Use of developmental Midazolam and 1-hydroxymidazolam data with pediatric physiologically based modelling to assess CYP3A4 and UGT2B4 ontogeny *in vivo.*

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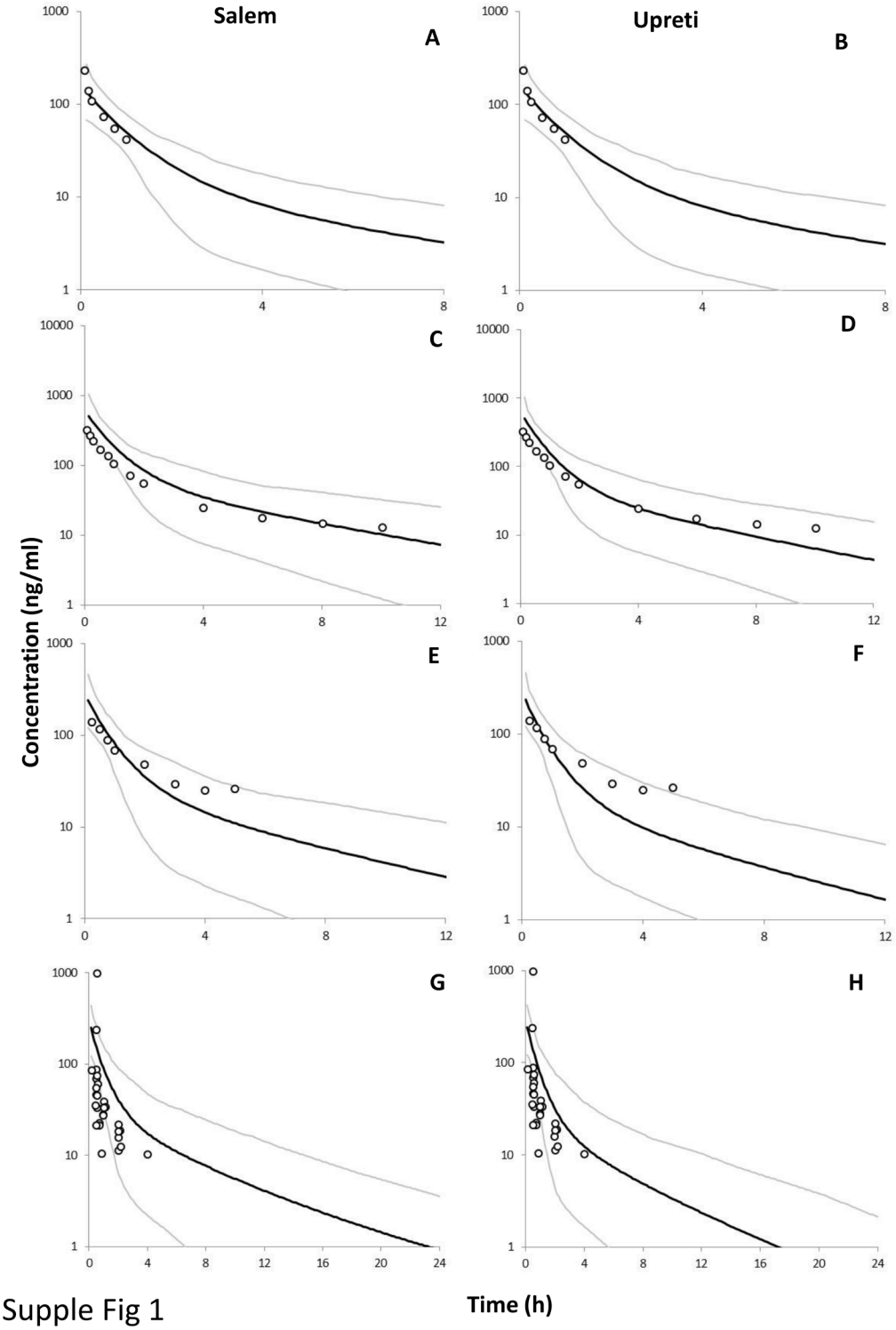
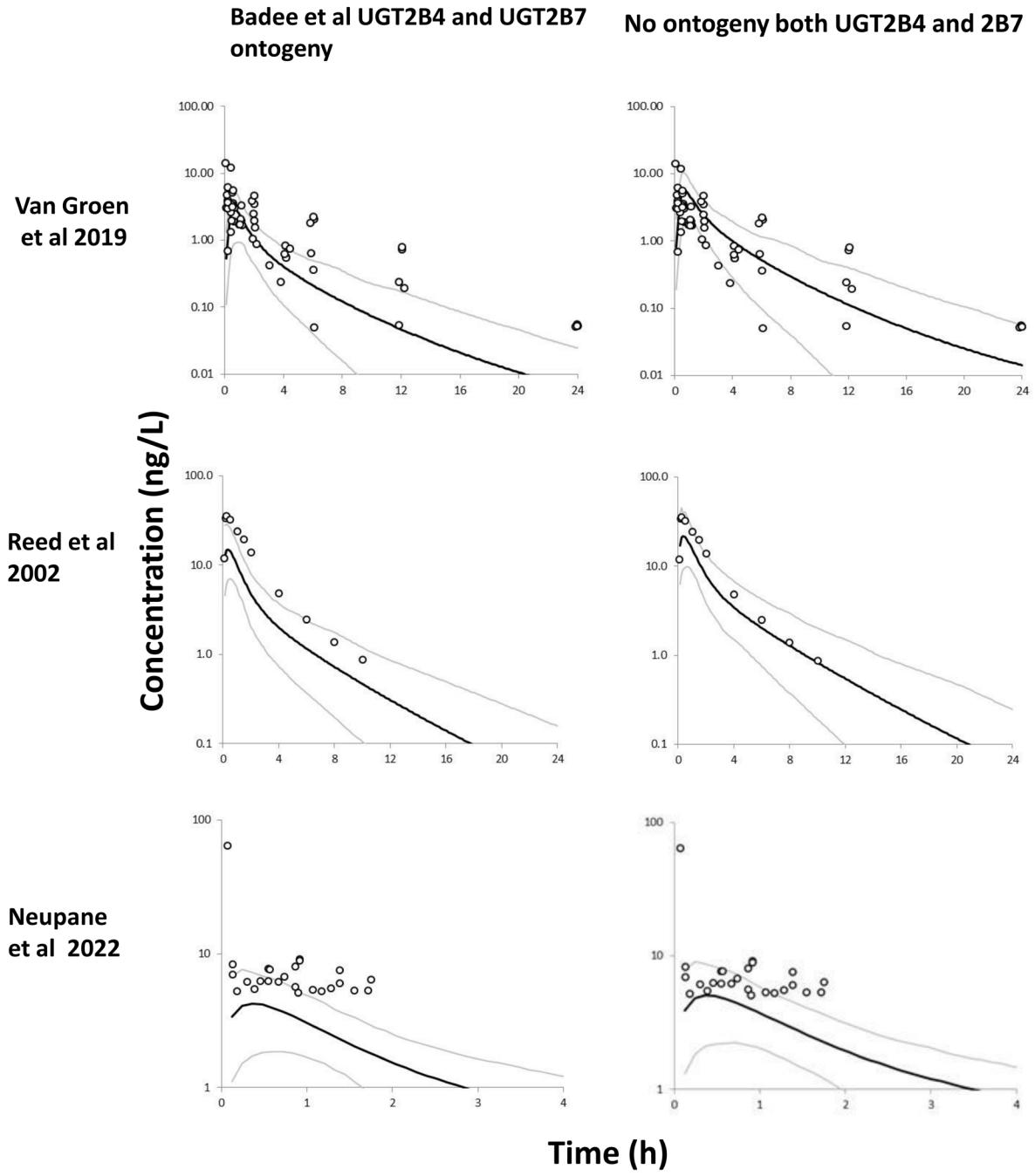


Supplementary Figure 1: Predicted and observed concentration time profiles for midazolam in different paediatric studies comparing the CYP3A4 ontogeny profiles of Salem et al 2012 (LHS) and Upreti and Wahlstrom 2016 (RHS). Black lines are the mean predicted profiles, grey lines are the 5th and 95th percentiles and black circles are the corresponding observed data (A,B) Tolia et al 1991, 0.08mg/kg in age 8 to 17y; (C,D) Matthews et al 1988, 0.3 mg/kg in age 0.5 to 10.26 years; (E,F) Payne et al 1989, 0.15mg/kg in age 3 to 10 years; (G,H) Hamano et al 2019, 0.15mg/kg in age 0.5 to 13.7 years.



Supple Fig 2

Supplementary Figure 2. Predicted and observed concentration time profiles for 1-OHMDZ in van Groen et al (2019), Reed et al (2002) and Neupane et al 2022 showing the UGT2B4 and UGT2B7 ontogeny profile of Badee et al (2019) and the assumption of no ontogeny (full adult expression of both enzymes) . Black lines are the mean predicted profiles, grey lines are the 5th and 95th percentiles and black circles are the corresponding observed data in individuals.