

Supplement 1

nuMoM2b Study Definitions of Hypertensive Disorders of Pregnancy

This supplement provides nuMoM2b study definitions of hypertensive disorders of pregnancy:

Exhibit S1.1 shows nuMoM2b definitions of hypertension and proteinuria at baseline (prior to pregnancy or prior to 20⁰ weeks gestation).

Exhibit S1.2 gives definitions of HELLP syndrome and eclampsia, which are new onset hypertensive disorders (occurring at or after 20⁰ weeks gestation). These definitions are applicable to all participants irrespective of baseline group (chronic hypertension, baseline proteinuria, both, neither).

Exhibit S1.3 provides a table of definitions of gestational hypertension, mild preeclampsia, severe preeclampsia, and superimposed preeclampsia, according to baseline group. Shown are the baseline groups, applicable diagnoses, and nuMoM2b clinical criteria (at or after 20⁰ weeks of gestation through 14 days postpartum) for these new onset maternal hypertensive disorders. In Section A, the occurrence of new onset hypertension (Section A.1) plus one or more of the criteria marked with an 'X' in Section A.2 establishes the diagnosis of preeclampsia. Given a diagnosis of preeclampsia, the occurrence of any criterion marked with an 'S' establishes the preeclampsia as severe; otherwise the diagnosis is mild preeclampsia. Note that some criteria, denoted with 'X, S' have a dual role as indicators of preeclampsia and of severe preeclampsia given a diagnosis of preeclampsia.

Abbreviations: SBP = systolic blood pressure; DBP = diastolic blood pressure

Exhibit S1.1 – Baseline hypertension and proteinuria

Chronic hypertension (CHTN) – (1) a diagnosis of hypertension prior to pregnancy or (2) hypertension (systolic ≥ 140 mmHg OR diastolic ≥ 90 mmHg on two occasions at least 6 hours apart or on one occasion followed by antihypertensive medication therapy) documented prior to pregnancy or prior to 20⁰ weeks gestation.

Baseline proteinuria ≥ 300 mg/ 24hr – total protein ≥ 300 mg in a 24-hour urine collection documented prior to pregnancy or prior to 20⁰ weeks gestation.

Exhibit S1.2 – New-onset hypertensive disorders (occurring at or after 20⁰ weeks of gestation through 14 days postpartum) applicable to all participants irrespective of baseline status regarding chronic hypertension (CHTN) and proteinuria

HELLP syndrome – the occurrence of all of the following criteria:

- a. Hemolysis – evidenced by (1) serum total bilirubin ≥ 1.2 mg/dL (20 μ mol/L), (2) serum lactate dehydrogenase (LDH) ≥ 600 IU/L, or (3) hemolysis on peripheral smear
- b. Thrombocytopenia (platelet count $< 100,000$ /mm³)
- c. Serum aspartate aminotransferase (AST) ≥ 100 IU/L

Eclampsia – the occurrence of a seizure without another known cause.

Exhibit S1.3 – nuMoM2b definitions for new onset hypertensive disorders, by baseline status regarding chronic hypertension (CHTN) and proteinuria

Baseline groups, applicable diagnoses, and nuMoM2b clinical criteria (at or after 20⁰ weeks of gestation through 14 days postpartum) for new onset maternal hypertensive disorders

A. Participants without CHTN or baseline proteinuria ≥ 300 mg/ 24hr

1. Gestational hypertension – the occurrence of new onset hypertension, defined as:

- a. SBP ≥ 140 or DBP ≥ 90 on 2 occasions ≥ 6 hr apart or 1 occasion with subsequent antihypertensive therapy, excluding blood pressures recorded during the second stage of labor

2. Preeclampsia – the occurrence of (1) new onset hypertension plus one or more criteria marked with an "X" below, or (2) HELLP syndrome

Severe preeclampsia – (1) a diagnosis of preeclampsia plus one or more criteria marked with an "S" below, or (2) HELLP syndrome

Mild preeclampsia – a diagnosis of preeclampsia that does not meet criteria for severe preeclampsia

- | | | |
|----|--|------|
| a. | Proteinuria ≥ 300 mg/ 24hr; or, if no 24-hour urine protein available, protein/creatinine ratio ≥ 0.3 or dipstick $\geq 2+$ | X |
| b. | Thrombocytopenia (platelet count $< 100,000$ /mm ³) | X, S |
| c. | Pulmonary edema | X, S |
| d. | Severe hypertension: SBP ≥ 160 or DBP ≥ 110 on 2 occasions ≥ 6 hr apart or 1 occasion with subsequent antihypertensive therapy, excluding blood pressures recorded during the second stage of labor | S |
| e. | Proteinuria $\geq 5,000$ mg/ 24hr | S |
| f. | Oliguria (urine output < 500 mL/ 24hr) | S |
| g. | Severe headache | S |
| h. | Epigastric pain | S |
| i. | Fetal growth restriction (antenatal diagnosis; operationalized as estimated fetal weight ≤ 10 th percentile for gestational age by ultrasound examination) | S |

Exhibit S1.3 (cont.) – nuMoM2b a definitions for new onset hypertensive disorders, by baseline status regarding chronic hypertension (CHTN) and proteinuria

Baseline groups, applicable diagnoses, and nuMoM2b clinical criteria (at or after 20⁰ weeks of gestation through 14 days postpartum) for new onset maternal hypertensive disorders

B. Participants with baseline proteinuria ≥ 300 mg/ 24hr only

1. Gestational hypertension – the occurrence of new onset hypertension, defined as:

- a. SBP ≥ 140 or DBP ≥ 90 on 2 occasions ≥ 6 hr apart or 1 occasion with subsequent antihypertensive therapy, excluding blood pressures recorded during the second stage of labor

2. Superimposed preeclampsia – the occurrence of one or more of the following:

- a. Sudden increase in proteinuria (5 times the baseline value, or 2 times a baseline value of $\geq 5,000$ mg/ 24hr)
- b. Thrombocytopenia (platelet count $< 100,000$ /mm³)
- c. Serum aspartate aminotransferase (AST) ≥ 100 IU/L
- d. Severe headache
- e. Epigastric pain

NOTE: the occurrence of HELLP satisfies superimposed preeclampsia criteria B.2.b and B.2.c

C. Participants with CHTN only

1. Superimposed preeclampsia – the occurrence of one or more of the following:

- a. Proteinuria ≥ 300 mg/ 24hr; or, if no 24-hour urine protein available, protein/creatinine ratio ≥ 0.3 or dipstick $\geq 2+$
- b. Thrombocytopenia (platelet count $< 100,000$ /mm³)

NOTE: the occurrence of HELLP satisfies superimposed preeclampsia criterion C.1.b

D. Participants with CHTN and baseline proteinuria ≥ 300 mg/ 24hr

1. Superimposed preeclampsia – the occurrence of one or more of the following:

- a. Worsening hypertension, as shown by two diastolic blood pressures ≥ 110 mm Hg taken four hours apart in the week before delivery, excluding blood pressures recorded during the second stage of labor; AND any of these findings:
 - i. Sudden increase in proteinuria (5 times the baseline value, or 2 times a baseline value of $\geq 5,000$ mg/ 24hr)
 - ii. Severe headache
 - iii. Epigastric pain
- b. Thrombocytopenia (platelet count $< 100,000$ /mm³)
- c. Serum aspartate aminotransferase (AST) ≥ 100 IU/L

NOTE: the occurrence of HELLP satisfies superimposed preeclampsia criteria D.1.b and D.1.c