Outpatient Medicine: Five Game Changing Articles for 2016

Heidi Lakanen, MD FACP
November 11, 2016
IN ACP Meeting
Case

- H is 76 yo community dwelling woman who presents for routine follow-up. She is bothered with some osteoarthritis but is satisfied that she feels well.
- Med: lisinopril 20 mg daily, HCTZ 12.5 mg daily, acetaminophen 325 PRN
- PE: BMI: 23, BP: 134/82
- Are you satisfied with her BP or does it warrant intensified therapy?
- How can some of the literature published this past year help us treat this patient?
**#1 Sprint Trial**

- Is a lower blood pressure target better in a non-diabetic population?
- 9361 patients
- RCT to intensive therapy (SBP < 120 mm Hg vs. standard therapy (SBP < 140 mm Hg))
- No drugs mandated but encouraged use of:
  - Chlorthalidone
  - Amlodipine
  - β-blockers (CAD population)
- Monthly adjustment to reach BP goal

Sprint: Who Were the Patients?¹

- ≥ 50 yo
- SBP 130-180 mm Hg
- Increased risk of CV events (1 of these)
  - CVD
  - CKD (GFR: 20-60 mL/min)
  - Framingham risk ≥15%
  - ≥ 75 yo
- Exclusion: CVA, DM

- Ethnically diverse
- 36% women
- 28% ≥ 75 yo
- Overweight
Did the Groups Achieve Different Blood Pressures?¹

**Mean BP:**
- Intensive: 121.5 mm Hg
- Standard: 134.6 mm Hg

**Number of medications:**
- Intensive: 2.8
- Standard: 1.8

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*Figure 2. Systolic Blood Pressure in the Two Treatment Groups over the Course of the Trial.*

The systolic blood-pressure target in the intensive-treatment group was less than 120 mm Hg, and the target in the standard-treatment group was less than 140 mm Hg. The mean number of medications is the number of blood-pressure medications administered at the exit of each visit. I bars represent 95% confidence intervals.
Results

Primary outcome: Composite of MI, ACS, stroke, HF or death from CV causes

RRR: 25%
ARR: 1.6%
NNT = 62 for 3 years of therapy

All-cause mortality:
RRR: 27%
ARR: 1.2%
NNT = 84
## Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>243/4678 (5.2)</td>
<td>319/4683 (6.8)</td>
<td>0.75 (0.64–0.89)</td>
</tr>
<tr>
<td>Previous CKD</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>135/3348 (4.0)</td>
<td>193/3367 (5.7)</td>
<td>0.70 (0.56–0.87)</td>
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<tr>
<td>Yes</td>
<td>108/1330 (8.1)</td>
<td>126/1316 (9.6)</td>
<td>0.82 (0.63–1.07)</td>
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<tr>
<td>Age</td>
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<tr>
<td>&lt;75 yr</td>
<td>142/3361 (4.2)</td>
<td>175/3364 (5.2)</td>
<td>0.80 (0.64–1.00)</td>
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<td>≥75 yr</td>
<td>101/1317 (7.7)</td>
<td>144/1319 (10.9)</td>
<td>0.67 (0.51–0.86)</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
<td>77/1684 (4.6)</td>
<td>89/1648 (5.4)</td>
<td>0.84 (0.62–1.14)</td>
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<tr>
<td>Male</td>
<td>166/2994 (5.5)</td>
<td>230/3035 (7.6)</td>
<td>0.72 (0.59–0.88)</td>
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<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Black</td>
<td>62/1454 (4.3)</td>
<td>85/1493 (5.7)</td>
<td>0.77 (0.55–1.06)</td>
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<tr>
<td>Nonblack</td>
<td>181/3224 (5.6)</td>
<td>234/3190 (7.3)</td>
<td>0.74 (0.61–0.90)</td>
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<tr>
<td>Previous cardiovascular disease</td>
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<tr>
<td>No</td>
<td>149/3738 (4.0)</td>
<td>208/3746 (5.6)</td>
<td>0.71 (0.57–0.88)</td>
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<tr>
<td>Yes</td>
<td>94/940 (10.0)</td>
<td>111/937 (11.8)</td>
<td>0.83 (0.62–1.09)</td>
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<tr>
<td>Systolic blood pressure</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>≤132 mm Hg</td>
<td>71/1583 (4.5)</td>
<td>98/1553 (6.3)</td>
<td>0.70 (0.51–0.95)</td>
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<tr>
<td>&gt;132 to &lt;145 mm Hg</td>
<td>77/1489 (5.2)</td>
<td>106/1549 (6.8)</td>
<td>0.77 (0.57–1.03)</td>
</tr>
<tr>
<td>≥145 mm Hg</td>
<td>95/1606 (5.9)</td>
<td>115/1581 (7.3)</td>
<td>0.83 (0.63–1.09)</td>
</tr>
</tbody>
</table>
## Harms

Overall serious adverse event:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive Tx (N= 4678)</th>
<th>Standard Tx (N=4683)</th>
<th>Hazard Ratio</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>2.4%</td>
<td>1.4%</td>
<td>1.67</td>
<td>.001</td>
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<tr>
<td>Syncope</td>
<td>2.3%</td>
<td>1.7%</td>
<td>1.33</td>
<td>.05</td>
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<tr>
<td>AKI</td>
<td>4.1%</td>
<td>2.5%</td>
<td>1.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Injurious Fall</td>
<td>2.2%</td>
<td>2.3%</td>
<td>0.95</td>
<td>.71</td>
</tr>
<tr>
<td>Orthostatic hypotension</td>
<td>16.6%</td>
<td>18.3%</td>
<td>.88</td>
<td>.01</td>
</tr>
</tbody>
</table>

Overall serious adverse event: 1793(38.3%) vs 1736(37.1%) 1.04 .25
Is SPRINT’S Statistical Significance Clinically Significant?

• Critique:2
  – Over emphasis on relative risk reduction of 25%
  – In the strictest sense:
    • IF you treat 1000 patients over 3.2 years to a SBP of <120 as opposed to 140 mm Hg
    • 16 patients will benefit
    • There are potential costs: more meds, more doctor visits, more co-pays

• “We should guard against a one-size-fits-all response to SPRINT”

2 Ortiz, E. Ann Intern Med 2016; 164:689-691
HOPE-3

- Does addition of ARB + thiazide in an intermediate risk population reduce CV events?
- Who is intermediate risk?
  - Men -> 55 + 1 RF
  - Women >65 + 1 RF or >60+2 RF
- Exclusion: established CAD, CKD

Result

- Result: No benefit with candesartan.
- Why the discordant results compared to SPRINT?
Comparators

**HOPE - 3**
- Average SBP lowering 6 mmHg
- Intermediate Risk population

**SPRINT**
- Average SBP lowering 15 mmHg
- High risk population
HTN Conclusion

• Theme:
  – Need to know inclusion criteria for trials
  – Individualize patient recommendations
    • Treatment goal dependent on risk

• Era of personalized medicine
  – “We believe SPRINT is an important study whose results should be applied judiciously in select patients incorporating EBM principles, patient preferences and individualized informed shared decision-making to ensure that patients treated more aggressively truly have a high likelihood of benefit from the intervention without being harmed.”

http://annals.org/article.aspx?articleid=2494542
GAME CHANGER #1

• Consider intensifying SBP targets
  – Is the patient 75 or older?
  – Do they have CVD?
  – Do they have CKD?
  – Is their Framingham risk $\geq$ 15%?
2. Aspirin?

- S is a 58 yo man who presents for his annual exam. He feels well other than the stress he experiences with his job. He brings his lab screening performed at his place of employment.
- He takes no medication other than aspirin which he started on his own because he heard it was good for him.
- RF: No tobacco use
- BP: 158/86 (he attributes to work stress)
- Labs: TC: 246, HDL: 38 TG: 156 LDL: 177
- How would you advise him?
Aspirin for Primary Prevention of CVD

Yesterday
• Framingham risk
• Differentiating by sex for first time MI

Today
• ACC/AHA Pooled Cohort Equation
  CHD Death
  Non-fatal MI
  Fatal CVA
  Non-fatal CVA
• ASA for CVD risk prevention for men and women
• Prevention of colorectal cancer
Aspirin Use for The primary Prevention of Cardiovascular Disease and colorectal Cancer: USPSTF Recommendation Statement

- **Key: Think Age and Risk**
  - 40’s – I
  - 50’s – B
    - ≥ 10% 10 y CVD risk
  - 60’s – C
    - ≥ 10% 10 y CVD risk
  - 70’s - I

- **Assumptions**
  - Primary prevention
  - Aspirin 81 mg

- **Cautions:**
  - GI bleeding risk
  - Intracranial bleeding

- **USPSTF Grades**
  - **A:** High certainty the net benefit substantial; offer service
  - **B:** High certainty of moderate benefit or moderate certainty of moderate/substantial benefit; offer service
  - **C:** Moderate certainty benefit is small; offer to selected patients
  - **D:** Moderate or high certainty of no net benefit or harm outweighs benefit
  - **I:** Evidence insufficient; patients need to understand uncertainty of risks vs benefits.

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4https://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions
Magnitude of Benefit

<p>| Table. Lifetime Events in 10 000 Men and 10 000 Women Taking Aspirin* |
|--------------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>CVD Risk</th>
<th>Nonfatal MIs Prevented</th>
<th>Nonfatal Ischemic Strokes Prevented</th>
<th>CRC Cases Prevented</th>
<th>Serious GI Bleeding Events Caused</th>
<th>Hemorrhagic Strokes Caused</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aged 50-59 y</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>10%</td>
<td>225</td>
<td>84</td>
<td>139</td>
<td>284</td>
<td>23</td>
</tr>
<tr>
<td>15%</td>
<td>267</td>
<td>86</td>
<td>121</td>
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<tr>
<td>20%</td>
<td>286</td>
<td>92</td>
<td>122</td>
<td>248</td>
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<tr>
<td>Aged 60-69 y</td>
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<td></td>
</tr>
<tr>
<td>10%</td>
<td>159</td>
<td>66</td>
<td>112</td>
<td>314</td>
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<tr>
<td>15%</td>
<td>186</td>
<td>80</td>
<td>104</td>
<td>298</td>
<td>24</td>
</tr>
<tr>
<td>20%</td>
<td>201</td>
<td>84</td>
<td>91</td>
<td>267</td>
<td>27</td>
</tr>
<tr>
<td><strong>Women</strong></td>
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<td>Aged 50-59 y</td>
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</tr>
<tr>
<td>10%</td>
<td>148</td>
<td>137</td>
<td>139</td>
<td>209</td>
<td>35</td>
</tr>
<tr>
<td>15%</td>
<td>150</td>
<td>143</td>
<td>135</td>
<td>200</td>
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<tr>
<td>20%</td>
<td>152</td>
<td>144</td>
<td>132</td>
<td>184</td>
<td>29</td>
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<tr>
<td>Aged 60-69 y</td>
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<tr>
<td>10%</td>
<td>101</td>
<td>116</td>
<td>105</td>
<td>230</td>
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<tr>
<td>15%</td>
<td>110</td>
<td>129</td>
<td>93</td>
<td>216</td>
<td>34</td>
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<tr>
<td>20%</td>
<td>111</td>
<td>130</td>
<td>97</td>
<td>217</td>
<td>33</td>
</tr>
</tbody>
</table>
Case

- 10 yr CVD risk = 15.6%
- NNT to prevent first CVD event or CRC = 21
- NNH: 35

Figure 2. Forest plot of aspirin use and long-term (0 to ≥20 y) risk for CRC death.

Game Changer #2

- Theme:
  - Benefit of therapy is dependent on baseline risk
  - Not a “one size fits all strategy”

- GI bleeding risk
- Preferences regarding taking aspirin
- Assess Age
- Assess CVD risk

- 50’s without CVD
  Low GI risk
  Pooled cohort ≥ 10%
  Consider ASA 81
- 60’s
  Consider risks vs. benefits of ASA
  “C”
- 70s
  Be careful
3. PPI: Friend or Foe?

- Case:
- A is a 73 yo woman with laryngeal reflux who has heard in the news lately about proton pump inhibitors. Is it really going to cause dementia, kidney disease and pneumonia?
- She is a speaker and her voice is gravely when she doesn’t take her PPI.
Case

• B is an 86 yo woman who comes in for routine follow-up.
• PMHx: paroxysmal afib, GERD, remote breast CA, CKD stage 2
• Social hx: widowed x 3 years and lives alone
• Meds: apixaban, esomeprozole, diltiazem, metoprolol
• She wonders about the recent news regarding PPIs. Should I be concerned?
PPI Use

- 2015:
  - Esomeprazole #4
  - $15 million scripts/month\(^7\)
  - 25-70% of these have no appropriate indication\(^8\)

- What is the data behind some of these potential side effects?

\(^7\)http://www.webmd.com/news/20150508/most-prescribed-top-selling-drugs


PPI Use and the Risk of CKD

- Prospective cohort study
- Atherosclerosis Risk in communities study (ARIC)
- Entry: 1987-1990
- Who?
  - 4 US communities
  - 15,792 adults
- Visits + annual telephone survey
- This study:
  - Attended visit #4, n= 11,656
  - Alb/Cr ratio obtained at this visit
  - Exclusion: baseline GFR > 60 mL/min
- Replication cohort
  - 248K
Results

- PPI user profile:
  - Higher BMI
  - Higher use of:
    - Anti-hypertensives, aspirin, statins

<table>
<thead>
<tr>
<th>Association Between PPI Use and Incident CKD</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted baseline PPI use vs no PPI use</td>
<td>1.45 (1.11-1.90)</td>
<td>.006</td>
</tr>
<tr>
<td>Baseline PPI use vs no PPI use</td>
<td>1.50 (1.14-1.96)</td>
<td>.003</td>
</tr>
<tr>
<td>Time-varying PPI ever use vs never PPI use</td>
<td>1.35 (1.17-1.55)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

- 10 yr. absolute risk difference for CKD in users compared to non-users
  - ARIC: 3.3%
  - Replication cohort: 1.7%
Results

• BID vs QD dosing
  – Replication cohort: HR = 1.46(CI 1.28-1.67)

• PPI use vs H₂ receptor antagonist
  – ACIR HR: 1.58(1.05-2.4)
  – Rep. cohort HR: 1.30(1.13-1.48)

• H₂ receptor antagonist vs. no H₂ receptor antagonist
  – ACIR HR: 1.15(.98-1.36)
  – Rep cohort HR: .93(0.88-0.99)
PPI Use and CKD

Figure 2. Association Between Proton Pump Inhibitor Use and Incident Kidney Disease Stratified By Subgroups

Atherosclerosis Risk in Communities Study

<table>
<thead>
<tr>
<th>Overall Population</th>
<th>Baseline PPI Users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Young</td>
<td>556</td>
</tr>
<tr>
<td>Old</td>
<td>882</td>
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<tr>
<td>Race</td>
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<tr>
<td>Yes</td>
<td>233</td>
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<tr>
<td>Overall</td>
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</table>

Geisinger Health System Replication Cohort

<table>
<thead>
<tr>
<th>Overall Population</th>
<th>Baseline PPI Users</th>
</tr>
</thead>
<tbody>
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<td>No. of Events</td>
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<td>Age</td>
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<td>Young</td>
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<td>Old</td>
<td>27386</td>
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<tr>
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<td>Overall</td>
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</table>
**PPI Adverse Events Summary**

<table>
<thead>
<tr>
<th>Source</th>
<th>Adverse Effect</th>
<th>Adjusted OR (95% CI)</th>
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<tbody>
<tr>
<td>Lazarus et al, 2015</td>
<td>Chronic kidney disease</td>
<td>1.50 (1.11-1.90)</td>
</tr>
<tr>
<td>Antoniou et al, 2015</td>
<td>Acute kidney disease</td>
<td>2.52 (2.27-2.79)</td>
</tr>
<tr>
<td>Antoniou et al, 2015</td>
<td>Acute interstitial nephritis</td>
<td>3.00 (1.47-6.14)</td>
</tr>
<tr>
<td>Cheungpasitporn et al, 2015</td>
<td>Hypomagnesemia</td>
<td>1.43 (1.08-1.88)</td>
</tr>
<tr>
<td>Kwok et al, 2012</td>
<td><em>Clostridium difficile</em></td>
<td>1.74 (1.47-2.85)</td>
</tr>
<tr>
<td>Eom et al, 2011</td>
<td>Community-acquired pneumonia</td>
<td>1.34 (1.14-1.57)</td>
</tr>
<tr>
<td>Filion et al, 2014</td>
<td>Community-acquired pneumonia</td>
<td>1.05 (0.89-1.25)</td>
</tr>
<tr>
<td>Zhou et al, 2015</td>
<td>Bone fracture</td>
<td>1.33 (1.15-1.54)</td>
</tr>
</tbody>
</table>

PPI: Friend or Foe?

- Observational studies
  - Do NOT prove causation
  - Only association
- Certainly use a PPI if indicated
- Frequently prescribed medication + potential adverse effect + use without clear indications = potential for harm.
- But....ask if the indication is still present
- Could lifestyle changes help?
- What about H₂ blocker?
- THINK before you prescribe or refill
- High value care issue
PPI Cases

75 yo with laryngeal reflux
• Perhaps she does not need 40 mg daily
• Trial of dose reduction

86 yo with GERD
• Trial at dose reduction
• Incorporate lifestyle measures

GAME CHANGER #3
We need to pause from the #90, 3 RF
Is there a compelling ongoing need for this medication?
4. Girlfriend Talk

• “Just found out my mammogram is normal. They say I have dense breasts and I need more testing.”

• They made it sound very alarming.

• “What should I do?”

• “I spoke to Dr. ____ through his nurse. He neither recommended nor discouraged it--said it was my decision. The nurse said that since my films have not changed from year to year, there is not really a need for it unless I think there's something more going on...which I don't. “

• “But nobody says absolutely one way or the other.”
Issue with Breast Density

- Increased breast density
  - Increased breast cancer risk
  - Problem with interval cancers
- April 2016 USPSTF published updated guidelines for breast cancer screening
  - Biennial screening in women 50-74 yo\textsuperscript{11}
- “Effects of supplemental screening on breast cancer outcomes remain unclear.”\textsuperscript{12}
- US, MRI and breast tomosynthesis do find more cancers
  - Most of it is invasive
- Problems:
  - NO MORTALITY DATA!!!!
  - Cost
  - More false positives

\textsuperscript{11} Ann Intern Med 2016;164:279-296
\textsuperscript{12} Ann Intern Med 2016;164:268-278.
Breast Density

- Patients must be notified.
- But what do we recommend beyond mammography as recommended by USPSTF?
Tailoring Breast Cancer Screening Intervals by Breast Density and Risk for Women aged 50 years or older: Collaborative Modeling of screening outcomes

• Factors:
  – Breast Density
    • Almost entirely fatty
    • Scattered fibroglandular density
    • Heterogeneously dense
    • Extremely dense
  – Relative risk of developing breast cancer
    • 1.3 = One first degree relative with breast Ca
    • = BMI > 30
    • 2 = 2 first degree relative with breast ca
    • 4 = LCIS, atypical hyperplasia
  – Age
    • 50-74
    • 65-74
• Outcomes
  Breast cancer deaths averted
  Median Life-years Gained
  Quality –adjusted life years gained
• Harms
  False-positive mammograms
  Benign biopsy results
  Overdiagnosis

13

13
<table>
<thead>
<tr>
<th>Relative Risk by Density</th>
<th>Median Breast Cancer Deaths Averted Per 1000 Women Screened</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Triennial</td>
</tr>
<tr>
<td>Almost entirely fatty (rr: 1.0)</td>
<td>3.4</td>
</tr>
<tr>
<td>Scattered fibroglandular density (rr: 1.0)</td>
<td>4.0</td>
</tr>
<tr>
<td>Heterogeneously dense (rr: 1.0)</td>
<td>4.8</td>
</tr>
<tr>
<td>Extremely dense</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>5.1</td>
</tr>
<tr>
<td>1.3</td>
<td>6.1</td>
</tr>
<tr>
<td>2.0</td>
<td>8.4</td>
</tr>
<tr>
<td>4.0</td>
<td>12.0</td>
</tr>
</tbody>
</table>
Practice Changes in Women with Dense Breasts

• “As we move toward more personalized medical interventions, tailoring one’s recommendation based on individualized risk and individualized harm becomes increasingly important.”\(^{14}\)

• Bottom line: Need more data for more informed decision making

Game Changer #4

• Consider breast density and personal risk factors when advising regarding mammography intervals
Case

• 48 yo woman presents to your office to establish care. She has a 30 pack year smoking hx and stage I COPD. She wants to quit and asks your advice.

• What evidence based suggestions can you provide?
5. Nicotine Cessation

• Question: Which method results in more abstinence?

- Taper vs abrupt

Methods:
- Primary care practices in UK
- Randomized
- Unblinded
- Followed for 6 months

Nicotine Cessation

• Who?₁⁵
  – 49 yo (avg age)
  – 50% men
  – 94% white
  – 51% post-secondary education
  – ≥ 15 cigarettes/day
  – ***Willing to quit 2 weeks after randomization***
Interventions

- Nicotine patches
- Gradual cessation:
  - Reduce smoking by 25% by end of second week (visit 0)
- May also use short acting NRT
- Abrupt cessation:
  - Do not reduce smoking
- Set quit date in 2 weeks
Randomly assigned \( (n = 697) \)

Allocated to abrupt-cessation group \( (n = 355) \)
- Discontinued intervention
  - No attendance at visit –1: 51
  - No attendance at visit 0: 59
- Abstinence status unknown
  - At 4-wk follow-up: 35
  - At 8-wk follow-up: 43
  - At 6-mo follow-up: 50

  Analyzed for primary outcome \( (n = 355) \)
  - Excluded from analysis: 0 (no withdrawals; ITT analysis carried out)

Allocated to gradual-cessation group \( (n = 342) \)
- Discontinued intervention
  - No attendance at visit –1: 63
  - No attendance at visit 0: 113
- Abstinence status unknown
  - At 4-wk follow-up: 48
  - At 8-wk follow-up: 58
  - At 6-mo follow-up: 59

  Analyzed for primary outcome \( (n = 342) \)
  - Excluded from analysis: 0 (no withdrawals; ITT analysis carried out)
### Results

<table>
<thead>
<tr>
<th>Abstinence Outcome</th>
<th>Abstinent, n (%)</th>
<th>Absolute Difference (95% CI)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gradual Cessation (n=342)</td>
<td>Abrupt Cessation (n=355)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 wk after quitting</td>
<td>134 (39.2)</td>
<td>174 (49.0)</td>
<td>9.8 (2.5-17.1)</td>
</tr>
<tr>
<td>6 months after quitting</td>
<td>53 (15.5)</td>
<td>78 (22.0)</td>
<td>6.5 (0.7-12.2)</td>
</tr>
</tbody>
</table>
Other Interesting Points

• Those who preferred gradual cessation were less likely to be abstinent at 4 weeks.
  – 38.3% vs. 52.2%, p = .007)
• Not abstinent at 4 weeks:
  – 61% preferred gradual cessation
• What about the pre-cessation nicotine?
  – No difference between groups with SE
  – Most symptoms of nicotine overdose were uncommon
Game Changer #5

- For the patient ready to quit, encourage abrupt cessation
- Encourage your patient to be: “ALL IN!”
Wrap-Up

• Have I chosen the right BP target for this patient?
• Who really benefits from aspirin?
• Does this patient really need #90, 3 RF of their PPI?
• Might this woman be served by more frequent mammography?
• How can I more effectively counsel this patient who is ready to stop smoking?
• Individualized medicine