Know Your Chances
AN EVIDENCED BASED APPROACH TO CLINICAL DECISION MAKING

DISCLOSURE STATEMENT
We have no direct financial or proprietary interest in any companies, products or services mentioned in this presentation

Jordan Keith, OD, FAAO
Minneapolis, MN
Objectives

Define a structured question

Find the best evidence and apply it clinically

See through hype in medical news and advertisements
Eye Doctor Roles

Vision
Pain
Rehabilitation
Iatrogenic
Systemic
Emotional/Psych
“Science is a way to keep us from fooling ourselves”
-Richard Feynman, PhD

“The most dangerous words in medicine are ‘In my experience’”
-Mark Crislip, MD
Don’t believe everything you think
“Teaches an important lesson – that we must critically evaluate any medical regimen, regardless of how time-honored. We must look for guidance from well-designed controlled trials when they are available, and we must recognize their absence when they are not.”

– Tim Harkins, OD
“One has only to review the graveyard of discarded therapies to discover how many patients might have benefited from being assigned to a control group.”

-Thomas Chalmers, MD
Steps of EBM

1. Formulate an answerable question
2. Find the best evidence
3. Critically appraise the evidence
4. Apply the evidence
“I see new flashes and floaters”

How often should I expect a RD?

Which patients need further monitoring?
“I see new flashes and floaters”

Acute, symptomatic PVD

Meta-analysis of 1568 patients

At initial presentation

20% retinal break

80% PVD

Follow-up?

- Hemorrhage in peripheral retina
- New symptoms
- Hemorrhage in vitreous

1.8% delayed retinal breaks

Acute symptomatic PVD

Retinal break
- Refer for treatment

No retinal break, risk factors
- Pigmented vitreous cells
- Retinal heme
- Vitreous heme
- New/many symptoms
- Lattice degeneration
- High myopia
- F/U 2-6 weeks

No retinal break, no risk factors
- Patient edu
- No F/U
1. Good Questions Lead to Good Answers

What is my diagnosis?
What are the threats to vision?
Are there treatments for this supported by evidence?
If so, when do we treat?
What do I do with the patient in my chair now?
2. Find the Best Evidence

- **Level 1**: Randomized clinical trials (RCT) with low study errors
- **Level 2**: RCT with high study errors
- **Level 3**: Nonrandomized clinical trials
- **Level 4**: Intervention Case Series
- **Level 5**: Intervention Case Report
3. Critical Appraisal

Who (where) did the study?

The goal of the study?
   Outcomes used?

How was the study carried out?
   Blind? Double blind? Randomized?
   Sample size (N) adequate?

What did they find out?

How does this affect us clinically?
   Are the benefits greater than the risk?
Discrepancy between Results and Abstract Conclusions in Industry- vs Nonindustry-funded Studies Comparing Topical Prostaglandins

“The published abstract conclusion was not consistent with the results of the main outcome measure in 62% of the industry-funded studies compared with 0% of the nonindustry funded studies.”

Twenty-four percent of the industry-funded publications had a statistically significant main outcome measure; however, 90% of the industry-funded studies had proindustry abstract conclusions.

E NANCIAL RELATIONSHIPS BETWEEN PHARMACEUTICAL companies and researchers and funding of medical research by drug companies has increased dramatically during the last two decades. This can result in industry bias where the source of funding of clinical research often has been associated with proindustry results and selective presentation of the results. Industry funding can result in overstate results without statistical support. The purpose of this study was to investigate the relationship between industry- vs nonindustry-funded publications comparing the intraocular pressure (IOP)-lowering efficacy of any or all of latanoprost, travoprost, or bimatoprost 0.03% by evaluating the correspondence between the statistical significance of the publication’s main outcome measure and its abstract conclusions.

PURPOSE: The published abstract conclusion was not consistent with the results of the main outcome measure in 62% of the industry-funded studies compared with 0% of the nonindustry-funded studies.

DESIGN: Retrospective, observational cohort study.

METHODS: English publications comparing the ocular hypotensive efficacy between any or all of latanoprost, travoprost, or bimatoprost 0.03% were searched from the initial search were reviewed. The complete articles were obtained and the references were searched to identify relevant publications of any combination of latanoprost, travoprost, or bimatoprost 0.03%.

RESULTS: Thirty-nine publications were included, of which 29 were industry funded and 10 were nonindustry funded. The published abstract conclusion was not consistent with the results of the main outcome measure in 62% of publications had a statistically significant main outcome measure; however, 90% of the industry-funded publications had a statistically significant main outcome measure and its abstract conclusions.

CONCLUSIONS: Discrepancies were resolved by consultation with the corresponding author. Each publication was reviewed by three independent observers and was evaluated for source of funding, industry author, study quality, statistically significant main outcome measure, correspondence between results of main outcome measure and abstract conclusion, number of abstract conclusions.

Inquiries to Yvonne M. Buys, Toronto Western Hospital, 399 Bathurst Street, Toronto, ON, M5T 2S8, Canada (Y.J.). From the Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada (T.A.). The School of Optometry, University of Ottawa, King Faisal University, King Fahad Hospital of the University, and its abstract conclusions.

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4. Apply the Evidence: Which is Best?

| Treatment A | • Reduced the rate of blindness by 34% |
| Treatment B | • Produced an absolute reduction in blindness of 0.06% |
| Treatment C | • Increased patients’ success rate from 99.82% to 99.88% |
| Treatment D | • 1592 patients needed to be treated to prevent 1 case of blindness |
Threats to vision?

What is my dx?

Diabetic Retinopathy

NPDR

PDR

Macular Disease

Pre-retinal/V-heme

TRD

NVG

Ischemia

Edema
Clinically Significant Macular Edema

**CSME**  
Retinal thickening within 500 microns of fovea

Exudate within 500 microns of fovea with adjacent thickening

Thickening of at least one disc area any part within one disc diameter of center of fovea

---

ETDRS. Ophthalmology. 1985; 103:1796-1806  
ETDRS. Ophthalmology. 1987; 94: 761-774
**Clinically Significant Macular Edema**

<table>
<thead>
<tr>
<th>CSME</th>
<th>Retinal <em>thickening</em> within 500 microns of fovea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Exudate within 500 microns of fovea with adjacent <em>thickening</em></td>
</tr>
<tr>
<td></td>
<td><em>Thickening</em> of at least one disc area any part within one disc diameter of center of fovea</td>
</tr>
</tbody>
</table>

ETDRS. *Ophthalmology*. 1985; 103:1796-1806

ETDRS. *Ophthalmology*. 1987; 94: 761-774
Treatments for DME

- **Laser**
  - ETDRS

- **Steroids**
  - DRCR.net

- **Anti-VEGF**
  - RESTORE
  - RISE and RIDE
  - DA VINCI
  - VIVID/VISTA

• < 3% of patients with CSME improved vision by 15 letters or more with laser over 3 years
“In patients with CSME, focal laser reduced the risk of moderate vision loss by 50%...”
Threats to vision?

What is my dx?

Diabetic Retinopathy

NPDR

Macular Disease

Ischemia

Edema

PDR

Pre-retinal/V-heme

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NVG
4-2-1 Rule: Raising the (Risk) Bar

4. Severe retinal hemorrhages in 4 quadrants
2. Venous beading in 2 quadrants
1. IRMA in 1 quadrant
NPDR $\rightarrow$ PDR in 1 Year

**Mild**
- 5% risk of progression to PDR

**Moderate**
- 15% risk of progression to PDR

**Severe**
- 52% risk of progression to PDR
- Meets **ONE** criteria of 4-2-1 Rule

**Very Severe**
- 75% risk of progression to PDR
- Meets **TWO** criteria of 4-2-1 rule

## Follow-up intervals in months

<table>
<thead>
<tr>
<th>Severity of NPDR</th>
<th>American Academy of Ophthalmology</th>
<th>American Optometric Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Mild</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>6-12</td>
<td>12</td>
</tr>
<tr>
<td>Severe</td>
<td>2-4</td>
<td>3-4</td>
</tr>
<tr>
<td>Very Severe</td>
<td>2-4</td>
<td>2-3</td>
</tr>
</tbody>
</table>

4-2-1 Rule

AAO. Preferred Practice Pattern. Diabetic Retinopathy. 2013
AOA. Evidence-Based Clinical Practice Guidelines. Eye Care of the Patient with Diabetes Mellitus. 2014
8-year Incidence of CHD and Stroke as a Hazard Ratio (HR) in Japanese Type 2 Diabetics (N=2033)

<table>
<thead>
<tr>
<th>Retinal Finding</th>
<th>Coronary Heart Disease</th>
<th>Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild-Mod NPDR</td>
<td>1.69 (95% CI 1.17-2.97)</td>
<td>2.69 (95% CI 1.03-4.86)</td>
</tr>
<tr>
<td>Retinal hemes/MA</td>
<td>1.63 (95% CI 1.04-2.56)</td>
<td>Not associated (P=0.06)</td>
</tr>
<tr>
<td>CWS</td>
<td>Not associated (P=0.66)</td>
<td>2.39 (95% CI 1.35-4.24)</td>
</tr>
</tbody>
</table>

Communicate Diabetic Eye Exam Results to PCP!

Kawasaki R, et al. Ophthalmology 2013;120(3)574-582
Threats to vision?

What is my dx?

Diabetic Retinopathy

NPDR

4-2-1 Rule

PDR

Macular Disease

Edema

Ischemia

Pre-retinal/V-heme

TRD

NVG

PDR

Macular Disease

Edema

Ischemia
High-Risk Characteristics

NVD $\geq \frac{1}{4}$ disc area

Any NVD or NVE with pre-retinal or vitreous heme
In patients with HRC, PRP reduces the risk of profound vision loss by 50%...”
What Was the Original Risk?

<table>
<thead>
<tr>
<th></th>
<th>No Tx</th>
<th>Tx</th>
<th>RRR</th>
<th>ARR</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>90%</td>
<td>45%</td>
<td>50%</td>
<td>45%</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>25%</td>
<td>12.5%</td>
<td>50%</td>
<td>12.5%</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>10%</td>
<td>5%</td>
<td>50%</td>
<td>5%</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>2/million</td>
<td>1/million</td>
<td>50%</td>
<td>0.0001%</td>
<td>1,000,000</td>
<td></td>
</tr>
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“In patients with CSME, focal laser reduced the risk of moderate vision loss by 50%…”

“In patients with HRC, PRP reduces the risk of profound vision loss by 50%…”
### Which Treatment is Best?

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Description</th>
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<tr>
<td>Treatment A</td>
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<td>Treatment C</td>
<td>Increased patients’ success rate from 99.82% to 99.88%</td>
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<tr>
<td>Treatment D</td>
<td>1592 patients needed to be treated to prevent 1 case of blindness</td>
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</table>
Treatment Studies

Relative Risk Reduction (RRR)
- Efficacy of treatments commonly reported this way in headlines/media/by pharmaceutical companies
- Use caution when reading this stat: can be misleading and commonly overstates the benefit

Absolute Risk Reduction (ARR)
- Much more meaningful clinically
- Tells us what % of patients benefited from the treatment

Number Needed to Treat (NNT)
Other Treatments for DME?

- Steroids as effective as laser but the side effects were worse
Anti-VEGF

DA VINCI Study
Trap-Eye anti-VEGF  Macular laser

Mean change in BCVA from baseline at 1 year
Gain 11 letters  Loss 1 letter

Eyes gained ≥ 3 lines BCVA
38%  11%

ARR = 27%
NNT = 3

RISE and RIDE

Mean change from baseline BCVA

+8.5-9.9 letters more in ranibizumab vs. sham

% with BCVA ≥20/40

60% ranibizumab  36% sham  ARR 24% NNT 4

Progression to PDR and needing PRP

< 1% ranibizumab  11% sham

RISE and RIDE. Ophthalmology 2012: 119: 789-801
Anti-VEGF iatrogenic?

Endophthalmitis = 1%
Transient IOP increase
Monthly injections
“My vision was fine until you sent me to that retinal specialist for laser”
PRP for PDR

5-9 letters loss from baseline

- 1 sitting (N=84)
- 4 sittings (N=71)

- 0%
- 5%
- 10%
- 15%
- 20%
- 25%
- 30%

- 3 day
- 4 weeks
- 17 weeks
- 34 weeks

PRP for PDR

≥ 10 letters loss from baseline

1 sitting (N=84)  4 sittings (N=71)

## Anti-VEGF for PDR: 2 Year Results

<table>
<thead>
<tr>
<th></th>
<th>Lucentis:</th>
<th>PRP:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in visual acuity</td>
<td>+2.8 letters</td>
<td>+0.2 letters</td>
</tr>
<tr>
<td>Change in visual field total point score</td>
<td>-23 dB</td>
<td>-422 dB</td>
</tr>
<tr>
<td>DME development</td>
<td>9%</td>
<td>28%</td>
</tr>
<tr>
<td>Eyes without PDR on fundus photos</td>
<td>35%</td>
<td>30%</td>
</tr>
</tbody>
</table>

DRCR.net. JAMA 2015;314(20):2137-2146
Patient Education

- Answer the question, “Why do I need yearly dilated eye exams?” every year even if they don’t ask it.
- Help them understand their vascular disease.
- Encourage them to be intimately aware of their numbers (BS, HbA₁C, BP, cholesterol).
- Keep in mind number one indicator of complications is duration.
- You don’t “know” how hard it is to control the disease unless you have lived with it.
These analyses of more than 4500 overweight adults with type 2 diabetes confirm that complete remission associated with an intensive lifestyle intervention, when defined by glucose normalization without need for hypoglycemic medications, is rare.

Diabetes traditionally has been considered a progressive, incurable condition wherein the best-case scenario after diagnosis is tight metabolic and risk factor management to forestall vascular and neuropathic complications. This notion that type 2 diabetes is an irreversible, incurable condition has been considered a progression of the type 2 diabetes to prediabetes or nondiabetic level of glycemia.”

“

**Context** The frequency of remission of type 2 diabetes achievable with lifestyle intervention is unclear.

**Objective** To examine the association of a long-term intensive weight-loss intervention with remission of type 2 diabetes.
Ocular HTN

Threats to vision?
Treatment?
When/who do we treat?
  Everyone?
  No one?
  Depends?
“Treating a patient with ocular hypertension reduces the risk of glaucoma by 50%...”
How Effective is Treatment?

<table>
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“Treating a patient with ocular hypertension reduces the risk of glaucoma by 50%...”

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713
What Were the Outcomes Used?

Surrogate endpoints vs. clinical endpoints

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713
How Was Ocular HTN Defined?

Age 40 – 80
IOP 24-32 mmHg in one eye and 21-32 mmHg in the other
Gonioscopically open angles
2 normal HVF tests each eye
Normal ONHs

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713
Treatment?

Reduction of IOP by 20% or more and reach an IOP of 24 or less

Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713
Treat everyone?

Treat no one?

It depends?
Iatrogenic to Treating Everyone?

$20/\text{bottle} \times 12 \text{ months} \times 5 \text{ years} \times 20 \text{ NNT} = \$24,000

\% \text{ of patients we didn’t help} = 95\%

\% \text{ of complication} = 100\%
Treat no one?
Is there penalty in delaying treatment?

- **At 5 years**
  - No Tx = 10%
  - Tx = 5%

- **At 7.5 years**
  - Start Tx
  - Continue Tx

- **At 13 years**
  - Delayed Tx = 22%
  - Early Tx = 16%

References:
- Kass MA et al. OHTS. Arch Ophthalmol. 2002;120:701-713
It Depends?

- Age, health status, patient preference
- Baseline risk determined by OHTS/EGPS calculator?
  - Age
  - IOP
  - CCT
  - PSD
  - C/D
After 13 years % developing glaucoma based on initial risk

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Delayed Tx (%)</th>
<th>Early Tx (%)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest risk at baseline (&lt;5%)</td>
<td>8</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>Moderate risk at baseline (5-15%)</td>
<td>19</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>High risk at baseline (&gt;15%)</td>
<td>40</td>
<td>28</td>
<td>8</td>
</tr>
</tbody>
</table>

Kass MA et al. OHTS. Arch Ophthalmol. 2010;128(3):276-287
What Do I Do With this Patient?

Assess risk
- Age, IOP, CCT, C/D

Testing
- HVF, ONH/RNFL analysis, stereo ONH photos, gonioscopy, pachymetry
Testing
“Medicine is a science of uncertainty and an art of probability”

-Sir William Olser, MD
Sensitivity vs. Specificity

Positive Predictive Value vs. Negative Predictive Value
Riddle
Probability of breast cancer = 0.8%

Mammography screening program of 40-50 yo women with no symptoms

What is the probability that a positive mammogram is actually breast cancer?

Has breast cancer

Positive mammogram 90%

Does not have breast cancer

False positive mammogram 7%

Positive mammogram 90%

Does not have breast cancer

False positive mammogram 7%
0.8% with breast cancer
90% sensitivity
93% specificity

Positive Predictive Value  = \( \frac{7}{77} = 9\% \)
1% adult population w/ glaucoma
90% sensitivity
90% specificity

Positive Predictive Value = 9/108 = 8%
10% adult population w/ glc when IOP >21
90% sensitivity
90% specificity

Positive Predictive Value = 50%
Testing

Sensitivity vs. Specificity

- Efficacy of tests commonly reported this way
- Clinically not valuable information in isolation
- Usefulness of test depends on initial risk of population

More judicious testing leads to fewer false positives and higher positive predictive value
“In general, tests do not make a diagnosis – you do, based on the test result in the context of how likely you believed the disease was to begin with.”

-Richard Gross, MD
“Because there is no need to show that an instrument has any real value in disease detection or management before it is brought to market, we have become enamored with sophisticated analysis algorithms and colorful printouts before we have studies that show what the results of the tests mean. This approach is fueled, of course, by economic interests. Industry is motivated to create product and we [ophthalmologists] provide the key opinion leaders to drive the use of what is developed . . .”

-Paul Lichter, MD
“... Cynical as it seems, these devices belong in the laboratory, before they are marketed as being of value and before billing codes are established for their use, which simply drive up the costs of care without making any impact whatsoever on the critical outcome in glaucoma—preservation of vision related QOL.”

-Paul Lichter, MD
Patient Education

- You don’t know your patient’s risk for glaucoma.
  - Help them understand what the risk is for people like them.
- Empower patients to make the decision to treat or not to treat on their own.
- Acknowledge their fear and help them understand why that won’t happen.
- Have a philosophy for treating glaucoma.
Dry ARMD

Nutrients

Retina

Choroid

Waste

RPE

Bruch’s
Dry AMD
Dry AMD
Wet AMD
Wet AMD
AMD

- Dry
  - 90%
  - 90% functional vision
  - 10% severe vision loss (GA)

- Wet
  - 10%
  - 90% severe vision loss
Threats to vision?

What is my dx?

AMD

Dry

Wet

RPE Atrophy

RPE Atrophy

CNVM
### MARINA for CNVM

#### 20/40 BCVA or better

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucentis</td>
<td>40%</td>
<td></td>
</tr>
<tr>
<td>Sham</td>
<td>11%</td>
<td>3.5</td>
</tr>
</tbody>
</table>

#### Lost ≤ 3 lines BCVA from baseline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucentis</td>
<td>94%</td>
<td>3</td>
</tr>
<tr>
<td>Sham</td>
<td>62%</td>
<td></td>
</tr>
</tbody>
</table>

#### Improved ≥ 3 lines BCVA from baseline

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Effect</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lucentis</td>
<td>30%</td>
<td>4</td>
</tr>
<tr>
<td>Sham</td>
<td>5%</td>
<td></td>
</tr>
</tbody>
</table>

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iatrogenic?

Endophthalmitis = 1%

Transient IOP increase

Monthly injections
“Despite the lack of convincing evidence, the marketing and use of antioxidants and zinc in eye-targeted formulations has become common practice.”

- AREDS I
“Taking AREDS I supplements reduces the risk of AMD progression by 25%...”
AREDS 1

- **Category 1**: No AMD. BCVA 20/32 or better in both eyes.
- **Category 2**: Mild/borderline AMD. BCVA 20/32 or better in both eyes.
- **Category 3**: Moderate AMD. BCVA 20/32 or better in one eye.
- **Category 4**: No signs of advanced AMD in the study eye and BCVA 20/32 in the fellow eye.

AREDS 1

Category 1
- Placebo
- Antioxidants
- Zinc
- Antioxidants + Zinc

Category 2
- Placebo
- Antioxidants
- Zinc
- Antioxidants + Zinc

Category 3
- Placebo
- Antioxidants
- Zinc
- Antioxidants + Zinc

Category 4
- Placebo
- Antioxidants
- Zinc
- Antioxidants + Zinc

Outcome: Progression to ADV AMD at 5 years

Probability by Category

- Category 1: 0.004%
- Category 2: 1.3%
- Category 3: 18%
- Category 4: 43%

Probability by Treatment (Placebo vs. Treatment)

- Category 1: Data not evaluated
- Category 2: No sig difference
- Category 3: Data not reported
- Category 4: Data not reported

Combined categories 3 AND 4

- Placebo = 28%
- Antioxidants + Zinc = 20%
- ARR = 8%
- NNT = 12.5

Outcome: 15-letter decrease from baseline at 5 years

Probability by Treatment (Placebo vs. Treatment)

<table>
<thead>
<tr>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
<th>Category 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data not evaluated</td>
<td>No sig difference</td>
<td>Data not reported</td>
<td>Data not reported</td>
</tr>
</tbody>
</table>

Combined categories 3 AND 4

| Placebo = 29%             | Antioxidants + Zinc = 23% | ARR = 6%                 | NNT = 17                 |

Iatrogenic?

$142/\text{year} \times 5 \text{ years} \times 17 \text{ NNT} =

\$12,070

\% \text{ of patients we didn’t help} = 92-94\%

\% \text{ of complication} = 100\%
Iatrogenic?

“We do not know the long-term health effects of supplementation with these high doses of vitamins and minerals”

-AREDS I

**Vitamin E and the Risk of Prostate Cancer: The Selenium and Vitamin E Cancer Prevention Study**


"Dietary supplementation with vitamin E significantly increased the risk of prostate cancer among healthy men"

**Main Outcome Measures**

Prostate cancer incidence was the primary outcome measure. The study lasted for a median follow-up of 13 years, with 48,420 person-years of follow-up. The risk of prostate cancer was compared between those who received vitamin E supplements and those who did not.

**Results**

Compared with the placebo group, the absolute increase in risk of prostate cancer per 1000 person-years was 0.8% for selenium, 0.4% for vitamin E, and 1.7% for both agents. The hazard ratio (HR) for prostate cancer in the selenium plus vitamin E group was 1.05 (99% CI, 0.89-1.22), compared with the placebo group. This increase was statistically significant (P=0.008). The HR for prostate cancer in the selenium group was 1.09 (99% CI, 0.93-1.27), also statistically significant (P=0.008).

**Conclusion**

Dietary supplementation with vitamin E and selenium did not significantly reduce the risk of prostate cancer. In fact, the risk of prostate cancer was increased by 5% in the selenium and vitamin E group, compared with the placebo group. This finding suggests that vitamin E supplementation may not be a beneficial strategy for preventing prostate cancer.

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**High dose vitamin E supplementation may increase the risk for hemorrhagic stroke and should be used with caution in people with heart disease**

Schurs et al. BMJ 2010; 341:c5702

**Less is More**

Dietary Supplements and Mortality Rate in Older Women

The Iowa Women’s Health Study


"In older women, several commonly used dietary vitamins and mineral supplements may be associated with increased total mortality rate"

**Methods**

We assessed the use of vitamin and mineral supplements and total mortality rate in a population-based cohort study of 78,136 cohorts.

**Results**

The use of 1 or more dietary supplements was associated with a 16% increase in total mortality rate. The associations were strongest for vitamin E supplements (hazard ratio, 0.91; 95% confidence interval, 0.88-0.94) and vitamin D supplements (hazard ratio, 0.90; 95% confidence interval, 0.88-0.92). The use of multiple dietary supplements was associated with a 21% increase in total mortality rate (hazard ratio, 0.79; 95% confidence interval, 0.76-0.82).

**Conclusion**

Dietary supplements may increase total mortality rate, particularly vitamin E and vitamin D supplements. The use of multiple dietary supplements was associated with a higher increase in total mortality rate.

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**Effects of Long-term Vitamin E Supplementation on Cardiovascular Events and Cancer: Results of a Randomized Controlled Trial**


"In patients with vascular disease or DM, long-term vitamin E supplementation may increase the risk for heart failure"

**Objective**

To evaluate the use of vitamin E and mineral supplements on total mortality rate; this association is strongest with supplemental iron. In contrast to the Iowa Women’s Health Study, results of epidemiologic studies in the United States, the United Kingdom, and Australia show a beneficial effect of dietary supplements on total mortality rate.

**Methods**

We evaluated the use of vitamin and mineral supplements and total mortality rate in a population-based cohort study of 78,136 cohorts.

**Results**

The use of 1 or more dietary supplements was associated with a 16% increase in total mortality rate. The associations were strongest for vitamin E supplements (hazard ratio, 0.91; 95% confidence interval, 0.88-0.94) and vitamin D supplements (hazard ratio, 0.90; 95% confidence interval, 0.88-0.92). The use of multiple dietary supplements was associated with a 21% increase in total mortality rate (hazard ratio, 0.79; 95% confidence interval, 0.76-0.82).

**Conclusion**

Dietary supplements may increase total mortality rate, particularly vitamin E and vitamin D supplements. The use of multiple dietary supplements was associated with a higher increase in total mortality rate.
“Taking AREDS 2 supplements reduces the risk of AMD progression by 26%...”
AREDS 2

AREDS 1 (placebo)  + Lutein & Zeaxanthin  + DHA & EPA  + L/Z + DHA & EPA

AMD Categories 3 and 4

Outcome: Progression to ADV AMD at 5 years

<table>
<thead>
<tr>
<th>AREDS I</th>
<th>+ L/Z</th>
<th>+ DHA &amp; EPA</th>
<th>+ L/Z &amp; DHA/EPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>31%</td>
<td>29%</td>
<td>31%</td>
<td>30%</td>
</tr>
</tbody>
</table>

Outcome: Moderate vision loss (≥ 3 lines of acuity) from baseline

| AREDS 1 | No additional effect | No additional effect | No additional effect |

Subgroup analysis: lowest dietary consumption of Lutein/Zeaxanthin

HR 0.74 (95% CI, 0.59-0.94; P=(0.01)

What Do I Do With My Patient?

- Patient Education: this is common and most don’t go blind
- Lifestyle changes (diet, smoking)
- Pros/cons supplements vs. no supplements
- Home Amsler grid?

1/10 develop CNVM → ¼ HAG find CNVM → 1/3 CNVM benefit Tx → NNT = 120

“Even when cure is impossible, healing is not necessarily impossible. While medical science has limits, hope does not.”

-Bernard Lown, MD

“To cure sometimes, to relieve often, to comfort always”

-Edward Trudeau, MD
Objectives

Define a structured question

Find the best evidence and apply it clinically

See through hype in medical news and advertisements
Resources