Appendix S1. Technical details of the data simulation

The model:
Setting: A cohort of fetuses is followed from week 22. Each fetus has a "target gestation", which represents the duration of pregnancy in the absence of any intervening factor. The target gestation follows a normal distribution (mean from last menstrual period: 280 days, standard deviation (SD): 12 days). If all babies were born at the target gestation, only about 4% would be born before 37 weeks, and virtually none before 32 weeks.

Background risks of fetal death and birth: All fetuses have a baseline weekly risk of fetal death of 8 per 100,000 ("frailty"), which is constant throughout pregnancy. A vanishingly small fraction of babies (4 per million per week) are born at each week, regardless of their target gestation, due to very rare external reasons that do not affect fetal health (e.g., due to an injury or condition that affects the mother and results in early delivery [1-3]). These rare occurrences, also independent of gestational age, may be considered as the obstetric equivalent of a lightning strike.

The four causes of preterm birth/neonatal death: Each of the four causes of preterm birth and mortality (A, B, C, and D), represents a "pathology" that affects the fetus and is characterized by:

1) Frequency (expressed in %)
2) Effect on gestational length (due to medically induced or spontaneous delivery), expressed by the mean reduction in days, and SD.
3) Effect on mortality, expressed by an odds ratio (OR), which can be either:
   a) Constant, i.e., the same OR applies at all weeks (factors A and B).
   b) Increasing, i.e., the baseline OR (at 22 weeks) increases by a given amount for each additional week that the fetus remains *in utero* (factors C and D). Unlike in situation (a), where risk is not reduced by early delivery, here the risk of early birth must be weighed against the increasing risk to the fetus.

The parameters are described in Table 1 of the paper. In this example, 1.5% of fetuses have A, which increases frailty by 50% (and the weekly probability of stillbirth from 8 to 12 per 100,000 fetuses per week). Factor B is similar, except that its effect on mortality risk is stronger. Factors C and D are rarer, reduce gestational length much more significantly, and the OR by which they multiply frailty increases by 20% for each additional week that the fetus remains *in utero*.

Outcome: Risk of neonatal death among babies who have none of the four pathologies is determined by the baseline frailty (comprising causes such as infection or injury incurred during or after birth) and physiological immaturity. In babies with one or more among A-D, risk is additionally influenced by the effect of the pathologies, which is carried over to the postnatal period. In this simulated universe, immaturity coincides with gestational age at birth and, unlike in the real world, its "pure" effect is known. Infants born at week 22 have a probability of 82% of dying neonatally; this probability goes down to 42.5% at week 23 (and is 0.5 per 1,000 at week 40; see Figure S1. As shown in the figure, gestational-age-specific mortality changes substantially as a result of the risk added by the introduction of the pathologies, as presumably would happen in the real world).

Relationship between the 4 pathologies: The four factors act independently of each other (i.e., having one does not influence the probability of having another). For babies with two or more factors, the effect on gestational length is the sum of the effects of each factor (with, e.g., both A and B, -40 days on average) and the effect on mortality is the product of the ORs (with both A and B, the OR will be 4.5;

when one of the factors is C or D, the OR to be multiplied will depend on week of birth). Figure S2 describes how all components of the simulation fit together.

Appendix S1 references

1. Hyde LK, Cook LJ, Olson LM, Weiss HB, Dean JM. Effect of motor vehicle crashes on adverse fetal outcomes. Obstetrics and gynecology. 2003 Aug;102(2):279-86.

2. Liu S, Basso O, Kramer MS. Association between unintentional injury during pregnancy and excess risk of preterm birth and its neonatal sequelae. American journal of epidemiology. 2015 Nov 1;182(9):750-8.

3. Amant F, Van Calsteren K, Halaska MJ, Gziri MM, Hui W, Lagae L, et al. Long-term cognitive and cardiac outcomes after prenatal exposure to chemotherapy in children aged 18 months or older: an observational study. Lancet Oncol. 2012 Mar;13(3):256-64.