Does Selenium protect against lung cancer?
Do Selenium supplements reduce the incidence of lung cancer in healthy individuals?

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The question

Mr Wilson’s father recently died of lung cancer. He is very worried about getting the same illness, and has heard that Selenium supplements help protect against lung cancers. He wants your advice before he buys any.

Do selenium supplements reduce the incidence of lung cancer in healthy adults?

<table>
<thead>
<tr>
<th>P</th>
<th>Healthy adults</th>
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<tbody>
<tr>
<td>I</td>
<td>Selenium supplements</td>
</tr>
<tr>
<td>C</td>
<td>No supplements</td>
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<tr>
<td>O</td>
<td>Incidence of lung cancer</td>
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</tbody>
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The search terms

We searched Pubmed, TRIP database and the Cochrane collaboration with the following search terms:

(selenium OR selenium supplement* or seleno*) AND (prevent* OR protect*) AND (lung cancer OR (lung OR pulmonary) carcinoma)

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<th>P</th>
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<tbody>
<tr>
<td>selenium</td>
<td>prevent* or protect*</td>
<td>lung cancer OR (lung OR pulmonary) carcinoma</td>
<td></td>
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<tr>
<td>OR</td>
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<td>selenium</td>
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<td>supplements</td>
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<td>OR</td>
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<td>seleno*</td>
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<td>AND</td>
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</table>
The search and search results

These searches produced the following results:
Scopus- 3562
PubMED- 38
Cochrane collaboration- 2 systematic reviews

Search results were ranked by “relevance” to the search criteria

We chose one paper to look at in more depth:


Reasons for study inclusion:
• It is a recent systematic review and includes a meta-analysis
• More narrow (and relevant) scope than the other systematic reviews
• Includes three RCTs on the chemopreventative effects of selenium in analysis
• Therefore, a good candidate to help us answer the clinical question
### The study appraisal - relevance

<table>
<thead>
<tr>
<th>PICO</th>
<th>What we wanted</th>
<th>What it looked at</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Healthy adults</td>
<td>• Selenium + cisplatin as lung cancer treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Selenium to prevent lung cancer recurrence</td>
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<tr>
<td></td>
<td></td>
<td>• Selenium to prevent lung cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 3 RCTs</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Selenium supplements</td>
<td>• Selenium supplement</td>
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<tr>
<td></td>
<td></td>
<td>• Lone-standing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ruled out confounding dietary/supplement studies</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>No supplements</td>
<td>• No supplements</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Lung cancer incidence</td>
<td>• All types of lung cancer included</td>
</tr>
</tbody>
</table>
The study appraisal - validity

Research aim:

A systematic review of clinical evidence to assess the risks and benefits of selenium supplementation in preventing lung cancer

1) Plasma selenium as predictor of lung cancer incidence

2) Selenium supplements as prevention of primary lung cancer

3) Selenium as preventer of secondary lung cancer (relapse)

No mention of smokers vs non-smokers
The study appraisal - validity

Literature search methodology:

*Scanned:* CINAHL, AltHealth Watch, Cochrane, National Library of Science and Technology, Pubmed, and EMBASE. Date limits not provided.

**Searches and search terms used:** appropriately broad to capture all relevant articles, updated searches three times during the data screening and extraction period. Two separate searches - efficacy and interactions/pharmacokinetics.

**Inclusion criteria:** Clinical surrogate trials, included if they examined endpoints directly related. Observational- objective selenium status and lung cancer risk prospectively or conducted in patients with lung cancer. Preclinical- +/-/0

**Exclusion criteria:** studies examining dietary intake were excluded, non-English

Interpretation: “In the absence of reported levels of significance, the authors’ interpretation was used to guide classification”
The study appraisal - validity

Data and interpretation:

Meta-analysis performed, heterogeneity assessed using $I^2$

No box-whisker plots

Good objective data analysis:
“odds ratio (OR) 0.93 (95% confidence interval 0.61–1.43);”

Mixed with subjective analysis and cherry-picking
Data from only 2 of 5 trials was pooled in one analysis
“Nutritional Prevention of Cancer (NPC) trial presents the strongest evidence in support of…”
The Results (interpretation of findings)

3994 articles screen, 130 included for full analysis. 78- efficacy analysis, 51- interactions analysis.

**Preclinical studies:** 36/41 showed results supporting an anti-cancer effect (biochemical markers)

**Surrogate trials:** 2 selenium supplementation to 300mcg/d= increases in serum glutathione peroxidase, increased neutrophil oxidative metabolic activity and immunological function however no clinical correlates stated in these results.

**Observational studies:** (23/26 were retrospective)
16/26- inverse relationship between selenium status and LC risk.
10/26- No sig. ef.
** 5/26- possibility of a U-shaped dose-effect curve. 1 showed sig. increased risk >90ng/ml (OR 10.32, 95% CI 1.88-138.2) 4 showed non-sig. authors noted interpretation/ pooling was limited due to different cut offs used.
The Results (interpretation of findings)

RCTs: 5.
3- prevention, 1- following early resection, 1- conjunction with cisplatin. Data was pooled from two trials- unclear how these trials were chosen. The authors quoted strongest evidence was from NPC trial- melanoma! mortality and risk of lung cancer sig. reduced.

Diabetes risk:
Two of the five RCT’s reported an increase in the diabetes risk with supplementation. NPC trial found 55% increase (95% CI 1.03–2.33), SELECT non-sig increase.

Authors overall interpretation:
“ The results of our review suggest that selenium supplementation may offer benefit with individuals at risk of lung cancer, however the association with diabetes warrants judicious use”. Authors cite the NPC trial frequently as having strong evidence...
The Implications

On balance: perhaps insufficient clinically relevant data to support advising Mr Wilson to begin taking selenium.

Reasons-
- Some suggestion that does >120ng/dl will increase cancer risk - although not fully corroborated
- Diabetes risk.
- Side effects of selenium toxicity and selenium supplementation (gastrointestinal and dermatological symptoms were reported in the trials. SELECT trial: SI rates of alopecia and dermatitis (RR 1.28, 1.17 resp)

Consider other factors which may be more important:
  - Smoking
  - Other lifestyle factors
  - Explanation of hereditary risk

What shall we do for Mr Wilson?
Reassurance, anxiety relief, and continued assessment of the literature r.e. further elucidation of dose response and RCTs.
- ? But it may put his worries at rest- would we go so far as to actively discourage?