

The Pharmacodynamics of Aging

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Resources for Further Reading

Baltimore Longitudinal Study on Aging: <https://www.blsa.nih.gov/>

American Geriatrics Society Updated Beers Criteria identifying medications that older adults should avoid or use with caution:

<https://geriatricscareonline.org/ProductAbstract/american-geriatrics-society-updated-beers-criteria-for-potentially-inappropriate-medication-use-in-older-adults/CL001>

Increase in elderly population

<https://www.census.gov/prod/2014pubs/p25-1140.pdf>

U.S. Department of Health and Human Services. HHS Initiative on Multiple Chronic Conditions. 2014. Available at: <http://www.hhs.gov/ash/initiatives/mcc/>

U.S. Department of Health and Human Services. Multiple Chronic Conditions – A Strategic Framework: Optimum Health and Quality of Life for Individuals with Multiple Chronic Conditions. Available at:

http://www.hhs.gov/sites/default/files/ash/initiatives/mcc/mcc_framework.pdf

References (in the order cited)

Table 1 from Zisook S, Downs NS. *J Clin Psych* 1998, 59 (suppl 4):80-91, data from Dorgan CA, editor. *Statistical record of health and medicine*. New York: International Thompson Publishing Co. 1995. (Slide 6)

Figure 1 from *Annals of Internal Medicine*, Vol 117, No 8, 685, 15 Oct 1992 (Slide 7)

Adapted from Cluff LE et al. *JAMA* 1964;188:976 (Slide 8)

Baltimore Longitudinal Study on Aging, <https://www.blsa.nih.gov/> (Slide 10)

Vestal et al. *Clin Pharmacol Ther* 1979;26:181-186 (Slide 11)

Abernethy et al. *Am J Cardiol* 1987;60:697-702 (Slides 12 and 13)

R. Clinton Webb. *Advan in Physiol Edu* 2003;27:201-206 (Slide 14)

O'Rourke, MF. *Arterial Function in Health and Disease*, 1982 (Slide 16)

Abernethy et al. *Ann Int Med*, 1986;105:329-336 (Slides 17-19)

JV Mombouli and PM Vanhoutte. *J Mol Cell Cardiol* 1999; 31:61-74 (Slide 21)

Andrawis et al. *J Am Geriatr Soc* 2000;48:193-198 (Slide 22)

Chauhan et al. *JACC* 1996; 28:1796-1804 (Slide 23)

Drug Interaction Table, Indiana University, Clinical Pharmacology Research Institute (Slide 27) (<http://medicine.iupui.edu/CLINPHARM/ddis/main-table>)

Greenblatt et al. *Br J Clin Pharmacol* 1983;15:303-309 (Slide 28)

Greenblatt et al. *Anesthesiology* 1984;61:27-35 (Slide 29)

Steinman et al. *J Am Geriatr Soc* 2012;60:1872-1880 (Slide 35)

Hilmer et al. *Arch Int Med* 2007;167:781-787 (Slide 38)

Additional References, Including Those from the Case Studies and Self-Assessment:

Polypharmacy

Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D. STOPP (Screening tool of Older Persons' Prescriptions) and START (Screening Tool to Alert Doctors to Right Treatment): Consensus validation. *Int J Clin Pharmacol Ther* 2008; 46(2):72-83.

Gnjidic D, Hilmer SN, Blyth FM, et al. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *J Clin Epidemiol* 2012;65:989-995.

Melzer D, Tavakoly B, Winder RE, et al. Much more medicine for the oldest old: trends in UK electronic clinical records. *Age Ageing* 2015;44(1):46-53.

National Action Plan for Adverse Drug Event Prevention. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. (2014). Washington, DC: <https://health.gov/hcq/pdfs/ade-action-plan-508c.pdf>

Quato DM, Wilder J, Schumm LP, et al. Changes in the prescription and over-the-counter medication and dietary supplement use among older adults in the United States, 2005 vs 2011. *JAMA Intern Med* 2016;176:473-482.

Steinman MA, Miao Y, Boscardin WJ, Komaiko KDR, Schwartz JB. Prescribing quality in older veterans: A multifocal approach. *J Gen Int Med* 2014; 29 1379-1386.

Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med* 2015;175(5):827-834.

Cardiovascular aging

Laurent S et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Heart J* 2006;27:2588-2605.

O'Rourke, MF, Hashimoto J. Mechanical factors in arterial aging: a clinical perspective. *J Am Col Cardiol* 2007;50:1-13.

Lakatta EG, Want M, Najjar SS. Arterial aging and subclinical arterial disease are fundamentally intertwined at macroscopic and molecular levels. *Med Clin North Am* 2009;93:3;583-604.

Impaired drug responses

Vestal RE, Wood AJ, Shand DG. Reduced beta-adrenoreceptor sensitivity in the elderly. *Clin Pharm Ther* 1979 Aug;26(2):181-6.

Craft N, Schwartz, JB. Effects of age on intrinsic heart rate, heart rate variability, and AV conduction in healthy humans. *Am J Physiol* 1995;268:H1441-1452.

Monahan KD. Effect of aging on baroreflex function in humans. *Am J Physiol Regul Integr Comp Physiol* 2007 Jul;293(1):R3-R12. Epub 2007 Apr 18.

Changes in renal drug clearance (including calculation of glomerular filtration rate)

Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31-41.

Levey AS, Greene T, Kusek JW, et. al. A simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol* 2000;11:A0828.

Levey A, Stevens L, Schmid C, Castro Ar, Feldman H, Kusek J, et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604-12.

Ix J, Wassel C, Stevens L, Beck G, Froissart M, Navis G, et al. Equations to estimate creatinine excretion rate: the CKD epidemiology collaboration. *Clin J Am Soc Nephrol* 2011;6(1):184-91.

Schwartz, JB. Potential impact of substituting estimated Glomerular Filtration Rate for estimated Creatinine Clearance for dosing of Direct Oral Anticoagulants. *J Am Geriatr Soc* 2016;1996-2002.

Changes in drug metabolism

Abernethy DR, Schwartz JB, Todd EI, et al. Verapamil pharmacodynamics and disposition in young and elderly hypertensive patients. *Ann Intern Med* 1986;105:339-336.

Cotreau MM, von Molte LL, Greenblatt DJ. The influence of age and sex on the clearance of cytochrome P4503A substrates. *Clin Pharmacokinet* 2005;44:33-60.

Schwartz JB, Abernethy DR. Aging and medications: Past, Present, Future. *Clin Pharmacol Ther* 2009;85:3-10.

Verotta D, Schwartz JB. Population analyses of atorvastatin inpatients living in the community and nursing homes. *Clin Pharmacol Ther* 2009;86:497-502.

Changes in body composition

Lesser GT, Markofsky J. Body water compartments with human aging using fat-free mass as the reference standard. *Am J Physiol* 1979 Mar;236(3):R215-20.

Chumlea WC, Roche AF, Webb P. Body size, subcutaneous fatness and total body fat in older adults. *Int J Obes* 1984;8(4):311-7.

Borkan GA, Hults DE, Gerzof SG, Robbins AH. Comparison of body composition in middle-aged and elderly males using computed tomography. *Am J Phys Anthropol* 1985 Mar;66(3):289-95.

Schwartz RS, Shuman WP, Larson V, et al. The effect of intensive endurance exercise training on body fat distribution in young and older men. *Metabolism* 1991;40(5):545-51.

Drug burden index and impaired functional status

Hilmer SN, Gnjdic D, Abernethy DR. Drug Burden Index for international assessment of the functional burden of medications in older people. *J Am Geriatr Soc* 2014;62(4):791-2.

Tinetti ME, Han L, Lee DS, et al. Antihypertensive medications and serious fall injuries in a nationally representative sample of older adults. *JAMA Intern Med* 2014 Apr;174(4):588-95.

Jamieson HA, Nishtala PS, Scrase R, et al. Drug Burden and its Association with Falls Among Older Adults in New Zealand: A National Population Cross-Sectional Study. *Drugs Aging* 2017 Dec 8. doi: 10.1007/s40266-017-0511-5. [Epub ahead of print]

Note that all websites were accessed on 08-Jan-2018