

[Access through your institution](#)to view subscribed content **from home**[Outline](#) [Get Access](#) [Share](#) [Export](#)

Free Radical Biology and Medicine

Volume 127, 1 November 2018, Pages 36-45

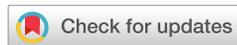
Review Article

Five threads: How U-shaped thinking weaves together dogs, men, selenium, and prostate cancer risk ☆

David J. Waters  , Emily C. Chiang

Center for Exceptional Longevity Studies, Gerald P. Murphy Cancer Foundation, 3000 Kent Avenue, Suite D1-104, West Lafayette, IN, USA

Received 5 November 2017, Revised 21 December 2017, Accepted 31 December 2017, Available online 2 January 2018.

[Show less](#) <https://doi.org/10.1016/j.freeradbiomed.2017.12.039>[Get rights and content](#)

Highlights

- A U-shaped dose response informs more selenium is not always better for risk reduction.
- Dog studies can integrate results of human studies and guide discovery of mechanisms.
- A dog U-curve provides a map for interpreting the results of men studied in SELECT.
- The critical hypothesis regarding selenium and prostate cancer risk remains untested.
- U-shaped thinking is an essential element of personalized (precision) medicine.

Abstract

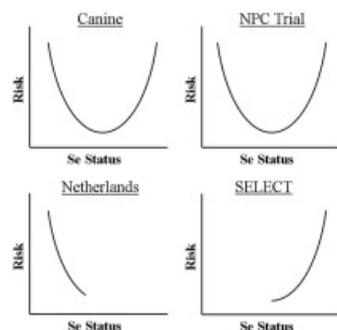
Prostate cancer is one of the leading causes of cancer-related mortality among men living in developed countries, making the development of safe, practical approaches to prostate cancer risk reduction a high research priority. The relationship

[Access through your institution](#)
to view subscribed content **from home**
[Outline](#)

[Get Access](#)
[Share](#)
[Export](#)

cancer risk. Our discovery of a [U-shaped dose-response](#) between toenail selenium concentration and prostatic DNA damage in dogs remarkably parallels data on the relationship between selenium status and prostate cancer risk in men. Notably, the dog U-curve provides a plausible explanation for the unanticipated increase in prostate cancer incidence among men with highest baseline selenium who received selenium supplementation in the largest-ever prostate cancer prevention trial (SELECT). Moreover, the dog U-curve guided the discovery of a non-antioxidant, anti-carcinogenic mechanism of organic selenium — the preferential triggering of [apoptosis](#) in DNA damaged cells, which we have termed “homeostatic housecleaning”. Taken together, the data from dogs and men indicate that increasing selenium status will not necessarily be associated with prostate cancer risk reduction. Landing in the trough of the U — achieving mid-range selenium status — is better than being too low or too high. Personalizing health promotion in a more-is-not-necessarily-better world poses distinctive challenges. Dog studies can be relied upon to contribute important insights into dose-dependent and form-dependent effects — two critical aspects of selenium biology that will have to be disentangled if the burgeoning science of selenium is to be translated into effective strategies for human [disease prevention](#). Beyond contributing to understanding the role of selenium in biology, our work situates the concept of U-shaped thinking at the core of personalized medicine and precision [nutrition](#).

Graphical abstract


[Download : Download high-res image \(81KB\)](#)
[Download : Download full-size image](#)
[Previous](#)
[Next](#)

Keywords

Translational research; Comparative oncology; Prostate cancer prevention; Non-linear dose response; Personalized medicine; Precision nutrition

[Special issue articles](#)
[Recommended articles](#)
[Citing articles \(6\)](#)

* A talk delivered at the Se 2017 Conference in Stockholm, Sweden August 16, 2017 titled “Of Dogs and Men: A Review of the Translational Impact of Dog Studies on Selenium and Prostate Cancer Risk”.

[View full text](#)

Access through your institution

to view subscribed content **from home**

-  [Outline](#)
-  [Get Access](#)
- [Share](#)
- [Export](#)



[About ScienceDirect](#)



[Remote access](#)

[Shopping cart](#)

[Advertise](#)

[Contact and support](#)

[Terms and conditions](#)

[Privacy policy](#)

We use cookies to help provide and enhance our service and tailor content and ads. By continuing you agree to the **use of cookies**.

Copyright © 2020 Elsevier B.V. or its licensors or contributors. ScienceDirect ® is a registered trademark of Elsevier B.V.

ScienceDirect ® is a registered trademark of Elsevier B.V.