

Extension of the Janmahasatian fat-free mass model to account for ethnicity-related bias



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Background

- Fat-free mass (FFM) is an alternative body size scaler of drug clearance.
- The Janmahasatian model (FFM_{Jan}) is commonly used for prediction.
- FFM_{Jan} was developed based on body composition data that arose from patients that were predominantly Caucasian (Figure 1).
- As body composition varies due to ethnicity, an ethnicity effect needs to be incorporated into this model.

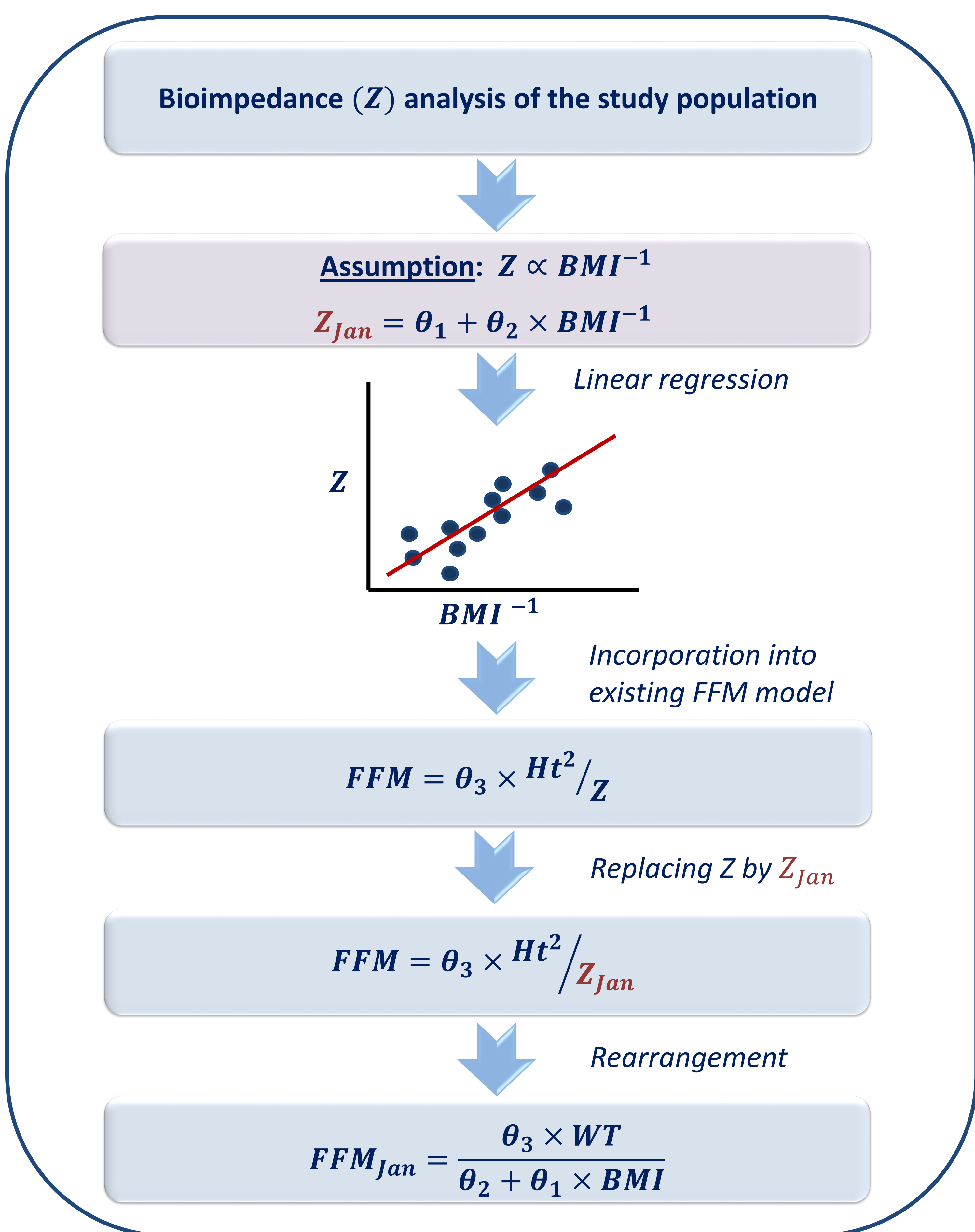


Figure 1. The implicit assumption of universal body composition in FFM_{Jan} model. WT total body weight, Ht Height, BMI body mass index

FFM_{Jan} model

For males: $FFM_{Jan} = \frac{9270 \times WT}{6680 + 216 \times BMI}$

For females: $FFM_{Jan} = \frac{9270 \times WT}{8780 + 244 \times BMI}$

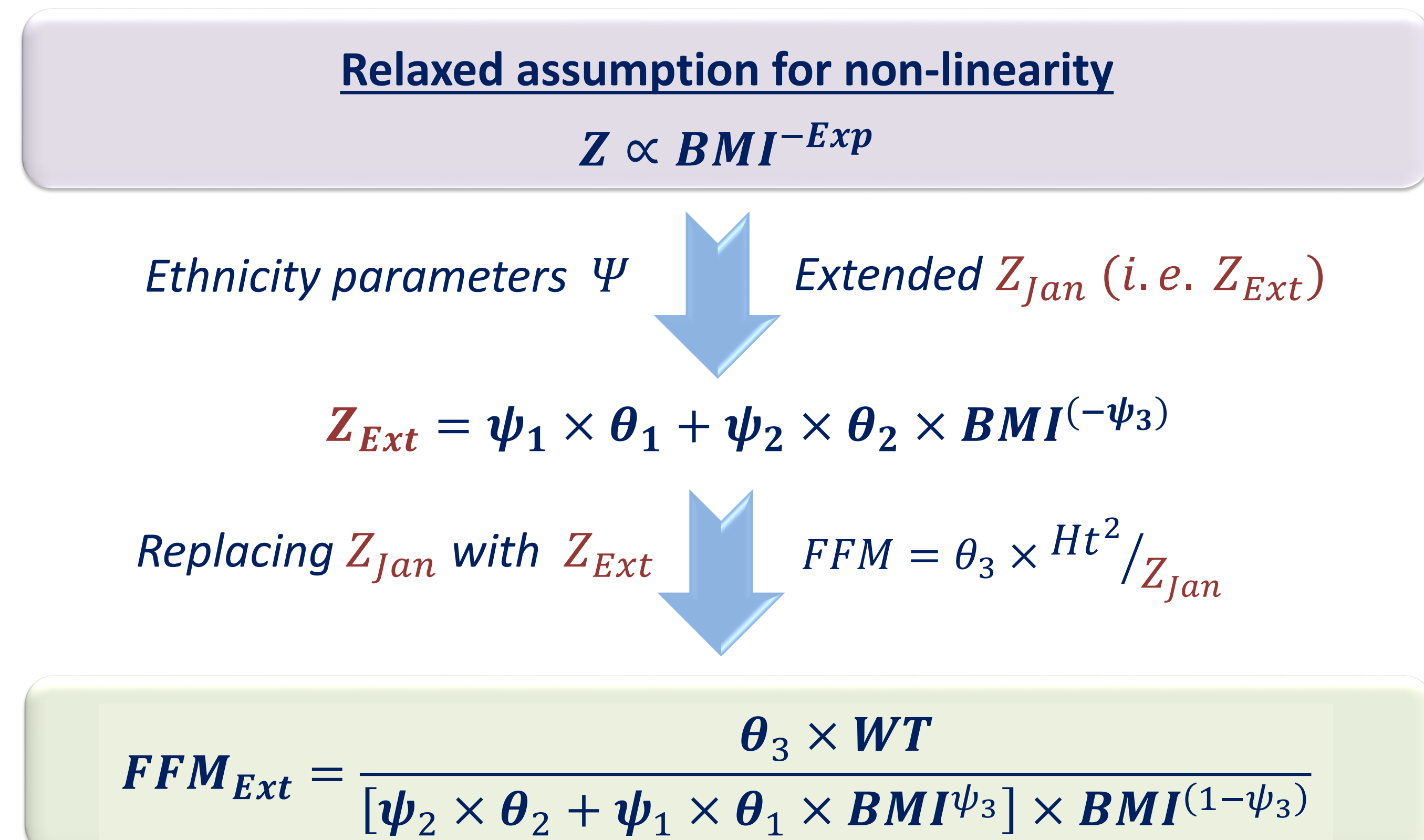
Influence of ethnicity on FFM_{Jan}

- Body composition vs. BMI relationship is curvilinear [2].
- Since Z is a reflective measure of body composition, a non-linear relationship is expected.
- Further, body composition relationship with body size differs between ethnicities [2]; FFM_{Jan} has been shown to over-estimate FFM in Indians.
- For Indians, FFM_{Jan} over-estimates FFM (~4 kg in average) [3].

Aims

- To extend the FFM model (FFM_{Ext}) by incorporating additional (estimable) body composition parameters (Ψ) that link to ethnicity.
- To estimate the value of Ψ in Indian population.

Adding ethnicity to FFM_{Jan} model



Ethnicity parameters Ψ for Indians

- FFM data were simulated for 100 adult Indian patients from a reference model (FFM_{Kul}).
- The reference model was developed specifically for the Indian population by Kulkarni et al. [4] and externally validated [3].
- The simulated data were used to estimate the Ψ parameters using NONMEM 7.3.

For Indian males: $\psi_1 = 0, \psi_2 = 0.77, \psi_3 = 0.72$

For Indian females: $\psi_1 = 0, \psi_2 = 0.70, \psi_3 = 0.72$

Conclusions

- An extended model of FFM was developed and estimated for Indians
- FFM_{Jan} can be extended from bioimpedance (Z) data only; FFM measurements are not required.

References

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2. Rush et al. *British Journal of Nutrition* 2009. 102(4): 632-641.
3. Srigiripura et al. *International Journal of Nutrition, Pharmacology, Neurological Diseases*. 2017. 7(4): 94-100
4. Kulkarni et al. *Journal of Applied Physiology*, 2013. 115(8): 1156-1162