 0.66 but NS

No significant adverse effects
NNT 20 to prevent one symptomatic fracture

Osteoporosis/Osteopenia

- Treatment after hip fracture is unacceptably low
- Infusion of zoledronate every 18 months (potentially longer intervals) prevents fracture in older women with few adverse events
  - Cost is relatively low
Early Surgery vs. PT for Nonobstructive Meniscal Tears

- 321 patients aged 45-70 with non-obstructive meniscal tear (no locking)
  - Randomized to arthroscopy vs. PT
    - PT consisted of 16 sessions over 8 weeks
  - Included traumatic and degenerative tears
  - Exclusions - locking, prior knee surgery, instability, severe OA, BMI > 35
  - Follow up 24 months
  - Outcome assessed by standardized questionnaire

JAMA 2018;320:1328-1337

No clinically significant difference in function
No statistically significant difference in activity level
29% of participants in the PT group crossed over to arthroscopy
Clinical and Cost Effectiveness of Steroid Injection or Night Splints for Carpal Tunnel

- 321 patients presenting with mild-moderate carpal tunnel symptoms
- Symptoms present for > 6 weeks
- Randomized to one injection of 20 mg Depo-Medrone vs. wrist splint for 6 weeks and gentle ROM exercises when removing the splint
- Primary outcome-Symptom Score on Boston Carpal Tunnel Questionnaire at 6 weeks
  - Performed cost-utility analysis

Lancet 2018;392:1423-33

Injection superior at 6 weeks
No difference at 6 months
No difference in surgical referral rates
Association of Basal Insulin Analogs vs NPH With Hypoglycemic Events in Type 2 DM

- Assessed records from Kaiser Permanente Northern California
- 25,489 adults with Type 2 DM initiated either NPH or basal analog insulin
- Propensity matched analysis of data
- Outcomes- hypoglycemia related ED visit or hospitalization, change in HgBA1C
- 92% started NPH, 8% (1928 patients) started insulin analogs
  - Co-payments $10 NPH, $20 insulin analogs
  - Starting HgBA1C 9.4%

JAMA doi:10.100/jama.2018.7993
Non-statistically significant greater improvement in glycemic control in patients treated with NPH insulin.

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**Table 3. Changes in Glycemic Control**

<table>
<thead>
<tr>
<th></th>
<th>Hemoglobin A1c, Mean (95% CI), %*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Insulin Analog</td>
</tr>
<tr>
<td>Baseline†</td>
<td>9.41 (9.34 to 9.50)</td>
</tr>
<tr>
<td>Postbaseline‡</td>
<td>8.16 (8.09 to 8.24)</td>
</tr>
<tr>
<td>No. of days between baseline and postbaseline measure, mean (SD)</td>
<td>298 (103)</td>
</tr>
<tr>
<td>Pre-post change</td>
<td>1.26 (1.16 to 1.36)</td>
</tr>
<tr>
<td>Unadjusted difference-in-differences estimate§</td>
<td>-0.22 (-0.09 to -0.37)</td>
</tr>
<tr>
<td>Adjusted difference-in-differences estimate§</td>
<td>-0.22 (-0.09 to -0.37)</td>
</tr>
</tbody>
</table>
Use of Intensive Glycemic Management in Older Adults with Diabetes Mellitus

- 42,269 patients with Type 2 DM aged 75 and older
  - Data extracted from EHR’s from practices participating in the Diabetes Collaborative Registry
  - Study period 2014-2016

- Patients with most co-morbidities and highest risk of intensive control with high risk agents
- >75% on a sulfonylurea, 30% insulin
Treatment of Diabetes Mellitus

- Most patients with Type 2 DM requiring insulin can safely be treated with NPH insulin with similar effectiveness and much lower cost
- Older patients can frequently have de-escalation of treatment, especially when on agents with hypoglycemic risk

Association of Thyroid Replacement Therapy with QoL and Thyroid Related Symptoms

- Meta-analysis and systematic review of 21 trials including 2192 adults
  - Baseline mean thyrotropin levels 4.4-12.8mIU/L
  - Therapy ranged from 3-18 months

JAMA 2018;320:1349-1359
In patients with subclinical hypothyroidism, treatment with thyroid hormone therapy was not associated with benefit for

- Quality of Life- General Health Questionnaire, SF-36, EQ-5D
- Thyroid related symptoms- ThyPro, ThyD QoL, Zulewski, Billewicz
- Fatigue-ThyPro tiredness scale
- Depression- Beck Depression Index, Hospital Anxiety and Depression Scale
- Cognitive Function-MMSE, Wechlser memory score, Letter-Digit Coding, Composite Cognitive Score

Association of Colonoscopy Findings With Long-term CRC Incidence

- Multicenter, prospective cohort study of participants in the PLCO Trial
  - 154,900 patients aged 55-74 enrolled
  - 15,935 underwent colonoscopy after a positive FS
    - Most initial colonoscopies performed prior to 2000
    - Polyps not removed at initial flexible sigmoidoscopy, but referred
    - 70% underwent colonoscopy
  - median follow up for CRC incidence 12.9 years

JAMA 2018;319:2021-2031
Carcinoid mortality 2.4 times higher in advanced adenoma cohort.
Carcinoid mortality did not differ in non-advanced adenoma cohort.

Long Term CRC Mortality After Adenoma Removal

- Patients with low risk adenomas do not have higher rates of CRC incidence or CRC mortality than patients with no adenoma.
- Current guidelines recommend surveillance 5-10 years after resection of low risk adenomas.
- Difficult to justify surveillance sooner than 10 years in low risk adenoma patients.
  - Poor prep or poor exam may warrant earlier follow up.
Use of Aspirin to Reduce Risk of Initial Vascular Events in Patients at Moderate CV Risk-ARRIVE

- 12,546 patients at moderate CV risk
  - Men ≥ 55 with 2 or more risk factors
  - Women ≥ 60 with 3 or more risk factors
  - Excluded diabetes, previous CV disease, CHF, high risk of bleed
  - Mean BMI 28.4
- Randomized to receive 100 mg enteric coated ASA vs. placebo
- Median follow up 60 months
- Primary outcome- Composite of first MI, CVA, unstable angina, TIA, CV death
- Assessed incidence of cancer
- Assessed adverse events and graded severity of GI bleed
- 10 year estimated event rates lower than expected (8.4%) using risk calculators

Lancet 2018;392:1036-46
Effect of Aspirin for Primary Prevention in Persons with DM

- 15,480 patients age ≥ 40 with DM and no known CVD
  - Excluded contraindication to ASA or significant conditions that might limit adherence.
  - Mean BMI 30.7
- 2x2 Randomization to 100 mg ASA and 1 G n-3 fatty acid capsule or placebo
- Subgroup analysis based on 5 year CV risk estimates of < 5%, 5 to <10%, and ≥ 10%
- Mean follow up 7.4 years

NEJM 2018:379;1529-1539
Aspirin for Primary Prevention of CV Events

- Primary Prevention
  - No evidence for average risk or moderate risk patients
  - ASA prevents CV events in patients with DM, but benefit is offset by GI bleeding

Statins for Primary Prevention of CV Events and Mortality in Old and Very Old Adults With and Without Type 2 DM

- Retrospective cohort study of 46,864 patients age ≥75 with and without DM and no known CVD.
  - Database of the Catalan primary care system 2006-2015
  - Compared outcomes between new statin users (no statin in previous 18 months vs. non-users
  - Primary outcome - incidence of CVD, all cause mortality
  - Assessed onset of liver toxicity, myopathy and cancer
  - Stratified results
    - Age 75-84 with and without DM
    - Age ≥ 85 with and without DM

BMJ 2018;362:k3359
Catheter Ablation for Atrial Fibrillation with Heart Failure

- 363 patients with CHF and EF ≤ 35%, symptomatic AF, no anti-arrhythmic drugs
  - All patients had an ICD or CRT-D to monitor a. fib recurrence
- Open label randomized trial to receive catheter ablation or medical therapy for atrial fibrillation
- Median follow-up 37.8 months
- Primary end point death or CHF hospitalization

NEJM 2018;378:417-27
Ablation patients had 8% improvement in LVEF.

Transcatheter Mitral Valve Repair in Patient with Heart Failure

- 614 patients with cardiomyopathy and EF 20-50% and Grade 3+ or 4+ secondary mitral regurgitation.
- Patient were symptomatic on stable, maximal doses of guideline based therapy plus CRT if indicated
- Randomized to transcatheter mitral valve repair plus medical therapy to medical therapy alone
- Primary outcome- Hospitalizations for CHF at 24 months, freedom from device related complications at 12 months

NEJM published online Sept 23, 2018
96.6% of patients were free of device related complications at 12 months

Cardiac Procedures in Heart Failure

- In patients with atrial fibrillation and congestive heart failure, catheter ablation is associated with lower all cause mortality, CHF hospitalization and improved LVEF
- In patients with secondary cardiomyopathy and secondary moderately-severe or severe mitral regurgitation, transcatheter mitral valve repair lowers all cause mortality, CHF hospitalization and improves symptomd