**PhD Thesis Title:** Framework for algorithmically optimizing longitudinal health outcomes: Examples in cancer radiotherapy and occupational radiation protection

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**ABSTRACT:**

Advancements in the treatment of non-infectious disease have enabled survival rates to steadily increase in recent decades (*e.g.*, diabetes, heart disease, and cancer). Epidemiological studies have revealed that the treatments for these diseases can have life–threatening and/or life–altering effects. Thus, realizing the full beneficial potential of advanced treatments necessitates new tools to algorithmically consider all major components of the health outcome, including benefit and detriment. The goal of this dissertation was to develop a framework for improving projected health outcomes following planned radiation exposures in consideration of all beneficial and detrimental, early and late, and fatal and non-fatal effects.

We designed a generally applicable framework for aggregating the benefits and detriments of planned exposures to individuals, groups, and populations. We demonstrated the utility of this framework with illustrative hypothetical example applications to emergency response, diagnostic radiology, and cancer radiotherapy. Finally, we used this new framework to directly optimize health outcomes in a population of men with prostate cancer receiving radiotherapy. We compared the resulting projected outcomes to those of conventional treatment-planning methods.

Applications of the comprehensive framework to three illustrative scenarios revealed the utility of this framework for guiding objective and algorithmic decision making. Radiotherapy outcome-optimization methods yielded equivalent or superior projected health outcomes compared to conventional dose-optimization methods for every patient in the population. On average, outcome-optimized plans increased the probability of treatment benefit by 1%, while simultaneously decreasing the cumulative probability of long- and short-term treatment side effects by 3% compared to conventional treatment plans. We estimate that this would add up to 7 additional healthy-life months to each patients' life expectancy compared to that from conventional treatment plans.

The major finding is that it is feasible to directly optimize the projected health outcome of planned radiation exposures (*e.g.*, industrial, diagnostic, or therapeutic) in a personalized or population-averaged manner. Furthermore, these methods are entirely compatible with current approaches and limits. This work, taken together, provides a comprehensive methodological framework that could enable a paradigm shift towards more objective and automated approaches to realizing the full beneficial potential of planned exposures.

**References to author publications that relate specifically to the dissertation**:

1. **Wilson LJ**, Newhauser WD, Schneider CW. *An objective method to evaluate radiation dose distributions varying by three orders of magnitude*. Medical Physics 2019; 46(4), 1888-1895. doi.org/10.1002/mp.13420

2. **Wilson LJ**, Schneider CW, Kamp F, Reiner M, Martins JC, Landry G, Kapsch RP, Schrader M, Meier M, Tappe O, Parodi K, Newhauser WD. *Method to quickly and accurately calculate absorbed dose from therapeutic and stray photon exposures throughout the entire body in individual patients*. Medical Physics 2020; 47(5), 2254-2266. doi.org/10.1002/mp.14018

3. **Wilson LJ** and Newhauser WD. *Justification and optimization of radiation exposures: a new framework to aggregate arbitrary detriments and benefits*. Radiation and Environmental Biophysics 2020; 59(3), 389-405. doi: 10.1007/s00411-020-00855-w

4. **Wilson LJ** and Newhauser WD. *Generalized approach for radiotherapy treatment planning by optimizing health outcome: preliminary results for prostate radiotherapy patients.* Physics in Medicine and Biology (In Preparation)