Understanding Therapy, Which strategy to choose, That is the question!

Enas El Gouhary, MBBCh, FRCPC
Objectives

✓ The evidence-based medicine cycle
✓ Start with a case scenario
✓ Ask the clinical question
✓ Key Concepts in RCT
  • Randomization
  • Allocation concealment
  • Blinding
  • Intention-to-treat
  • Treatment effect
✓ Return to case scenario
THE PATIENT

Evidence-based Medicine Cycle

The 5 A’s

ASSESS

ASK

ACQUIRE

APPLY

APPRAISE
Case scenario

✓ Lara was born at 26 weeks. She is now one month old. She will go home in 3 months
✓ 5 years of infertility Rx
✓ Parents were asking how to make the home environment safer for Lara
✓ The neonatologist met with parents and highly recommended to Mike to quit smoking.
✓ Smoking in the household is known to increase the risk of SIDS and Asthma.
Mike is 45 y. Smoking for 20 years. One pack a day. He did not try quitting before because he claims Smoking helps him relax as he feels his job is very stressful.

Today, he is willing to do anything for Lara’s benefit. He is otherwise healthy. He is overweight with BMI of 27.

Mike has googled it and he found this article in reputable journal that talks about how e-cigarettes is superior to Nicotine Patch. Mike would like to discuss with you.
Swapping Cigarettes for Vaping

Aggie Mika | Oct 19, 2017

New evidence suggests e-cigarettes are not without risks to human health, but can be useful in getting people to kick their smoking habit.

Vaping Damages Immune Cells, Researchers Find

Kids in Vancouver school district addicted to nicotine thanks to vaping, says VSB official
Key findings: Aug 2017

There is limited evidence that e-cigarettes may be effective aids to promote smoking cessation.

E-cigarette use is associated with increased risk of ever smoking, and increased frequency and intensity of subsequent smoking among youth and young adults.

More research on the effectiveness of e-cigarettes (with or without nicotine) as a smoking cessation aid is required.
Vaporizers, E-Cigarettes, and other Electronic Nicotine Delivery Systems (ENDS)

Statistics about E-cigarette Use among U.S. Youth

- Among middle and high school students, 3.62 million were current users of e-cigarettes in 2018.¹
- E-cigarette use, from 2017 to 2018, increased 78 percent among high school students (11.7% to 20.8%) and 48 percent among middle school students (3.3% to 4.9%) from 2017 to 2018.¹
- According to a 2013-2014 survey, 81 percent of current youth e-cigarette users cited the availability of appealing flavors as the primary reason for use.²
THE PATIENT

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The 5 A’s

Evidence-based Medicine Cycle
Clinical question formation

**P** - Population

**I** - Intervention

**C** - Comparison

**O** - Outcome

**T** - Type of Question

**T** - Type of (ideal) study design
Clinical question

**P** - Middle aged Smokers

**I** - Electronic cigarettes

**C** - Nicotine Patch

**O** - Smoking Cessation

**T** - Therapy question

**T** - Randomized controlled trial or meta analysis
Search strategy
Therapeutics

E-cigarettes were more effective than nicotine replacement for smoking cessation at 1 year

Clinical impact ratings: ******* ******* *******

Question
How do refillable e-cigarettes and nicotine replacement therapy (NRT) compare for smoking cessation?

Methods
Design: Randomized controlled trial (RCT). ISRCTN60477608.
Allocation: Concealed.*
Blinding: Blinded* (data analysts).
Follow-up period: 1 year after target quit date.
Setting: 3 stop-smoking service sites in England, UK.
Patients: 886 adults (median age 41 y; 52% men) who did not have a strong preference for using e-cigarettes or NRT. Exclusion criteria included current use of either product type, pregnancy, or breastfeeding.

Intervention: Refillable e-cigarettes (n = 439) or NRT (n = 447) added to behavioral support, including weekly individual sessions with clinicians. The e-cigarette group received a starter pack with a 30-mL bottle of e-liquid containing nicotine, 18 mg/mL. Patients were asked to purchase additional e-liquid as needed. The NRT group received a 3-month supply of their choice of nicotine-replacement products (i.e., patch, gum, inhalator, mouth spray, mouth strips, lozenges, microlab, and nasal spray) and were free to switch between products. Patients were asked not to use the nonassigned treatment for ≥4 weeks.

Outcomes: 52-week sustained abstinence (self-report of smoking ≤ 5 cigarettes from 2 wk after target quit date and validated by expired carbon monoxide level < 8 ppm at 52 wk). Secondary outcomes included abstinence at 4 weeks, presence of cough or phlegm, and urge severity.

Patient follow-up: 79% for primary and other outcomes at 52 weeks and 63% at 4 weeks.

Main results
Results are in the Table.

E-cigarettes vs nicotine replacement therapy (NRT) for smoking cessation

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Event rate</th>
<th>RR (95% CI)</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstinence at 4 wk†</td>
<td>44†%</td>
<td>30†%</td>
<td>45 (22 to 74)</td>
</tr>
<tr>
<td>Abstinence at 52 wk</td>
<td>18%</td>
<td>13 (7 to 14)</td>
<td></td>
</tr>
<tr>
<td>Cough at 52 wk</td>
<td>31%</td>
<td>20 (10 to 40)</td>
<td></td>
</tr>
<tr>
<td>Phlegm at 52 wk</td>
<td>20 (9%)</td>
<td>10 (7 to 13)</td>
<td></td>
</tr>
<tr>
<td>Mean change (CO)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity of urge at 1 wk†</td>
<td>2.6</td>
<td>3.0</td>
<td>0.4 (-0.6 to -0.2)</td>
</tr>
<tr>
<td>Severity of urge at 4 wk†</td>
<td>2.0</td>
<td>2.3</td>
<td>0.3 (-0.5 to -0.1)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary. RR, RR, NNT, and CI calculated from nicotine replacement event rates and relative risks in article.
†Self-report of ≤ 5 cigarettes from 2 wk after target quit date plus expired carbon monoxide (CO) level < 8 ppm at 52 wk.
‡Self-report of no smoking from 2 wk after target quit date plus expired CO level < 8 ppm at 4 wk.
§Scores range 1 to 6; higher score = more severe urges.

Conclusion
E-cigarettes were more effective than nicotine replacement therapy for smoking cessation at 1 year.

*See Glossary.

Sources of funding: National Institute for Health Research and Cancer Research UK Prevention Trials Unit.
For correspondence: Dr. D. Pruzi, Queen Mary University of London, London, England, UK. E-mail d.pruzil@gmul.ac.uk.

Commentary
Studies have shown that e-cigarettes have comparable effectiveness to NRT, but the studies used e-cigarettes with low nicotine levels (1).

The RCT by Hajek and colleagues compared the effectiveness of e-cigarettes with an NRT method of patient’s choice on smoking cessation at 1 year when accompanied by behavioral support. It is encouraging that the e-cigarette group had a higher rate of abstinence at 1 year and improved symptoms of nicotine withdrawal. However, use of NRT was low and most abstinent patients in the e-cigarette group (80%) continued to use the products at 1 year.

The use of refillable e-cigarettes with a variety of flavors and nicotine doses may explain the increased efficacy found in this study. Unfortunately, the initial e-cigarette model was discontinued during the trial and a successor had to be substituted. Neither model is currently available for purchase from the manufacturer, which limits the clinician’s ability to implement the treatment as delivered in their practice.

Unlike other medications, e-cigarettes are minimally regulated and have unclear long-term risks, a concern compounded by high rates of long-term e-cigarette use. In this trial, 40% of the e-cigarette group, many of whom were still smoking, continued to use e-cigarettes at 1 year. The safety of dual use of e-cigarettes and combustible tobacco is unknown, and exposure to potential carcinogens with dual use may not be lower than with cigarette smoking alone (2). The risks are too poorly defined to routinely recommend e-cigarettes rather than established treatment methods. However, for patients unable to quit with standard therapies, these data suggest that e-cigarettes may be a useful alternative.

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References

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JC50
ACP Journal Club
Annals of Internal Medicine
21 May 2019
### Search strategy

<table>
<thead>
<tr>
<th>Search Term</th>
<th>Query</th>
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<tbody>
<tr>
<td>smokers</td>
<td>&quot;smokers&quot;[MeSH Terms] OR &quot;smokers&quot;[All Fields]</td>
</tr>
<tr>
<td>nicotine</td>
<td>&quot;nicotine&quot;[MeSH Terms] OR &quot;nicotine&quot;[All Fields]</td>
</tr>
<tr>
<td>replacement</td>
<td>&quot;replantation&quot;[MeSH Terms] OR &quot;replantation&quot;[All Fields] OR &quot;replacement&quot;[All Fields]</td>
</tr>
<tr>
<td>smoking cessation</td>
<td>&quot;smoking cessation&quot;[MeSH Terms] OR (&quot;smoking&quot;[All Fields] AND &quot;cessation&quot;[All Fields]) OR &quot;smoking cessation&quot;[All Fields]</td>
</tr>
</tbody>
</table>
A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy

Peter Hajek, Ph.D., Anna Phillips-Waller, B.Sc., Dunja Przulj, Ph.D., Francesca Pesola, Ph.D., Katie Myers Smith, D.Psych., Natalie Bisal, M.Sc., Jinhao Li, M.Phil., Steve Parrott, M.Sc., Peter Sasieni, Ph.D., Lynne Dawkins, Ph.D., Louise Ross, Maciej Gomienicz, Ph.D., Pharm.D., Qi Wu, M.Sc., and Hayden J. McRobbie, Ph.D.

ABSTRACT

BACKGROUND
E-cigarettes are commonly used in attempts to stop smoking, but evidence is limited regarding their effectiveness as compared with that of nicotine products approved as smoking-cessation treatments.

METHODS
We randomly assigned adults attending U.K. National Health Service stop-smoking services to either nicotine-replacement products of their choice, including product combinations, provided for up to 3 months, or an e-cigarette starter pack (a second-generation refillable e-cigarette with one bottle of nicotine e-liquid [18 mg per milliliter]), with a recommendation to purchase further e-liquids of the flavor and strength of their choice. Treatment included weekly behavioral support for at least 4 weeks. The primary outcome was sustained abstinence for 1 year, which was validated biochemically at the final visit. Participants who were lost to follow-up or did not provide biochemical validation were considered to not be abstinent. Secondary outcomes included participant-reported treatment usage and respiratory symptoms.

RESULTS
A total of 886 participants underwent randomization. The 1-year abstinence rate was 18.0% in the e-cigarette group, as compared with 9.9% in the nicotine-replacement group (relative risk, 1.83; 95% confidence interval [CI], 1.30 to 2.58; P=0.001). Among participants with 1-year abstinence, those in the e-cigarette group were more likely than those in the nicotine-replacement group to use their assigned product at 52 weeks (80% [63 of 79 participants] vs. 9% [4 of 44 participants]). Overall, throat or mouth irritation was reported more frequently in the e-cigarette group (65.3%, vs. 51.2% in the nicotine-replacement group) and nausea more frequently in the nicotine-replacement group (37.9%, vs. 31.3% in the e-cigarette group). The e-cigarette group reported greater declines in the incidence of cough and phlegm production from baseline to 52 weeks than did the nicotine-replacement group (relative risk for cough, 0.8; 95% CI, 0.6 to 0.9; relative risk for phlegm, 0.7; 95% CI, 0.6 to 0.9). There were no significant between-group differences in the incidence of wheezing or shortness of breath.

CONCLUSIONS
E-cigarettes were more effective for smoking cessation than nicotine-replacement therapy, when both products were accompanied by behavioral support. (Funded by the National Institute for Health Research and Cancer Research UK; Current Controlled Trials number, ISRCTN60477605)
Orientation to paper (PICOT)

- **P**: 886 adults attending U.K. National Health Service stop-smoking services (funding)
- 3 service sites May 2015-February 2018.
- Exclusion criteria:
  - pregnant or breast-feeding,
  - strong preference to use or not to use nicotine replacement or e-cigarettes, or currently using either type of product.
All patients received behavioural counselling sessions
Orientation to paper (PICOT)

• Primary **outcome:**

Self-report of smoking ≤ 5 cigarettes from 2 wk after target quit date and validated by expired carbon monoxide level < 8 ppm at 52 wk).
Orientation to paper (PICOT)

- Secondary outcomes:

1 week
- Smoking urge
- Respiratory Sx

4 weeks
- Smoking urge

26 weeks
- Smoking urge

52 weeks
- Smoking urge
- Respiratory Sx
The 5 A’s

Evidence-based Medicine Cycle

THE PATIENT

ASK

ASSESS

ACQUIRE

APPLY

APPRAISE
### Therapy Worksheet = Randomized Controlled Trial

<table>
<thead>
<tr>
<th>How serious is the risk of bias?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Did intervention and control groups start with the same prognosis?</strong></td>
</tr>
<tr>
<td><strong>Were patients randomized?</strong></td>
</tr>
<tr>
<td><strong>Was randomization concealed?</strong></td>
</tr>
<tr>
<td><strong>Were patients in the study groups similar at baseline with respect to prognostic factors?</strong></td>
</tr>
<tr>
<td><strong>Was prognostic balance maintained as the study progressed?</strong></td>
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<tr>
<td><strong>To what extent was the study blinded?</strong></td>
</tr>
<tr>
<td><strong>Were groups prognostically balanced at the study’s conclusion?</strong></td>
</tr>
<tr>
<td><strong>Was follow-up complete?</strong></td>
</tr>
<tr>
<td><strong>Were patients analyzed in the groups to which they were randomized?</strong></td>
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<td><strong>Was the trial stopped early?</strong></td>
</tr>
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</table>

Therapy Worksheet = Randomized Controlled Trial

Critical appraisal
Flow of an RCT
To evenly distribute all **known and unknown** prognostic variables between the groups
Focus on Randomization

P

R

O

List generation
List generation-Simple Randomization

Heads: (A)

Tails: (B)
Goal vs. Outcome of randomization

We may not always achieve this goal
Sentence from the paper...

- Randomization sequences:
  - 1:1 ratio
  - permuted blocks of 20
  - stratified according to trial site
  - Individually randomised
Stratification by Centre and randomization by permuted blocks of 20

<table>
<thead>
<tr>
<th>Centre 1</th>
<th>Centre 2</th>
<th>Centre 3</th>
</tr>
</thead>
</table>
Stratification and Blocking

✓ Stratification: is used to achieve approximate balance of important characteristics without sacrificing the advantages of randomization

✓ Blocking: is used to keep the numbers in each group very close at all times
Randomisation flow chart

Was the study randomized?
Did randomization work?

Table 1. Characteristics of the Participants at Baseline.*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>E-Cigarettes (N=438)</th>
<th>Nicotine Replacement (N=446)</th>
<th>Total (N=884)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) — yr</td>
<td>41 (33–53)</td>
<td>41 (33–51)</td>
<td>41 (33–52)</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>211 (48.2)</td>
<td>213 (47.8)</td>
<td>424 (48.0)</td>
</tr>
<tr>
<td>Employed — no. (%)</td>
<td>299 (68.3)</td>
<td>316 (70.9)</td>
<td>615 (69.6)</td>
</tr>
<tr>
<td>Entitled to free prescriptions — no. (%)</td>
<td>181 (41.3)</td>
<td>179 (40.1)</td>
<td>360 (40.7)</td>
</tr>
<tr>
<td>Median no. of cigarettes per day (IQR)</td>
<td>15 (10–20)</td>
<td>15 (10–20)</td>
<td>15 (10–20)</td>
</tr>
<tr>
<td>Score on the Fagerström Test for Cigarette Dependence†</td>
<td>4.5±2.5</td>
<td>4.6±2.4</td>
<td>4.6±2.4</td>
</tr>
</tbody>
</table>

*Data are presented as median (IQR) or n (%) unless otherwise indicated.
Focus on Randomization

P

R

O

List Generation

Stratification

Blocking
Allocation concealment

P

R

O

List generation

Allocation concealment
The person who is enrolling participants cannot know, predict, or manipulate the list.

Trials with inappropriate allocation concealment are associated with larger estimates of treatment effect.

Was allocation concealed in the study?
Randomization sequences were generated with the of Stata software and were embedded into an application that only revealed the next treatment assignment once a participant had been entered into the database.
Allocation concealment vs. Blinding

• Why all the confusion?
Why all the confusion?

Because both allocation concealment and blinding are about *someone not knowing something*.
<table>
<thead>
<tr>
<th></th>
<th>Allocation Concealment</th>
<th>Blinding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Who?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>What?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>When?</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Allocation Concealment vs. Blinding
<table>
<thead>
<tr>
<th></th>
<th>Allocation Concealment</th>
<th>Blinding</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Who?</strong></td>
<td>Enroller</td>
<td></td>
</tr>
<tr>
<td><strong>What?</strong></td>
<td>The list</td>
<td></td>
</tr>
<tr>
<td><strong>When?</strong></td>
<td>Part of randomization</td>
<td></td>
</tr>
</tbody>
</table>
## Allocation Concealment vs. Blinding

<table>
<thead>
<tr>
<th>Who?</th>
<th>Allocation Concealment</th>
<th>Blinding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who?</td>
<td>Enroller</td>
<td>Patients, caregivers, data collectors, outcome adjudicators, analysts</td>
</tr>
<tr>
<td>What?</td>
<td>The list</td>
<td>Group assignments</td>
</tr>
<tr>
<td>When?</td>
<td>Part of randomization</td>
<td>Starts once allocated</td>
</tr>
</tbody>
</table>
What about Blinding?

Diagram showing the process of allocation concealment and list generation.
Blinding

✓ is masking the group assignment to ensure all groups are treated the same apart from the intervention through the follow up period

✓ Trials with inappropriate blinding are also associated with larger estimates of effect, but not as much as with inappropriate allocation concealment

✓ Is our study blinded?
Data analyses were conducted with blinding to treatment assignments.

Participants were contacted by telephone at 26 and 52 weeks.

Interviewers asked about product use and thus were aware of the treatment assignments.

Participants who reported abstinence or a reduction in smoking of at least 50% at 52 weeks were invited back to provide a carbon monoxide reading at the 52-week validation visit.

Was the study blinded?
Intention-to-treat and follow up

✓ ITT: Were patients analyzed in the groups to which they were randomized

✓ Preserves prognostic balance between the groups (protects ‘the list’)

✓ Reflects real life
Was the study data analysed according to ITT?
Follow up... Why??

✓ Preserves prognostic balance between the groups (protects ‘the list’)
Lost to Follow up for the primary outcome:

886 Underwent randomization

- 439 Were assigned to the e-cigarette group
  - 432 Attended ≥1 session after quit date
    - 376 Completed 4-wk follow-up
      - 352 Completed 6-mo follow-up
        - 356 Completed 12-mo follow-up
          - 438 Were included in primary analysis
            1 Died during the trial

- 447 Were assigned to the nicotine-replacement group
  - 431 Attended ≥1 session after quit date
    - 356 Completed 4-wk follow-up
      - 337 Completed 6-mo follow-up
        - 342 Completed 12-mo follow-up
          - 446 Were included in primary analysis
            1 Died during the trial

19% vs. 23%
In the study:

✓ Participants who were lost to follow-up or did not provide biochemical validation were classified as not being abstinent in the primary analysis.

✓ Another way of dealing with LFU is to do worst case scenario sensitivity analysis.
In the study:

- To assess the effect of missing data on the primary outcome, conducted sensitivity analysis which:
  - excluded participants who did not attend at least 1 behavioral-support session
  - Excluded participants who used the Non-assigned product for at least 5 consecutive days,
  - excluded participants who did not complete the 52-week follow-up
In the study:

-Imputed missing information with the use of multiple imputation by chained equations.
Review: Risk of Bias?

- Randomized: Yes
- Allocation: Yes
- Similar at Baseline: Yes
- Blinding: Not patients or providers but Data analysts
- Follow up: about 80% LTF assumed not having the outcome
- Stopped early for benefit: No
- Intention to treat: Yes
Back to the paper: What are the results?
## Primary Outcome

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>E-Cigarettes</th>
<th>NRT</th>
<th>Relative Risk (95% C.I.)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstinence at 4 weeks</td>
<td>192 (43.8)</td>
<td>134 (30.0)</td>
<td>1.45 (1.22–1.74)</td>
<td>significant</td>
</tr>
<tr>
<td>Abstinence at 52 weeks</td>
<td>79 (18.0)</td>
<td>44 (9.9)</td>
<td>1.83 (1.30–2.58)</td>
<td>significant</td>
</tr>
</tbody>
</table>
### Secondary Outcomes

<table>
<thead>
<tr>
<th>Outcomes At 52 weeks</th>
<th>E-Cigarettes (N = 315)</th>
<th>NRT (N = 279)</th>
<th>Relative Risk (95% C.I.)</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough</td>
<td>97 (30.8)</td>
<td>111 (39.8)</td>
<td>0.8 (0.6–0.9)</td>
<td>significant</td>
</tr>
<tr>
<td>Phlegm</td>
<td>79 (25.1)</td>
<td>103 (36.9)</td>
<td>0.7 (0.6–0.9)</td>
<td>significant</td>
</tr>
<tr>
<td><em>Use of assigned products at 52 wk — no. (%)</em></td>
<td>173 (39.5)</td>
<td>19 (4.3)</td>
<td>9.18</td>
<td></td>
</tr>
<tr>
<td>Continued use in Participants with 1 year abstinence</td>
<td>63/79 (80%)</td>
<td>4/44 (9%)</td>
<td>8.8</td>
<td></td>
</tr>
</tbody>
</table>
Outcome#1: Cough at 52 weeks:

**Step 1:**

- NRT: 40%
- E-Cigarettes: 31%

**Step 2:** Subtract: $40\% - 31\% = 9\%$

**Step 3:** Divide: $31 / 40\% = 0.78$

Risk difference: 9%
Risk ratio: 0.78
What is the risk difference of 9% telling you?

In order to prevent cough in 9 adult smokers, you need to offer E-Cigarettes as Cessation aid to 100.

In order to prevent cough in 1 adult smokers, how many do you need to offer E-Cigarettes as cessation aid?

**Formula**

\[
\text{NNT: } 100 / \text{RD } \%
\]
Number Needed to Treat

✓ Formula: \( NNT = \frac{100}{RD} \)

\[
NNT = \frac{100}{9} = 11.1 \rightarrow 12
\]

NNT = 12

✓ You need to offer E-Cigarettes as Cessation aid to 12 smokers in order to prevent one smoker from having cough
Relative Risk Reduction

✔ Formula: \[ \text{RRR} = 1 - \text{Risk Ratio} \]
\[ \text{RRR} = 1 - 0.78 \]
\[ \text{RRR} = 0.22 \]

✔ Words: The risk of cough in smokers using E-Cigarettes as smoking cessation aid is reduced by 22% compared to NRT.
Outcome#2: Abstinence at 52 w.:

Step 1: NRT 9.9%  E-Cigarettes 18%

Step 2: Subtract: 18% – 9.9% = 8.1%  Risk difference

Step 3: Divide: 18 / 9.9% = 1.8  Risk ratio
What is the risk difference of 8% telling you?

In order to achieve abstinence in 9 adult smokers, you need to offer E-Cigarettes as Cessation aid to 100. In order to achieve abstinence in 1 adult smoker, how many do you need to offer E-Cigarettes as cessation aid?

Formula
NNT: 100 / RD %
Number Needed to Treat

✓ Formula: \[ NNT = \frac{100}{RD} \]

\[ NNT = \frac{100}{8} = 12.5 \rightarrow 13 \]

\[ NNT = 13 \]

✓ You need to offer E-Cigarettes as Cessation aid to 13 smokers in order to achieve abstinence at 1 year for 1 smoker
What is the risk ratio of 1.8 telling you?

The chance for smokers who use E-Cigarettes as smoking cessation aid for abstinence at 52 Weeks is 1.8 times higher than those who use NRT.
Relative Benefit Increase

✔️ Formula: \( RBI = \text{Risk ratio} - 1 \)
\[ RBI = 1.8 - 1 \]
\[ RBI = 0.8 \]

✔️ Words: The probability of smoking Abstinence at 1 year in smokers using E-Cigarettes as smoking cessation aid is 80% higher compared to those using NRT.
Outcome #3: Continued use of Assigned intervention at 52 w.

Step 1:

Step 2: Subtract: \( 39.5\% - 4.3\% = 35.2\% \)

Step 3: Divide. \( 100 / 35.2\% = 2.8\approx 3 \)

Risk difference

NNH
The 5 A’s

THE PATIENT

Evidence-based Medicine Cycle

ASSESS

ASK

ACQUIRE

APPLY

APPRAISE
To use E-Cigarettes for cessation of smoking in comparison to NRT:
- Absolute benefit increase in smoking cessation by 9% NNT 13
- Absolute risk increase of continued use of E-cigarettes 35.2% NNH 3
Back to our Scenario...

✓ Raise hands: how many would recommend E-Cigarettes as Smoking Cessation aid to Mike?

✓ How many will not recommend E-Cigarettes as first line therapy to Mike?

✓ Raise hands: how many will provide E-Cigarettes as an option with further counselling on side effects?
Back to our Scenario...

✓ The best is to have shared decision making with the patient balancing potential benefit and potential harm. Also there is a need to consider alternative available therapy.
Take-home points

- The EBM cycle begins and ends with a patient
- Randomization intends to equally distribute prognostic factors between groups.
- There are multiple factors that may threaten the equal prognosis that we seek to achieve through randomization:
  - Play of chance (small sample size)
  - Improper allocation concealment
  - Not following intention to treat
  - Lost to follow up
Take-home points

✓ Stratification and blocking are about making the list

✓ Allocation concealment is about the enroller not being able to manipulate the random list during enrollment

✓ Blinding is a later step (after allocation) that prevents 5 important groups from being able to treat patients differently based on their group allocation.

✓ Therapy math: simply subtract (Risk Difference) or divide (Risk Ratio).
Take-home points

✓ This is just the beginning...

And also the *END*...
Thank you!