Maksym *et al.*
International Breastfeeding Journal (2025) 20:53
https://doi.org/10.1186/s13006-025-00743-3

International Breastfeeding Journal

RESEARCH

Open Access

Development of lactation and breast/chestfeeding adverse event terminology (LaBAET) through a Delphi consensus approach

Katarzyna M. Maksym[1], Kinga Kalita-Kurzyńska[2*], Diane Spatz[3], Melinda Boss[4], Maria Carmen Collado[5], Anna Gonciarz-Dytman[6], Bei Han[7], Asma Khalil[8], Joanna Kozakiewicz[9], Ernest Kuchar[10], Karolina Morze[11], Rebecca Powell[12], Natalie Shenker[13], Sławomir Wątroba[14], Anna L. David[1] and Aleksandra Wesołowska[2]

Abstract

Background Most women who give birth will initiate lactation and breast/chestfeeding, with up to 40% of infants globally receiving human milk exclusively for the first 6 months of life. One of the studies indicates that 40% of breastfeeding women had used at least one prescription medication in the first 3 months postpartum. The lack of information on the safety of medications during lactation may lead to cessation of lactation in favor of treatments, therefore contribute to suboptimal breastfeeding rates. Inadequate terminology to define and grade adverse events for lactation and breast/chestfeeding limits the understanding of potential therapeutic harms. This results in lactating women commonly being excluded from participation in clinical trials, leading to inequitable access to effective treatments. We developed a comprehensive framework with new definitions and grades for breastfeeding Adverse Events (AEs) through consideration of the physiology and pathology of lactation.

Methods We performed the Delphi consensus process between January 2021 and November 2023. An international multidisciplinary group of lactation and breast/chestfeeding experts identified a gap in AE terminology and developed definitions and grading of AEs based on the generic Common Regulatory Criteria for Adverse Events (CTCAE) structure. These underwent two rounds of a modified Delphi procedure involving an international multidisciplinary team of experts and patient representatives. The web platform REDCap® was used to collect the results of the Delphi surveys.

Results Three new definitions, delayed secretory activation, primary lactation insufficiency, and secondary lactation insufficiency, were developed and mapped to the Medical Dictionary of Regulatory Activities (MedDRA, March 2023). Oversupply of milk and other changes in lactation/feeding patterns were mapped to existing MedDRA terms. Grading for all five definitions was developed and agreed upon through consensus.

Conclusions These new definitions and grading of adverse events in lactation and breast/chestfeeding fill the gap in existing classifications and should encourage the inclusion of postpartum individuals into clinical trials.

Keywords Adverse event, Pharmacovigilance, Lactation, Breastfeeding, Definition

*Correspondence:
Kinga Kalita-Kurzyńska
kinga.kalita-kurzynska@wum.edu.pl
Full list of author information is available at the end of the article

Inclusivity comment

The authors recognise that not all people who chestfeed/breastfeed their neonate and infant will identify as women. However, for consistency reasons, we will use the term breastfeeding throughout this study to describe the process. Similarly, the terms women and woman will be used to describe all pregnant and postnatal people.

Background

In the 1970s, use of medicines during pregnancy led to unexpected and delayed serious adverse events in newborns [1]. This created ethico-legal challenges resulting in changes leading to pregnant and lactating women being routinely and systematically excluded from participation in clinical trials. Since the policy changes, the clinicians caring for women and the women themselves must decide about the safety, dosage, and efficacy of medication use during pregnancy/lactation in an evidence vacuum [2, 3]. This is a major inequity in healthcare.

Globally only about 40% of infants are exclusively fed human milk for six months [4, 5]. Rates of pre-existing maternal medical conditions are increasing amongst pregnant and lactating women, in the context of rising obesity and other non-communicable diseases [6–8]. This in turn increases the chance of women needing regular treatment for a pre-existing condition. The lack of information on the safety of medications during lactation may contribute to suboptimal breastfeeding rates. A recent Canadian study found that 40% of breastfeeding women had used at least one prescription medication in the first 3 months postpartum [9]. Various medications administered to the mother are known to be excreted into human milk and some in quantities that could adversely affect the infant [10]. There is therefore a pressing need to improve the inclusion of pregnant and breastfeeding women in clinical trials to fill this information gap [11].

Initiatives are being developed to allow for improved recruitment of pregnant and breastfeeding persons into clinical trials [12]. Despite these efforts, it is estimated that only around 5% of medical products available on the market are properly controlled, tested, and marked with up-to-date information on their safety during the perinatal period and lactation. This limited evidence can lead to miscommunication, with patients being advised against the use of life-saving treatments or medications being stopped due to conception [13, 14]. The problem of routinely excluding women from clinical trials resurfaced during the COVID-19 pandemic when the lack of data on this population compounded concerns and doubts about the use of the COVID-19 vaccine [15, 16].

Additionally, the manufacturer is legally responsible for any adverse reactions that occur after medicinal products are used, regardless of whether there is evidence of a cause-and-effect relationship. This is often an insurmountable barrier to including breastfeeding women in clinical trials [14].

An adverse event (AE) is defined as any abnormal sign, symptom, laboratory test, syndromic combination of such abnormalities, untoward or unplanned occurrence, or unexpected deterioration in a concurrent illness associated with the use of a therapeutic product, either as a medicine or medical device [17]. The reporting of AEs is essential during a clinical trial and for the ongoing monitoring of the safety and effectiveness of therapeutic medicinal products. Specific and standardised terminology for reporting AE facilitates a meaningful analysis of safety and the exchange of information between trial personnel and the regulatory authorities. While a detailed framework exists for preferred terms relating to most human organ systems, such a tool needs to be better described for lactation.

Lactation is a normal, complex physiological process within the reproductive cycle that involves initiation of milk secretion, transition from colostrum to secretion of mature milk, and the interplay of hormonal signals to continue regular synthesis and secretion of milk for the neonate once supply is established. Lactation commences at conception, triggering breast tissue remodeling to synthesise unique milk components. Milk secretion commences between 16 and 20 weeks of gestation to produce colostrum, while secretory activation is then triggered by the delivery of the placenta (REFS) [18]. Sustained lactation then requires frequent and effective milk removal in the context of normal breast physiology through breastfeeding. Most women who give birth will initiate breastfeeding of their newborn. This process can also be termed chestfeeding [18, 19].

Current terminologies fail to capture the intricacies of lactation and breastfeeding. The Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [20] lists 837 potential AEs, of which only one generic 'Lactation disorder' relates to lactation and breastfeeding, describing a disorder with two grades characterised by disturbances of milk secretion. At the time this study was initiated, the Medical Dictionary of Regulatory Activities (MedDRA version 25) contained two definitions of AEs related to "Oversupply of milk" and "Other change in lactation/feeding pattern" that were inadequate and insufficient to describe the complex physiological and behavioural interplay between two individuals during breastfeeding.

This study convened an international group of lactation and breastfeeding experts to develop standard definitions with severity grading of AEs based on lactation physiology. The objective was to enable the structured reporting of AEs during lactation in clinical trials.

Methods

In summary, we performed a two-stage consensus process using the Delphi method between January 2021 and November 2023. After review of existing available terminology for lactation and breastfeeding AEs, a first draft of definitions and grading as well as measurable indicators definitions were developed by the Steering Group. It was an international, multidisciplinary group of experts in midwifery, obstetrics, fetal medicine, neonatology, pediatrics, lactation, pharmacology, biomedicine, human nutrition, and also parent representatives (Fig. 1). New lactation/breastfeeding AE terms were integrated with MedDRA (Medical Dictionary for Regulatory Activities) requirements and mapped to their terms list in discussion with the MedDRA Maintenance and Support Services Organization (MSSO) (26th edition of MedDRA). The draft of the new terms and grading of the terminology were finalised before entering a two-stage international modified Delphi consensus procedure, which was conducted between November 2021 and October 2023. A final set of lactation and breastfeeding AE definitions and severity criteria were agreed.

Identification of existing AE terminology relevant to lactation and breastfeeding

At the start, we consulted internationally with academic and industry experts on lactation and clinical triallists to identify existing definitions of lactation and breastfeeding and the severity of the grading criteria for clinical trials. A search of existing databases (MedDRA 25th edition, WHO ICD-11, GAIA terminology 16.2d and CTCAE 5.0, Division of AIDS (DAIDS) Adendum1: female Grading table for use in Microbicide Studies, NAESS, International Classification of Functioning, Disability and Health) using keywords attracting definitions of postnatal period, breastfeeding and lactation was performed [20–27]. The search was limited to English language. Existing definitions and severity grading criteria were reviewed with MedDRA-preferred terms for AEs (Table 1).

Development of terminology and grading framework relevant to lactation and breastfeeding

The Steering Group considered the physiological process of lactation to categorize AEs. The terminology also considered definitions developed by researchers from the LactaResearch Group [28].

Whenever possible, consideration was made to concentrate on milk synthesis and breastfeeding, taking into account the unique interplay of the mother-infant dyad. Both maternal and neonatal measurable indicators were defined to aid definitions and grading. AE grades were based on the generic Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. (U.S. Department of Health and Human Services, 27th November, 2017)

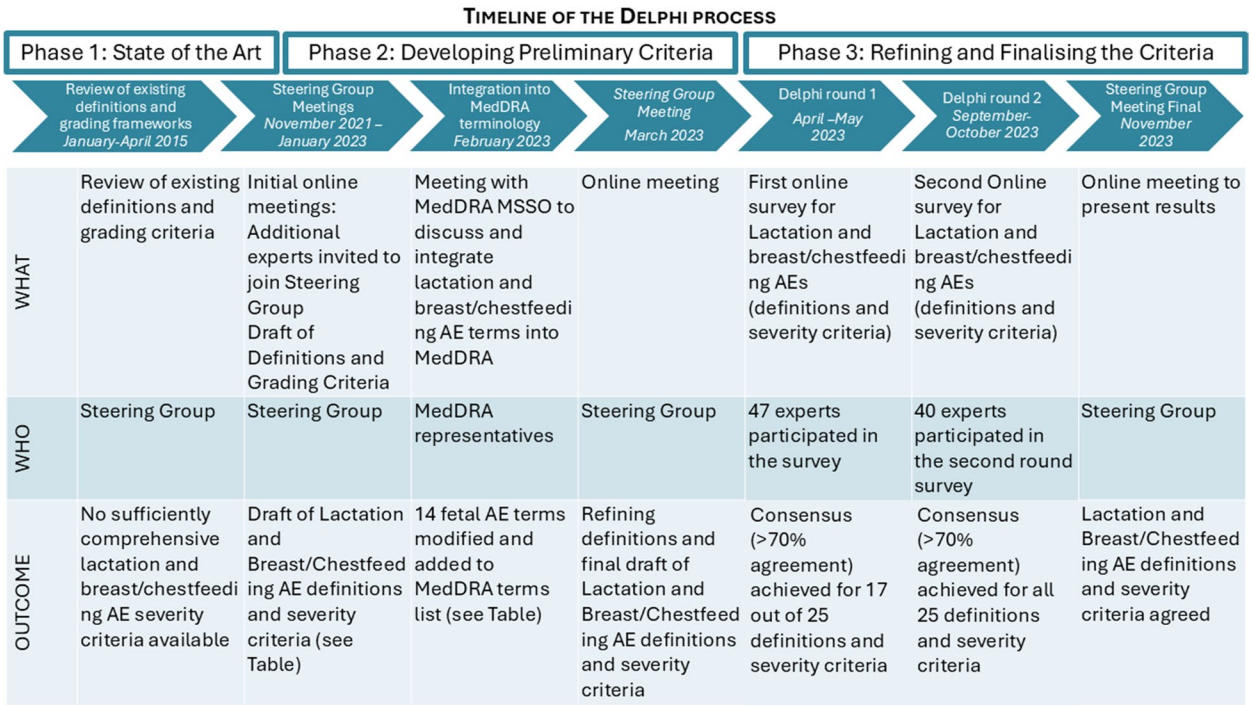

Fig. 1 Timeline of the Delphi process. Abbreviations used in Fig. 1: AE – adverse event; MedDRA – Medical Dictionary for Regulatory Activities; MSSO—Maintenance and Support Services Organization

Table 1 Existing Adverse Events (AE) terminology relevant to breast/chestfeeding and lactation

1. MedDRA 25th edition

Exposures associated with pregnancy, delivery, and lactation (Exposures, chemical injuries, and poisoning)

Code	English PT	HLT	HLGT	SOC	Primary SOC
10069496	Vaccine exposure before pregnancy	Exposures associated with pregnancy, delivery, and lactation	Exposures, chemical injuries, and poisoning	Injury, poisoning, and procedural complications	Y
10069496	Vaccine exposure before pregnancy	Exposures associated with pregnancy, delivery, and lactation	Pregnancy, labour, delivery, and postpartum conditions	Pregnancy, puerperium, and perinatal conditions	N
10057982	Vaccine exposure during pregnancy	Exposures associated with pregnancy, delivery, and lactation	Exposures, chemical injuries, and poisoning	Injury, poisoning, and procedural complications	Y
10057982	Vaccine exposure during pregnancy	Exposures associated with pregnancy, delivery, and lactation	Pregnancy, labour, delivery, and postpartum conditions	Pregnancy, puerperium, and perinatal conditions	N
Lactation					
Code	English PT	HLT	HLGT	SOC	Primary SOC
10061261	Lactation disorder	Lactation disorders	Breast disorders	Reproductive system and breast disorders	Y
10061261	Lactation disorder	Postpartum breast disorders	Postpartum and puerperal disorders	Pregnancy, puerperium, and perinatal conditions	N
10069058	Lactation inhibition therapy	Obstetric therapeutic procedures	Obstetric and gynecological therapeutic procedures	Surgical and medical procedures	Y
10082625	Lactation normal	Normal pregnancy, labour, and delivery	Pregnancy, labour, delivery, and postpartum conditions	Pregnancy, puerperium, and perinatal conditions	Y
10023671	Lactation puerperal increased	Lactation disorders	Breast disorders	Reproductive system and breast disorders	Y
10023671	Lactation puerperal increased	Postpartum breast disorders	Postpartum and puerperal disorders	Pregnancy, puerperium, and perinatal conditions	N
10079806	Lactation stimulation therapy	Obstetric therapeutic procedures	Obstetric and gynecological therapeutic procedures	Surgical and medical procedures	Y
10042576	Suppressed lactation	Lactation disorders	Breast disorders	Reproductive system and breast disorders	Y
10042576	Suppressed lactation	Postpartum breast disorders	Postpartum and puerperal disorders	Pregnancy, puerperium, and perinatal conditions	N
Infant/neonate					
10075317	Excessive feeding neonatal	Overfeeding of infant	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders
10075317	Excessive feeding neonatal	Overfeeding of infant	Neonatal metabolic and endocrine disorders	Neonatal and perinatal conditions	Pregnancy, puerperium, and perinatal conditions
10016316	Feeding disorder neonatal	Selective eating disorder	Eating disorders NEC	Eating disorders and disturbances	Psychiatric disorders
10016316	Feeding disorder neonatal	Selective eating disorder	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders
10028938	Neonatal feeding disorder	Selective eating disorder	Eating disorders NEC	Eating disorders and disturbances	Psychiatric disorders
10028938	Neonatal feeding disorder	Selective eating disorder	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders

Table 1 (continued)

10075318	Poor feeding neonatal	Poor feeding infant	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders
10075318	Poor feeding neonatal	Poor feeding infant	Neonatal metabolic and endocrine disorders	Neonatal and perinatal conditions	Pregnancy, puerperium, and perinatal conditions
10016320	Feeding problems in a newborn	Poor feeding infant	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders
10016320	Feeding problems in a newborn	Poor feeding infant	Neonatal metabolic and endocrine disorders	Neonatal and perinatal conditions	Pregnancy, puerperium, and perinatal conditions
10016321	Feeding problems in a newborn	Poor feeding infant	General nutritional disorders NEC	Appetite and general nutritional disorders	Metabolism and nutrition disorders
10016321	Feeding problems in a newborn	Poor feeding infant	Neonatal metabolic and endocrine disorders	Neonatal and perinatal conditions	Pregnancy, puerperium, and perinatal conditions
2. The Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) terminology, version 16.2d					
No definition on Breastfeeding, lactation, puerperium or postnatal mother					
3. International Classification of Functioning, Disability and Health					
B6603: Lactation		Description: Functions involved in the production of milk and making it available to the child		Related impairments: agalactorrhea, alactation, galactorrhea	
D6608 Other specified assisting others		All index terms: Other specified assisting others Breastfeeding infants and children			
4. Division of AIDS (DAIDS) Adendum1: female Grading table for use in Microbicide Studies					
No definition on breastfeeding or lactation					
5. NAESS					
No definition or grading on breastfeeding or lactation					
6. WHO (ICD-11)					
JB45 Infections of the breast associated with childbirth					
JB45.0				Abscess of the breast associated with childbirth	
JB45.1				Nonpurulent mastitis associated with childbirth	
JB45.Y				Other specified infections of the breast associated with childbirth	
JB45.Z				Infections of the breast associated with childbirth, unspecified	
JB46 Certain specified disorders of breast or lactation associated with childbirth					
JB46.0				Retracted nipple associated with childbirth	
JB46.1				Cracked nipple associated with childbirth	
JB46.2				Other or unspecified disorders of the breast associated with childbirth	
JB46.3				Agalactia	
JB46.4				Hypogalactia	
JB46.5				Suppressed lactation	
JB46.6				Galactorrhoea	
JB46.7				Other or unspecified disorders of lactation	
MF31				Breast or lactation symptoms or complaints	

Table 1 (continued)

MF35		Postpartum symptoms or complaints
JB4Z		Complications predominantly related to the puerperium, unspecified
7. CTCAE 5.0		
C143336	Breast Infection	A disorder characterized by an infectious process involving the breast
C144554	Grade 2 Breast Infection, CTCAE	Local infection with moderate symptoms; oral intervention indicated (e.g., antibiotic, antifungal, or antiviral)
C145170	Grade 3 Breast Infection, CTCAE	IV antibiotic, antifungal, or antiviral intervention indicated; severe infection; axillary adenitis
C145770	Grade 4 Breast Infection, CTCAE	Life-threatening consequences: urgent intervention indicated
C146238	Grade 5 Breast Infection, CTCAE	Death
C143335	Breast atrophy	A disorder characterized by underdevelopment of the breast
C144010	Grade 1 Breast Atrophy, CTCAE	Minimal asymmetry; minimal atrophy
C144553	Grade 2 Breast Atrophy, CTCAE	Moderate asymmetry; moderate atrophy
C145169	Grade 3 Breast Atrophy, CTCAE	Asymmetry > 1/3 of breast volume; severe atrophy
C146742	Breast Pain	A disorder characterized by a sensation of marked discomfort in the breast region
C56026	Grade 1 Breast Pain, CTCAE	Mild pain
C56027	Grade 2 Breast Pain, CTCAE	Moderate pain; limiting instrumental ADL
C56028	Grade 3 Breast Pain, CTCAE	Severe pain; limiting self-care ADL
C143634	Lactation Disorder	A disorder characterized by disturbances of milk secretion. It is not necessarily related to pregnancy observed in females; it can be observed in males
C144234	Grade 1 Lactation disorder, CTCAE	Mild changes in lactation, not significantly affecting production or expression of breast milk
C144805	Grade 2 Lactation disorder, CTCA	Changes in lactation, significantly affecting breast production or expression of breast milk
C143706	Nipple Deformity	A disorder characterized by a malformation of the nipple
C144291	Grade 1 Nipple Deformity, CTCAE	Asymptomatic: asymmetry with slight retraction and/or thickening of the nipple-areolar complex
C144867	Grade 2 Nipple Deformity, CTCAE	Symptomatic: asymmetry of a nipple-areolar complex with moderate retraction and/or thickening of the nipple-areolar complex
C143808	Reproductive System and Breast Disorders—Other, Specify	
C144380	Grade 1 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
C144974	Grade 2 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
C145597	Grade 3 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; limiting self-care ADL
C144974	Grade 2 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL

Table 1 (continued)

C145597	Grade 3 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of existing hospitalization indicated; limiting self-care ADL
C146094	Grade 4 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Life-threatening consequences; urgent intervention indicated
C146529	Grade 5 Reproductive System and Breast Disorders—Other, Specify, CTCAE	Death

The terms listed are drawn from the 25th edition of MedDRA (Medical Dictionary for Regulatory Activities), the Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) terminology, International Classification of Functioning, Disability and Health (ICF), Division of AIDS (DAIDS) Female Grading Table, WHO ICD-11, and the Common Terminology Criteria for Adverse Events (CTCAE) v5.0. MedDRA terms include multiple System Organ Class (SOC) assignments, with primary SOC indicated. Definitions specific to lactation were absent in GAIA, DAIDS, and NAESS. The ICF provides functional descriptors and impairment classifications. WHO ICD-11 and CTCAE describe infectious, structural, and symptomatic conditions associated with lactation and postpartum breast health. There is noticeable gap in standardised, physiology-aligned terminology to capture the range of lactation-related experiences and outcomes in clinical and regulatory frameworks

The name of regulatory body or classification system given in **bold**

grading system (Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. Grade 2 Moderate; minimal, local or non-invasive intervention indicated. Grade 3 Severe or medically significant but not immediately life-threatening; hospitalisation or prolongation of hospitalisation indicated. Grade 4 Life-threatening consequences; urgent intervention indicated. Grade 5 Death related to AE), with the well-being of the newborn/infant used as the surrogate marker of adequate milk production and transfer. Terms were limited to objective indicators of maternal milk synthesis and adequacy of infant milk intake and factors relating more broadly to infant and/or maternal health were outside of scope as they would be defined by other terminology (CTCAE, MFAET or NAESS) [29–31].

Modified Delphi consensus process

Experts in clinical and academic fields related to lactation and breastfeeding as well as representatives of parents' organisations, were identified via the Steering Group network through snowballing and were invited to participate in the Delphi procedure. Participants were identified with expertise in biomedical and nutrition science, obstetrics, and maternal and fetal medicine, immunology, microbiology, lactation, midwifery and nursing, neonatology and pediatrics, pharmacy, pharmacology and pharmacovigilance.

We assured a broad global coverage, inviting participants from twenty-three countries across Europe, North America, Asia, Africa, South America, and Australia. Data was carefully anonymized in order to avoid identification of individual experts during analysis. Agreement of $\geq$ 70% participants was taken as consensus. Systematically missing responses where participants stopped partway through the survey were excluded from analysis; non-systematically missing responses were included as non-agreement.

The web platform REDCap® was used to collect the results of the Delphi surveys [32, 33]. Participation was tracked with individual logins. The first round of Delphi allowed participants to answer whether they agreed or disagreed with the proposed definitions and grades, with additional space for free comments. All definitions and grades were presented to the participants for the second round, but they were only asked to consider and agree on unresolved items.

Results

Phase 1: current terminology

A review of the terminology, classification of diseases and adverse events grading systems (MedDRA 25th edition, WHO ICD-11, GAIA terminology 16.2d and CTCAE 5.0) identified two existing AE definitions but no grading of AEs relevant to lactation/breastfeeding. The existing MedDRA definitions related to "Oversupply of milk" and "Other change in lactation/feeding pattern".

Phase 2: development of AE definitions and grading

Considering the physiological stages of lactation, the Steering Group agreed on the following specific AE areas: initial inadequate activation of copious milk synthesis (delayed secretory activation), and two types of lactation insufficiency according to the timing following initial lactation activation (primary lactation insufficiency and secondary lactation insufficiency). Additionally, we defined two other AEs related to oversupply and potential other changes in lactation or breastfeeding related to, for example, a change in human milk appearance, smell, and taste.

Measurable indicators were identified from the literature search to aid the classification of AEs [34]. The effects of disrupted lactation breastfeeding on neonates were defined and used as a surrogate marker of the severity of the AE.

Mapping new definitions to MedDRA

In the process of developing the definitions for Adverse Events in lactation and breastfeeding Steering Group members reviewed the new proposed definitions with the MSSO (Maintenance and Support Services Organization) team from MedDRA, the Medical Dictionary of Regulatory Activities. Three new lactation definitions were mapped and described in the MedDRA 26th edition in March 2023: Delayed secretory activation, Primary lactation insufficiency and Secondary lactation insufficiency. The Oversupply and Other changes in lactation/feeding patterns were mapped to existing MedDRA terms (Table 2).

Modified Delphi consensus process

We invited fifty-five experts via e-mail to participate in the Delphi process. We received forty-seven responses to the First Round (85% of all invitees). Forty-seven experts from eleven countries completed the First Round questionnaire which launched in April 2023 and closed in May 2023 after two reminders. We noted one non-systematic error when an expert missed the answer to the question and this was treated as non-agreement. Consensus was reached for 17 out of the 25 proposed grades. Four grades achieved borderline consensus equal to 70% and for another four grades, the consensus threshold was not reached. Based on the comments from the First Round experts, changes were made to the terminology of AE grades which had not achieved agreement of > 70%. This included changing the definitions of the terms primary and secondary lactation 'failure' to 'insufficiency'. Another change was the addition of a definition

Table 2 Adverse events related to the lactation and breast/chestfeeding mapped to MedDRA 26th edition, March 2023

Adverse Event	MedDRA LLT v26.0	MedDRA LLT Code
Delayed secretory activation	Delayed onset of lactation	10088878
Primary lactation insufficiency	Primary lactation insufficiency	10088880
Secondary lactation insufficiency	Secondary lactation insufficiency	10088881
Oversupply	Milk overproduction	10027634
Other change in lactation/feeding pattern	Lactation disorder	10061261

Three new definitions were added to MedDRA 26th edition, and two definitions were mapped to previously established terms

Abbreviations: MedDRA Medical Dictionary for Regulatory Activities, *LLT* Lowest Level Term

for neonatal medical interventions and the impact of the AE grade on neonates for Grade 3 Delayed Secretory Activation and Grade 3 Other change in lactation/feeding pattern.

All changes were reflected in the Second Round questionnaire, which was sent to all experts who completed the First Round. The second round launched in September and closed in October 2023 after two reminders. Forty experts (85%) returned the questionnaire for the Second Round. After two rounds of the modified Delphi procedure the consensus was reached in all the AE grades (Table 3).

Lactation and Breastfeeding Adverse Events Terminology (LaBAET)

The final version of the Lactation and Breastfeeding Adverse Event Terminology (LaBAET) version 1.0 is presented in Table 4.

Discussion

Main findings

The Lactation and Breastfeeding Adverse Events Terminology (LaBAET) version 1.0 has been developed to standardise definitions and grade the severity of AEs related to lactation and breastfeeding. To the best of our knowledge this is the first collaboration to address AEs related to lactation and breastfeeding with such methodology. By working with world-class experts in the field, developing the terminology and grading in line with the CTCAE framework, mapping definitions to MedDRA, and following the well-established Delphi consensus procedure we developed the terminology to be as robust as possible within the constraints of current knowledge. This resulted in defining five domains of AE definitions and grading the severity within each domain using standard criteria.

With the exception of Secondary lactation insufficiency (Grades 2–5) and Oversupply (Grades 1–4), we defined five grades for each AE definition. Measurable indicators for the Secondary Lactation Insufficiency were not considered to define a mild event, therefore Grade 1 is absent in this AE.

Together with the Maternal and Fetal Adverse Events Terminology (MFAET) [30] and the Neonatal Adverse Event Severity Score (NAESS) [25] LaBAET fills an important gap in clinical trial safety terminology and will help researchers and clinicians improve assessment and recording of AEs in pregnant and lactating persons.

Application

We hope that developing detailed descriptions and grading of the severity of AEs in lactation and breastfeeding will help researchers to safely develop and deliver clinical trials to postpartum persons as it enables the unification of terminology used and helps with communicating the findings. The terminology can be applied to the control group participants and patients undergoing medical intervention. The physiological approach to defining and grading AE makes LaBAET version 1.0 easy to apply in clinical and research-related settings.

We believe that the development of LaBAET version 1.0 will fill the gap identified by the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC), which found difficulties with developing safe and effective therapies for pregnant and lactating women due to gaps in knowledge and research from limited existing scientific literature [2]. Having available terminology to define and grade lactation and breastfeeding AEs will improve the safe conduct of trials of therapeutics. Participation in clinical trials not only improves medical knowledge and allows the development of new and novel therapies but also, independently from applied treatment, improves outcomes for participants [35–37]. This is especially important in emergencies such as the recent COVID-19 pandemic, when the rapid development of vaccines played a crucial role in managing the immunity of the pregnant population. Evidence shows that pregnancy vaccination improves neonatal immunity response to COVID-19 [38].

Strengths and limitations

The strength of our process is that we began by considering the physiology of lactation and breastfeeding followed by a careful examination of existing terminology

Table 3 Modified Delphi procedure results

Adverse Event	First Round Agreement (%, $n=47$)	Proposed changes in the Second Round	Second Round Agreement ($n=40$)			
			Respondents (n)		% agreement	% agreement (corrected for absent 2nd round experts)
			Yes	No		
Delayed secretory activation						
Grade 1*	72					
Grade 2	72	addition of 'onset' to Grade 2 and 3	39	1	98	83
Grade 3	68	addition of 'onset' to Grade 2 and 3	40	0	100	85
Grade 3	68	additions of definitions of medical interventions and impact of the AE on neonate to Grades 3, 4 and 5	38	2	95	81
Grade 4	70	replacement of 'lactation failure' with 'lactation insufficiency	40	0	100	85
Grade 5	72	replacement of 'lactation failure' with 'total lactation insufficiency'	39	1	98	85
Primary lactation insufficiency						
Grade 1*	74					
Grade 2*	72					
Grade 3*	77					
Grade 4	72	replacement of 'lactation failure' with 'lactation insufficiency'	39	1	98	83
Grade 5	68	replacement of 'lactation failure' with 'total lactation insufficiency'	37	3	93	79
Secondary lactation insufficiency						
Grade 1	70	removal of Grade 1	39	1	98	83
Grade 2*	77					
Grade 3*	72					
Grade 4	72	replacement of 'lactation failure' with 'lactation insufficiency'	40	0	100	85
Grade 5	70	replacement of 'lactation failure' with 'total lactation insufficiency'	37	3	93	79

Table 3 (continued)

Adverse Event	First Round Agreement (%, $n=47$)	Proposed changes in the Second Round	Second Round Agreement ($n=40$)			
			Respondents (n)		% agreement	% agreement (corrected for absent 2nd round experts)
			Yes	No		
Oversupply						
Grade 1*	85					
Grade 2*	79					
Grade 3*	74					
Grade 4*	83					
Other change in lactation/feeding pattern						
Grade 1*	85					
Grade 2*	74					
Grade 3	70	additions of definitions of medical interventions and impact of the AE on neonate to Grades 3, 4 and 5	38	2	95	81
Grade 4	74	replacement of 'lactation failure' with 'lactation insufficiency'	40	0	100	85
Grade 5	68	replacement of 'lactation failure' with 'total lactation insufficiency'	38	2	95	82

A two-round modified Delphi process was conducted with 47 expert panel members participating in Round 1 and 40 in Round 2. Agreement was defined as ≥ 70% of responses endorsing the proposed grade or change. Grades that met this threshold in Round 1 were considered agreed and did not proceed to Round 2. In Round 2, the percentage agreement was calculated both among respondents and corrected for the full Round 1 cohort, assuming non-agreement from non-respondents

Names of Adverse Events given in **bold**

Abbreviations: *AE* adverse event

* agreement reached in Round 1

Table 4 Definitions and grading of the Adverse Events in lactation and breast/chestfeeding

Grade Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Delayed secretory activation	Mild delay in copious milk synthesis of < 72 h after placenta separation	Onset of copious milk synthesis delayed > 72 h and < 10 days after placenta separation. Breast/chestfeeding or human milk feeding established afterwards	Onset of copious milk synthesis delayed > 10 days after placenta separation. Neonate affected (Loss of more than 10% body weight in the first 72 h, still passing meconium on day 5, not back to birthweight by day 14, less than normal output for age, poor weight gain for age), and/or needs medical intervention (ie need to introduce donor milk or formula). Breast/chestfeeding or human milk feeding or mixed feeding established afterwards	Lactation insufficiency. Neonate severely affected (dehydration/urine output reduced < 1 ml/kg/h), and/or medical intervention required (IV supplementation/hospitalisation)	Total lactation insufficiency, no other source of nutrition available for the neonate. Neonatal death
Primary lactation insufficiency	Mixed feeding with < 20% of formula or donor human milk or mixed feeding with 20–80% of formula or donor human milk but amount of supplementation reduced to 0 afterwards	Mixed feeding with > 80% of formula or donor human milk	Lactation insufficiency. Formula or donor human milk feeding with no or token human milk available. And/or neonate affected, needs medical intervention	Lactation insufficiency. Neonate/infant severely affected (dehydration/urine output reduced < 1 ml/kg/h), and/or needing medical intervention (IV supplementation/hospitalisation)	Total lactation insufficiency, no other source of nutrition available for the neonate. Neonatal death
Secondary lactation insufficiency	-	Neonate weight loss of > 10% or inadequate infant weight gain. Need to introduce mixed feeding	Lactation insufficiency. Neonate weight loss of > 10% or infant weight gain significantly below expected. Formula or donor human milk feeding with no or token human milk available. Neonate affected, needs medical intervention	Lactation insufficiency. Neonate/infant severely affected (dehydration/urine output reduced < 1 ml/kg/h), and/or needing medical intervention (IV supplementation/hospitalisation)	Total lactation insufficiency, no other source of nutrition available for the neonate/infant. Neonate/infant death
Oversupply	Symptoms present for less than 4 weeks postpartum and managed with non-pharmacological interventions such as varying breast/chestfeeding position	Symptoms present for more than 4 weeks postpartum and managed with non-pharmacological interventions such as varying breast/chestfeeding position or symptoms present for less than 4 weeks postpartum managed with pharmacological interventions (pain relief, treatment to reduce milk synthesis)	Symptoms present for more than 4 weeks postpartum, need for professional support/hospitalisation. Symptoms managed with pharmacological interventions (pain relief, treatment to reduce milk synthesis)	Symptoms so overwhelming that complete breast/chestfeeding cessation required despite nonpharmacological and/or pharmacological intervention	-

Table 4 (continued)

Grade Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Other change in lactation/ feeding pattern	Parental reassurance required with no effect on breast/chest-feeding and the baby (normal weight gain of neonate/infant, no need to introduce mixed feeding)	Reduced parental breast/chest-feeding confidence with disruption of neonate infant well-being, need to introduce mixed feeding. Exclusive breast/chestfeeding and parental confidence re-established after intervention (non-pharmaceutical or pharmaceutical)	Lactation/feeding pattern leading to lactation insufficiency. Formula or donor human milk feeding with no or token human milk available. Unable to re-establish breast/chest-feeding despite nonpharmacological and/or pharmacological intervention. Neonate/infant affected (less than normal output for age, poor weight gain), and/or needing medical intervention (need to introduce donor milk or formula)	Lactation insufficiency. Neonate/infant severely affected (dehydration/urine output reduced < 1 ml/kg/h), and/ or needing medical intervention (IV supplementation/ hospitalisation)	Total lactation insufficiency, no other source of nutrition available for the neonate/infant. Neonate/infant death

This table presents the outcome of a multidisciplinary expert consensus process using a modified Delphi method to define and grade adverse events related to lactation and breast/chestfeeding. Events were assessed across five severity grades (Grade 1–5), with specific definitions applied to each level of severity for the following categories: Delayed secretory activation, Primary lactation insufficiency, Secondary lactation insufficiency, Oversupply, and Other change in lactation/feeding pattern

Definitions account for clinical signs in the mother, impact on the neonate or infant, and whether interventions (pharmaceutical or non-pharmaceutical) were required. Adverse events graded 3 or higher typically reflect significant disruption to lactation or infant well-being, with Grades 4 and 5 associated with severe compromise or death

Grades and names of Adverse Events given in **bold**

Abbreviations: *AE* Adverse Event, *IV* Intravenous, < less than, > more than

and literature to identify gaps in assessment for AEs. Our Steering Group and Delphi consensus experts included multiple key stakeholders involved in developing clinical trials in pregnancy and postpartum. There was international participation in the process with clinicians and researchers, industry representatives, midwifery and parent representatives.

A considerable problem that impacts lactation medical care is the absence of reference ranges to objectively define parameters for normal function. This represents a major gap in the continuum of care that does not exist for other major organs. Definitions have been proposed to describe parameters for biological normality [34]. This has collated published data to provide preliminary markers for the initiation of lactation and to describe objective tests once lactation is established. For example, reference limits have been calculated for maternal markers of secretory activation, such as progesterone in maternal blood and total protein, lactose, sodium, and citrate in maternal milk. Nevertheless, some indicators (oversupply and changes in lactation/feeding pattern) were arbitrarily proposed and agreed by expert consensus. Future refinement and expansion will continue to improve these criteria. The terminology should undergo validation within real-life clinical environments, or during clinical trials as done recently with the NAESS terminology [39] and be updated as new knowledge on lactation and breastfeeding becomes available.

The terminology is also limited by the complex physiological processes underlying lactation and breastfeeding. For example, the terms Delayed secretory activation and Primary lactation insufficiency might be assumed to overlap. Trial staff classifying AEs will therefore need to carefully collect data on the timing of lactation onset to decide how to classify an individual AE. Additionally, it is difficult to separate lactation, the physiological process of milk synthesis, from breastfeeding, which refers to the dyadic mother-baby transfer of milk. The neonate and infant can be affected by lactation, breastfeeding disturbance, and the actual medicinal product being excreted and transferred within the milk. These types of AEs should be classified through neonatal definitions [38].

The dyadic nature of the lactation and breastfeeding process allowed us to use the neonate/infant as a surrogate marker of lactation insufficiency. This approach generated debate within the Delphi consensus in more severe grades, especially for Grade 5 which is for neonatal death. The Steering Group considered the very low chance that total lactation insufficiency would result in a neonatal death as almost certainly alternative feeding would be undertaken. However, consensus was reached to keep these severe grades for completeness as we believe that LaBAET would not be comprehensive without them.

Conclusion

Using an international Delphi consensus process a comprehensive terminology (LaBAET version 1.0) has been developed to standardise definitions and grade the severity of adverse events related to lactation and breastfeeding. This new terminology fills the gap in existing classifications and should encourage the safe inclusion of pregnant and postpartum individuals into clinical trials.

Acknowledgements

Magdalena Babiszewska-Aksamit, Medical University of Warsaw, Warsaw, Poland; Sofia Badilla, Pzifer, Warsaw, Poland; Barbara Baranowska, Postgraduate Centre of Medical Education, Warsaw, Poland; Urszula Bernatowicz-Łojko, Postgraduate Centre of Medical Education, Warsaw, Poland; Agnieszka Bzikowska-Jura, Medical University of Warsaw, Warsaw, Poland; Jarosław Bryda, Voivodship Veterinary Inspectorate, Lublin, Poland; Pavel Calda, Charles University, Prague, Czech Republic; Tanya Cassidy, Maynooth University, Maynooth, Ireland; Chris Gale, Imperial College London, London, UK; Wessel Ganzevoort, Amsterdam UMC Care, Amsterdam, Netherlands; Donna Geddes, The University of Western Australia, Western Australia, Australia; Roslyn Giglia, Department of Health Western Australia, Western Australia, Australia; María Gormaz Moreno, La Fe University and Polytechnic Hospital, Valencia, Spain; Maria Hoeltzenbein, Charité – Berlin University Medicine, Berlin, Germany; Sue Jordan, Swansea University, Swansea, UK; Meg Kawan, Children's Hospital of Philadelphia, Philadelphia, USA; Kaytlin Krutsch, Texas Tech University Health Sciences Center, Lubbock, USA; Desirée Mena Tudela, Jaume I University, Castelló de la Plana, Spain; Alicja Misztal, Żelazna Medical Center, Warsaw, Poland; Nancy Mohrbacher, Nancy Mohrbacher Solutions, Inc., Chicago, USA; Aneta Nitsch-Osuch, Medical University of Warsaw, Warsaw, Poland; Ryan Pace, University of Idaho, Moscow, USA; Douglas Pritchard, University of Western Australia, Western Australia, Australia; Juan Miguel Rodríguez, Complutense University of Madrid, Madrid, Spain; Elena Sinkiewicz-Darol, Kazimierz Wielki University, Bydgoszcz, Poland; Edyta Socha, Ludwik Rydygier Collegium Medicum, Bydgoszcz, Poland; Agnieszka Szymanek, Sunnaas sykehus, Norway; Dawid Szymonik, Independent Public Healthcare, Puławy, Poland; Jingjie Yu, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China.

Authors' contributions

KMM: Conceptualization; formal analysis; methodology; investigation; resources; validation; visualization; writing – original draft. KKK: Conceptualization; data curation; methodology; investigation; resources; visualization; writing – original draft. DS: Conceptualization; methodology; resources; validation; writing – review & editing. MB: Methodology; resources; validation; writing – review & editing. MCC: Methodology; resources; validation; writing – review & editing. AGD: Methodology; resources; validation; writing – review & editing. BH: Methodology; resources; validation; writing – review & editing. AK: Methodology; resources; validation; writing – review & editing. JK: Methodology; resources; validation; writing – review & editing. EK: Methodology; resources; validation; writing – review & editing. KM: Methodology; resources; validation; writing – review & editing. RP: Methodology; resources; validation; writing – review & editing. NS: Methodology; resources; validation; writing – review & editing. SW: Methodology; resources; validation; writing – review & editing. ALD: Conceptualization; methodology; resources; supervision; validation; writing – review & editing. AW: Conceptualization; funding acquisition; methodology; project administration; resources; supervision; validation; writing – review & editing.

Funding

The implementation of the study was a part of the project entitled 'Development of a tool for pharmacovigilance on breastfeeding and analysis of the impact of post-vaccination effects on lactation in women after receiving the COVID-19 vaccine in the perinatal period' and financed under 'Urgency Grants' by the Polish National Agency for Academic Exchange (in Polish: Narodowa Agencja Wymiany Akademickiej). Number of financed project: BPN/GIN/2021/1/00040/U/00001.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The survey was performed in compliance with the principles outlined in the Declaration of Helsinki. The Bioethical Committee of the Medical University of Warsaw in Warsaw, Poland has taken note of the information about the investigation and has raised no objections (number of decision: AKBE/177/2023).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Institute for Women's Health, University College London, London, United Kingdom. [2]Laboratory of Human Milk and Lactation Research, Regional Human Milk Bank at Holy Family Specialist Hospital, Department of Medical Biology, Medical University of Warsaw, Warsaw, Poland. [3]Department of Family and Community Health and the Center for Pediatric Nursing Research and Evidence Based Practice at Children's Hospital of Philadephia, University of Pennsylvania School of Nursing, Philadelphia, PA, USA. [4]School of Allied Health, The University of Western Australia, Crawley, WA, Australia. [5]Institute of Agrochemistry and Food Technology – National Research Council (IATA-CSIC), Valencia, Spain. [6]Pfizer Polska Sp. Z O.O, Warsaw, Poland. [7]Department of Nutrition and Food Safety, School of Public Health, Health Science Center of Xi'an Jiaotong University Xi'an, Xi'an, China. [8]St George's Hospital, University of London, London, United Kingdom. [9]IBCLC Private Practice, Wroclaw, Poland. [10]Department of Pediatrics With Clinical Assessment Unit, Medical University of Warsaw, Warsaw, Poland. [11]Department of Clinical Pharmacy and Biopharmacy, Poznan University of Medical Sciences, Poznan, Poland. [12]Department of Medicine, Division of Infectious Diseases, Department of Immunology and Immunotherapy, Icahn School of Medicine at Mount Sinai New York, New York, United States of America. [13]Department of Surgery and Cancer, Imperial College London, London, United Kingdom. [14]Department of Neonatology and Neonatal Intensive Care, Independent Public Specialist Hospital, Chełm, Poland.

Received: 9 February 2025 Accepted: 4 June 2025
Published online: 04 July 2025

References

1. Saunders EJ, Saunders JA. Drug therapy in pregnancy: the lessons of diethylstilbestrol, thalidomide, and Bendectin. Health Care Women Int. 1990;11:423–32.
2. Eunice Kennedy Shriver National Institute of Child Health and Human Development. Task force on research specific to pregnant women and lactating women. 2018. Available from:https://www.nichd.nih.gov/sites/default/files/2018-09/PRGLAC_Report.pdf. Cited 2024 Apr 3.
3. Byrne JJ, Saucedo AM, Spong CY. Evaluation of drug labels following the 2015 pregnancy and lactation labeling rule. JAMA Netw Open. 2020;3:e2015094.
4. North K, Gao M, Allen G, Lee AC. Breastfeeding in a global context: epidemiology, impact, and future directions. Clin Ther. 2022;44:228–44.
5. UNICEF Data. Breastfeeding. 2023 Available from:https://data.unicef.org/topic/nutrition/breastfeeding/. Cited 2024 Apr 8.
6. Radulescu L, Munteanu O, Popa F, Cirstoiu M. The implications and consequences of maternal obesity on fetal intrauterine growth restriction. J Med Life. 2013;6:292–8.
7. Lean SC, Derricott H, Jones RL, Heazell AEP. Advanced maternal age and adverse pregnancy outcomes: a systematic review and meta-analysis. PLoS ONE. 2017;12:e0186287.
8. Robledo CA, Yeung EH, Mendola P, Sundaram R, Boghossian NS, Bell EM, et al. Examining the prevalence rates of preexisting maternal medical conditions and pregnancy complications by source: evidence to inform maternal and child research. Matern Child Health J. 2017;21:852–62.
9. Soliman Y, Yakandawala U, Leong C, Garlock ES, Brinkman FSL, Winsor GL, et al. The use of prescription medications and non-prescription medications during lactation in a prospective Canadian cohort study. Int Breastfeed J. 2024;19:23.
10. Bowes WA. The effect of medications on the lactating mother and her infant. Clin Obstet and Gynecol. 1980;23:1073–80.
11. Eunice Kennedy Shriver National Institute of Child Health and Human Development. List of recommendations from the task force on research specific to pregnant women and lactating women (PRGLAC). 2019. Available from:https://www.nichd.nih.gov/about/advisory/PRGLAC/recommendations. Cited 2024 Apr 3.
12. Committee on Developing a Framework to Address Legal, Ethical, Regulatory, and Policy Issues for Research Specific to Pregnant and Lactating Persons, Board on Health Sciences Policy, Health and Medicine Division, National Academies of Sciences, Engineering, and Medicine. Advancing clinical research with pregnant and lactating populations: overcoming real and perceived liability risks. Riley MF, Helman A, March A, editors. Washington, D.C.: National Academies Press; 2024. p. 27595. Available from:https://www.nap.edu/catalog/27595. Cited 2024 May 2.
13. Global egulators envision paradigm shift toward inclusion of pregnant and breastfeeding women in clinical research for medicines and vaccines. Available from:https://www.fda.gov/news-events/fda-voices/global-regulators-envision-paradigm-shift-toward-inclusion-pregnant-and-breastfeeding-women-clinical.
14. Manca TA, Sadarangani M, Halperin SA, Langley JM, McClymont E, MacDonald SE, et al. Vaccine regulation should require and enforce the inclusion of pregnant and breastfeeding women in prelicensure clinical trials. Hum VaccinImmunother. 2022;18:2104019.
15. Gianfredi V, Stefanizzi P, Berti A, D'Amico M, De Lorenzo V, Lorenzo AD, et al. A systematic review of population-based studies assessing knowledge, attitudes, acceptance, and hesitancy of pregnant and breastfeeding women towards the COVID-19 vaccine. Vaccines. 2023;11:1289.
16. Sportiello L, Capuano A. It is the time to change the paradigms of pregnant and breastfeeding women in clinical research! Front Pharmacol. 2023;14:1113557.
17. Aronson JK. When I use a word … Medical definitions: adverse events, effects, and reactions. BMJ. 2023;381:917.
18. Hassiotou F, Geddes D. Anatomy of the human mammary gland: current status of knowledge. Clin Anat. 2013;26:29–48.
19. Pang WW, Hartmann PE. Initiation of human lactation: secretory differentiation and secretory activation. J Mammary Gland Biol Neoplasia. 2007;12:211–21.
20. U.S. Department of Health and Human Services. Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. 2017.
21. MEDRA. What's new MedDRA version 25.0. 2022.
22. World Health Organization. International statistical classification of diseases and related health problems (ICD). Available from:https://www.who.int/standards/classifications/classification-of-diseases.
23. Bonhoeffer J, Kochhar S, Hirschfeld S, Heath PT, Jones CE, Bauwens J, et al. Global alignment of immunization safety assessment in pregnancy – The GAIA project. Vaccine. 2016;34:5993–7.
24. Division of AIDS table for grading the severity of adult and pediatric adverse events. Available from:https://www.mtnstopshiv.org/sites/default/files/attachments/DAIDS_AE_GradingTable_ClarificationAug2009_Final_%5B1%5D.pdf.
25. Salaets T, Turner MA, Short M, Ward RM, Hokuto I, Ariagno RL, et al. Development of a neonatal adverse event severity scale through a Delphi consensus approach. Arch Dis Child. 2019;104:1167–73.
26. World Health Organization. International classification of functioning, disability and health (ICF). Available from:https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health.
27. Common Terminology Criteria for Adverse Events (CTCAE). Available from:https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm.
28. Boss M, Hartmann P, Frauenfeld (CH): Family Larsson-Rosenquist Foundation. LactaResearch Group. LactaPedia. 2018. Available from:https://www.lactapedia.com. Cited 2021 Dec 1.
29. CTCAE dictionary. Available from:https://safetyprofiler-ctep.nci.nih.gov/safety-profiler/static/#/home/(body:ctcDictionary)?version=5.0. Cited 2024 Sep 4.

30. Spencer RN, Hecher K, Norman G, Marsal K, Deprest J, Flake A, et al. Development of standard definitions and grading for maternal and fetal adverse event terminology. Prenat Diagn. 2022;42:15–26.
31. INC Terminology Files. Available from:https://evs.nci.nih.gov/ftp1/Pediatric_Terminologies/INC/About.html.
32. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. J Biomed Inform. 2019;95:103208.
33. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J of Biomed Inform. 2009;42:377–81.
34. Boss M, Gardner H, Hartmann P. Normal human lactation: closing the gap. F1000Res. 2018;7:801.
35. Majumdar SR. Better outcomes for oatients treated at hospitals that participate in clinical trials. Arch Intern Med. 2008;168:657.
36. West J. Do clinical trials improve quality of care? A comparison of clinical processes and outcomes in patients in a clinical trial and similar patients outside a trial where both groups are managed according to a strict protocol. Qual Saf Health Care. 2005;14:175–8.
37. Nijjar S, D'Amico M, Wimalaweera N, Cooper N, Zamora J, Khan K. Participation in clinical trials improves outcomes in women's health: a systematic review and meta-analysis. BJOG. 2017;124:863–71.
38. Nir O, Schwartz A, Toussia-Cohen S, Leibovitch L, Strauss T, Asraf K, et al. Maternal-neonatal transfer of SARS-CoV-2 immunoglobulin G antibodies among parturient women treated with BNT162b2 messenger RNA vaccine during pregnancy. Am J of Obstet Gynecol MFM. 2022;4:100492.
39. Allegaert K, Salaets T, Wade K, Short MA, Ward R, Singh K, et al. The neonatal adverse event severity scale: current status, a stakeholders' assessment, and future perspectives. Front Pediatr. 2024;11:1340607.

Publisher's Note