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We thank Dr. Watchko and Dr. Maisels for their knowledgeable comments on our study and would like to address their questions.

One concern was the use of a higher bilirubin threshold for phototherapy and exchange transfusion (ET) at our centre for infants with haemolytic disease of the foetus and newborn (HDFN). The relationship between haemolysis and high bilirubin levels is clear, but it is unclear whether infants with HDFN have a higher risk of bilirubin neurotoxicity compared to infants without HDFN in case of similar levels of serum bilirubin [1]. We have no reason to assume that HDFN alters the blood–brain barrier and therefore do not assume that the studied, term infants have a higher risk of bilirubin encephalopathy. Moreover, the maximum bilirubin level at birth remained stable for group II (2005–2015) and III (2015–2020), with maximum values of 257 (standard deviation [SD] of 89) and 262 $\mu\text{mol/L}$ (SD of 80) after birth. Local policy also indicates the near-immediate start (within 15 min after birth) of intensive phototherapy for infants with HDFN regardless of the first measured bilirubin after birth or other risk factors and will therefore not delay treatment. Other risk factors include prematurity, asphyxia, suspected infection/sepsis and low albumin levels.

With regard to phototherapy, technological advancements of the used (LED) lamps very likely also contributed to more effective treatment of hyperbilirubinaemia and decreased use of ET. In our study, the median duration of phototherapy per infant remained stable over the years, with a median of 4 (interquartile range [IQR] 3–5), 5 (IQR 3–6) and 5 (IQR 4–6) days in our three time cohorts. The timing of the start of phototherapy (within 15 min after birth) has not changed over the years.

The relationship between intrauterine transfusion (IUT) and ET(s) was previously reported by our study group [2, 3]. Infants treated with more IUTs required fewer ET(s); the rate of ET dropped from 39% of infants treated with one IUT to 25% after two IUTs and further declined to 8% for infants treated with five IUTs (infants born 2005–2018) [2]. The decline in ET rate in this study does not show a similar trend as the IUT rate has declined in the three time cohorts in our study from a median of three IUTs (IQR 2–4) in group I to two (IQR 2–4) and two (IQR 1–3) in group II and III.

The standard blood product in the Netherlands for neonatal ET has a haematocrit of around 0.50; no additional albumin is transfused prior to or during the procedure. As stated, the product

consists of a two donor combination of washed red blood cells and adult plasma.

We hope to have clarified the raised issues and welcome all further thoughts on our study.

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CONFLICT OF INTEREST

There are no conflicts of interest to report.

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