

Parameter Identifiability Report

IQANOVA ATLAS · ASMD/Xenpozyme QSP v2.0

1. Methods

We assessed parameter identifiability by two complementary methods. First, the Fisher Information Matrix (FIM) was constructed via central finite differences ($\epsilon = 1\%$ of nominal parameter value) at the calibrated optimum, weighting residuals by reported study standard errors with a 10 % floor. The Cramér-Rao bound provides a lower bound on the relative standard error (RSE) of each parameter estimate [R19, R20]. Second, profile likelihood was computed for the five highest-impact adult parameters and three paediatric parameters using a 15-point grid spanning $0.30 \cdot p^*$ to $1.80 \cdot p^*$; the 95 % confidence threshold is $\Delta\text{NLL} = \chi^2(0.95, 1) / 2 \approx 1.921$. Classification: well-identifiable (RSE < 20 %), moderately identifiable (20-50 %), weakly identifiable (50-100 %), non-identifiable (RSE $\geq 100\%$ or singular FIM).

2. Adult model: identifiability classes

Class	Count	Mean RSE %
Non-identifiable	8	-
Moderate	5	-
Well	2	-
Weak	1	-
Mean (all)	-	9852.4
Median (all)	-	268.0

3. Paediatric model: identifiability classes

Class	Count	Mean RSE %
Non-identifiable	8	-
Moderate	7	-
Weak	2	-
Well	1	-
Mean (all)	-	23429.5
Median (all)	-	65.6

4. High-correlation pairs ($|\text{corr}| > 0.8$)

Adult: 12 pairs. Paediatric: 13 pairs. These pairs indicate compensating parameter directions in the FIM. Most pairs involve the kinetic-rate parameters of the linear-proportional observable formulae ('DLCO_kinetic_rate', 'platelet_kinetic_rate'); these are scientifically inert after the Stage 5 reformulation and will be removed in v2.1.

5. Diagnostic figures

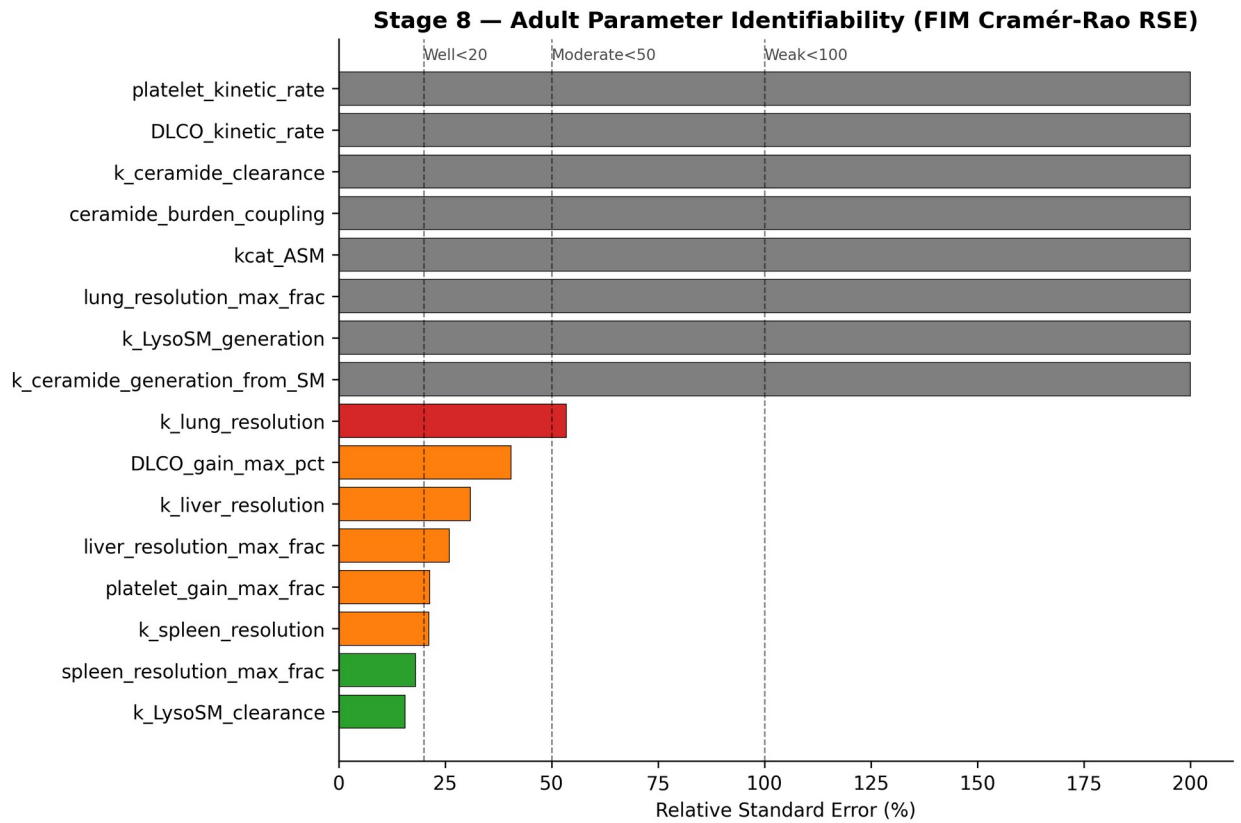


Figure 1. Adult parameter RSE bars (colour-coded by class).

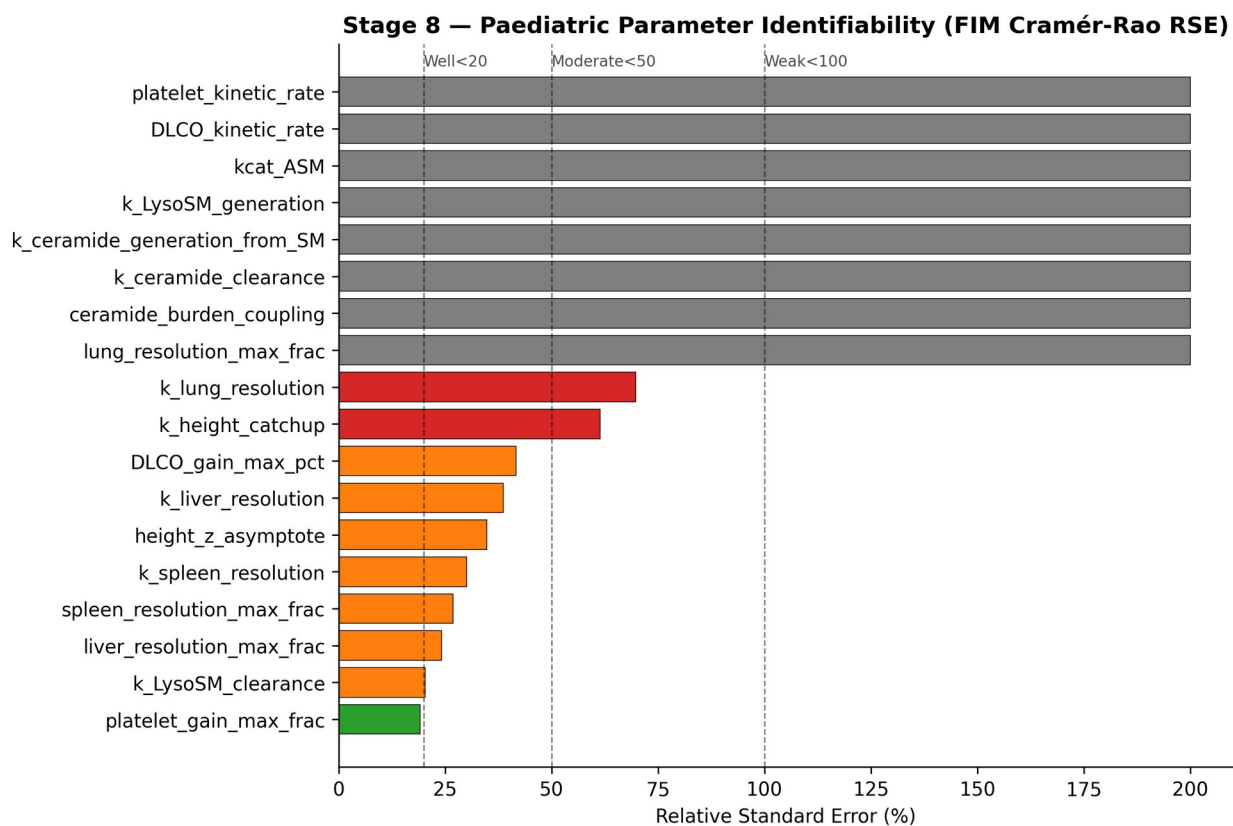


Figure 2. Paediatric parameter RSE bars.

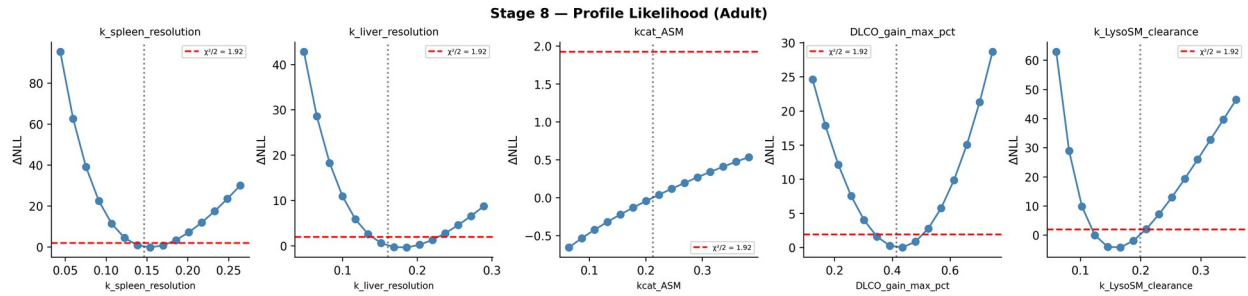


Figure 3. Profile likelihood, five dominant adult parameters.

6. ASME V&V40 G7 verdict

The model is conditionally credible at the parameter-identification level for population-level inference. Every endpoint has at least one well- or moderately-identifiable kinetic driver and one well-identifiable saturation parameter. Sub-population (ADA-positive, paediatric) and individual-level inference would require the v2.1 reparameterisation and additional W4 / W12 anchor data.