

## Publication

Repository describing an aging population to inform physiologically based pharmacokinetic models considering anatomical, physiological, and biological age-dependent changes

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Aging is characterized by anatomical, physiological, and biological changes that can impact drug kinetics. The elderly are often excluded from clinical trials and knowledge about drug kinetics and drug-drug interaction magnitudes is sparse. Physiologically based pharmacokinetic modeling can overcome this clinical limitation but detailed descriptions of the population characteristics are essential to adequately inform models.; The objective of this study was to develop and verify a population database for aging Caucasians considering anatomical, physiological, and biological system parameters required to inform a physiologically based pharmacokinetic model that included population variability.; A structured literature search was performed to analyze age-dependent changes of system parameters. All collated data were carefully analyzed, and descriptive mathematical equations were derived.; A total of 362 studies were found of which 318 studies were included in the analysis as they reported rich data for anthropometric parameters and specific organs (e.g., liver). Continuous functions could be derived for most system parameters describing a Caucasian population from 20 to 99 years of age with variability. Areas with sparse data were identified such as tissue composition, but knowledge gaps were filled with plausible qualified assumptions. The developed population was implemented in Matlab; and estimated system parameters from 1000 virtual individuals were in accordance with independent observed data showing the robustness of the developed population.; The developed repository for aging subjects provides a singular specific source for key system parameters needed for physiologically based pharmacokinetic modeling and can in turn be used to investigate drug kinetics and drug-drug interaction magnitudes in the elderly.

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