

MATURATION OF GLOMERULAR FILTRATION THROUGHOUT THE PAEDIATRIC AGE-RANGE; A COMPARISON OF DIFFERENT FUNCTIONS

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Objectives

Glomerular filtration (GF) has a key role in the renal elimination of many drugs. An accurate ontogeny function for this route could guide paediatric dosing regimens of drugs eliminated through GF.

Aim: Compare the performances of published functions [1-6] describing the maturation of GF rate (GFR) to observed values collected from literature [7-12].

Methods

Published functions [1-6] - main characteristics:

- Developed using estimates of ‘true’ GFR (i.e. Cr-EDTA, inulin, mannitol) [1-5] or clearance estimates of drugs mainly excreted through GF (i.e. aminoglycosides) [6].
- GFR maturation functions based on single demographic characteristics (i.e. body surface area, bodyweight [5-6]) or in combination (i.e. bodyweight with postmenstrual age [1-4]).

Conclusions

- GFR maturation functions derived using ‘true’ GFR values [1-5] perform better than functions based on drug clearance [6].
- All functions overpredict GFR in the very young (<6 mo.).
- None of the functions is a good GFR predictor in children with disease.

Results

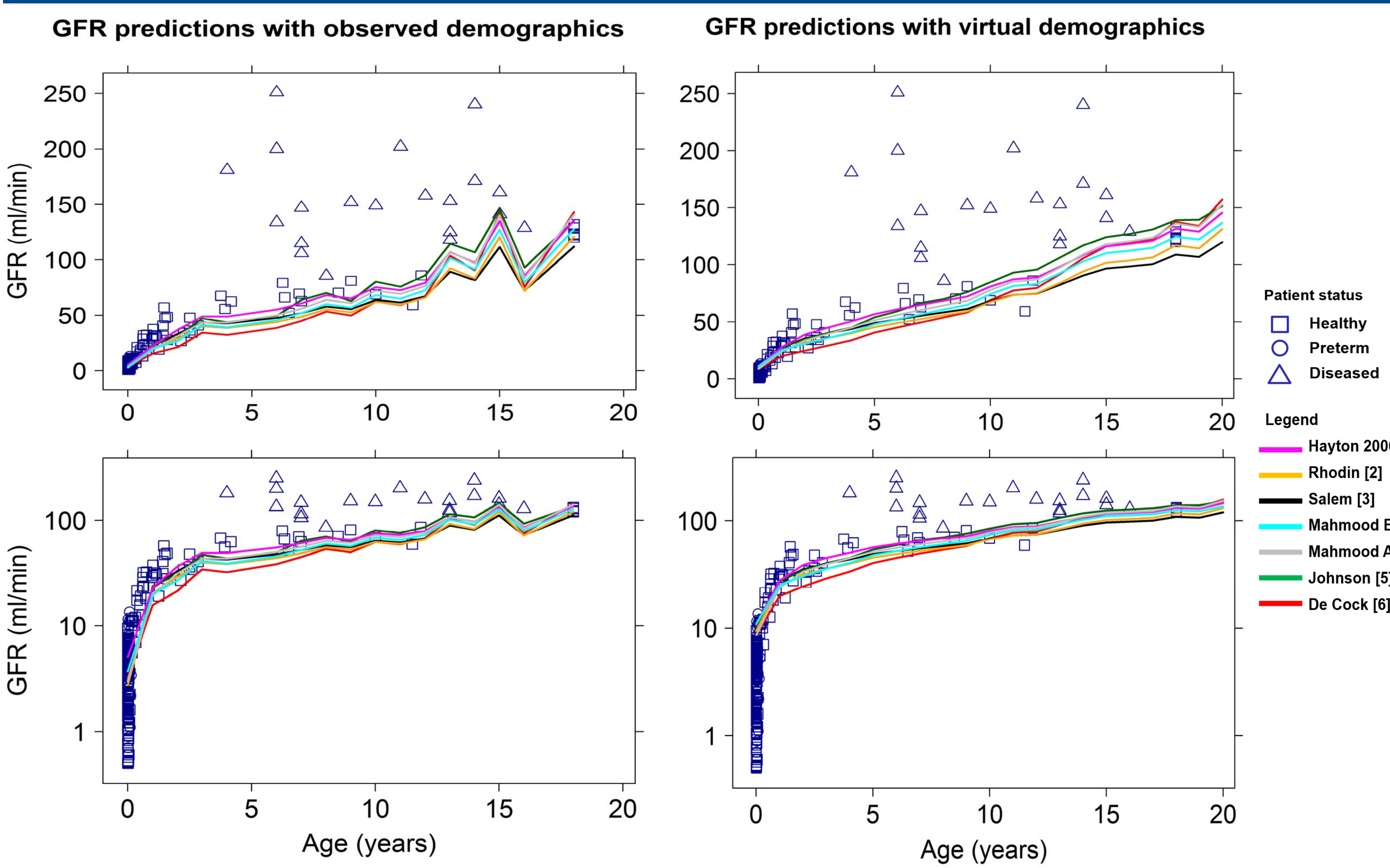


Figure 1. Published function predictions (lines) versus observed values of GFR (symbols).

- All functions [1-6] overpredict GFR for the smallest children. For children older than 6 months, all functions describe similar maturation patterns, within 25-39% mean PE% range (Figure 2).
- Salem [3], Mahmood ADE [4] and Rhodin [2] predict within the accepted $\pm 50\%$ PE for all ages (Table 1) even though Figure 2 shows some extreme overpredictions for the very young ages.
- Overall, Salem [3] has the best GFR predictions, however, for children older than 6 months, Hayton [1] performs best (Table 1 and Figure 2).
- None of the functions is a good predictor for GFR in disease states (Figure 1 (Δ)).

- A virtual paediatric population (N=3200) of ages between 2.5 weeks and 20 years was simulated using Simcyp v13. Its demographic characteristics were used as input for the GFR published functions (Figure 1).
- The comparison of published functions [1-6] to observed values [7-12] was performed at two levels:
 - Qualitative: visual comparison of GFR predictions
 - Quantitative: % prediction error (PE%)

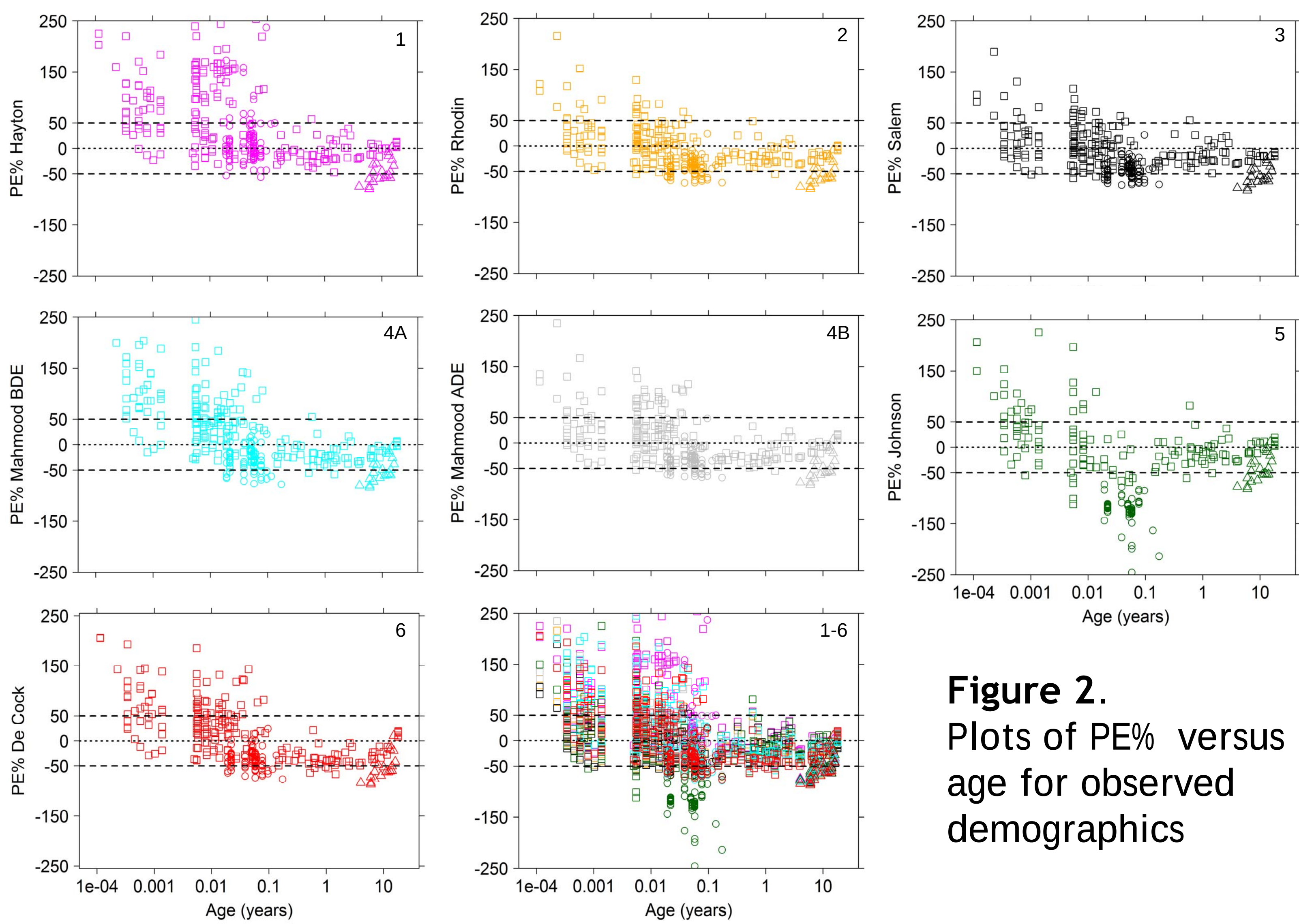


Figure 2. Plots of PE% versus age for observed demographics

Absolute Mean %Prediction Error							
Functions	De Cock 2014	Mahmood BDE 2016	Mahmood ADE 2016	Salem 2014	Johnson 2006	Rhodin 2009	Hayton 2000
Age bins							
< 1 mo.	50	60	41	35	106	36	94
< 6 mo.	39	31	33	33	130	32	45
6 mo. - 1 yr.	39	32	32	26	29	29	26
1-5 yrs.	41	29	25	23	22	26	22
6 -18 yrs.	38	32	30	35	28	35	28
Overall	47	52	38	34	86	35	76
Overall (>6 mo.)	39	31	28	31	26	32	25

Table 1. Quantitative level: Absolute mean PE% – Age stratified

References

[1] Hayton et. al. 2000; [2] Rhodin et. al. 2009; [3] F. Salem et. al. 2014; [4] Mahmood et. al. 2016; [5] Johnson et. al. 2006; [6] De Cock et. al. 2014; [7] Barnett et. al. 1948; [8] Coulthard et. al. 1975; [9] Dean et. al. 1947; [10] Leak et. al. 1976; [11] Oh et. al. 1966; [12] Rubin et. al. 1949;



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