

**National Birth Defects Prevention Network (NBDPN)
NBDPN Abstractor's Instructions**

Congenital Microcephaly	
Description	<p>Microcephaly, or microcephalus, is the clinical finding of a small head when compared with infants of the same sex and age. The head circumference (HC), also known as the occipitofrontal circumference (OFC), is considered a reliable assessment of the volume of the underlying brain. Congenital microcephaly is microcephaly that is present prenatally or at the time of birth/delivery.</p>  <p align="right"></p>
Inclusions	<p>Congenital microcephaly is defined as a HC at birth (or at delivery for stillbirths and elective terminations) less than the 3rd percentile for gestational age and sex based on standard growth charts (http://www.cdc.gov/zika/public-health-partners/microcephaly-case-definitions.html).</p> <p>If the HC at birth is not available, a HC less than the 3rd percentile for age and sex within the first 6 weeks of life can be used to define congenital microcephaly. For preterm infants, this measurement should be adjusted for gestational age when comparing with standard growth charts.</p> <p>Children for whom the only available HC measures less than the 3rd percentile for age and sex beyond 6 weeks of life can be included in surveillance data as having possible congenital microcephaly.</p> <p>Some clinicians use other cut-points, such as less than the 5th or less than the 10th percentile, to make a diagnosis of microcephaly. These children should be included in birth defects surveillance data, along with the relevant HC values, if their medical record states they have congenital microcephaly.</p>

	<p>Children for whom no HC measurement is available but the medical record states that congenital microcephaly has been diagnosed should be included in birth defects surveillance data as having congenital microcephaly.</p> <p>The diagnosis of microcephaly should not be assigned by surveillance staff based only on the HC value in the medical record.</p>
Exclusions	<p>Acquired microcephaly – Microcephaly that develops after birth due to a delivery complication or a postnatal insult, trauma, or infection in infancy or childhood. In this instance, the head circumference (HC) is normal for sex and age at birth. However, as the baby grows in length, the head does not grow and becomes disproportionately smaller.</p> <p>Relative microcephaly – This term may be noted in the medical record to indicate that the HC measures in the normal range for age and sex but is small relative to the baby’s weight and length. <i>Note: Programs that wish to ascertain “relative microcephaly” need to be able to distinguish this from congenital microcephaly in the data.</i></p> <p>Proportionate microcephaly – This is where the HC, weight and length all are small for the infant’s age and sex but proportional to each other. This usually is seen with intrauterine growth restriction and many genetic syndromes.</p>
ICD-9-CM Code	742.1
CDC/BPA Code	742.10
ICD-10-CM	Q02
Diagnostic Methods	<p>Head circumference measurements should be taken using a tape measure that cannot be stretched. The tape is securely wrapped around the widest possible circumference of the head, 1-2 finger widths above the eyebrow on the forehead and at the most prominent part of the back of the head. Ideally, the measurement should be taken 3 times and the largest measurement recorded to the nearest 0.1 cm.</p> <p>The shape of the head after delivery can affect the accuracy of the HC measurement as an estimate of brain volume due to molding of the head from the birth canal. The optimal time to measure HC is at 24-36 hours after birth when molding of the head has subsided.</p>
Prenatal Diagnoses Not Confirmed Postnatally	<p>Microcephaly can be detected on a mid-pregnancy anomaly scan (ultrasound) at 18-20 weeks. However, it may not be evident until the late 2nd or into the 3rd trimester. Microcephaly is usually present by 36 weeks gestation. Serial prenatal ultrasounds may be needed to detect the development of microcephaly <i>in utero</i>.</p>

	<p>Stillborn infants and pregnancies electively terminated after prenatal diagnosis can be included in surveillance data as having possible congenital microcephaly in the absence of available postnatal HC measurements, depending on the certainty of the prenatal diagnosis. Every effort should be made to identify a HC measurement at birth to verify the presence of microcephaly, if possible.</p>
<p>Information to Collect</p>	<p>Identifying information (child, parents, physicians)</p> <p>Maternal information</p> <ul style="list-style-type: none"> - Dates of last menstrual period (LMP) and estimated date of delivery(EDD) - Chronic and acute conditions during pregnancy, e.g., diabetes, epilepsy, infections - Timing and results of prenatal testing, e.g., ultrasound, amniocentesis - Maternal exposures, e.g., medications, mercury <p>Infant/fetal information</p> <ul style="list-style-type: none"> - Pregnancy outcome - live birth, fetal death, elective termination after prenatal diagnosis - Measurement of weight, length, and HC at delivery and HC at 24-36 hours, if available - Gestational age assigned at delivery and infant sex - Findings on physical exam, including all major and minor defects - Evaluations performed to evaluate microcephaly, date, and results, e.g., cranial ultrasound, head CT or MRI scan - Subspecialty evaluations, date, and results, e.g., neurology, ophthalmology, audiology, genetics <p>Results of any Zika virus testing^{4,5}</p> <p><i>Note: Zika virus testing may be done at CDC or a state health laboratory and results may not be available in the medical record.</i></p> <ul style="list-style-type: none"> - Testing of maternal serum during pregnancy or after delivery, amniotic fluid, cord blood, infant serum, and cerebrospinal fluid after birth <ul style="list-style-type: none"> o Zika virus RNA by reverse transcription-polymerase chain reaction (RT-PCR) o Zika virus-specific immunoglobulin (Ig) M and neutralizing antibodies - Histopathologic evaluation of fixed and frozen tissue from the placenta and umbilical cord <ul style="list-style-type: none"> o Zika virus immunohistochemical staining o Zika virus RNA by RT-PCR <p>Results of testing for other <i>in utero</i> virus infections (see known causes of</p>

	<p>congenital microcephaly below)</p> <ul style="list-style-type: none"> - Testing of maternal serum during pregnancy or after delivery for virus-specific IgM and IgG antibodies - Testing of cord blood and/or infant serum for virus-specific IgM and IgG antibodies - Infant urine culture for cytomegalovirus (CMV)
<p>Data Sources</p>	<p>Locations where deliveries occur:</p> <ul style="list-style-type: none"> - Birth hospitals, birthing centers/midwifery practices - Locations where elective terminations are performed after prenatal diagnosis <p>Vital records - Head circumference is not a field on the U.S. Standard Birth Certificate, but has been added by some states.</p> <p>Locations where children with microcephaly are seen:</p> <ul style="list-style-type: none"> - Pediatric and family practice offices - Subspecialty clinics, e.g., neurology, genetics - Developmental clinics, early intervention programs <p>Reporting by healthcare providers and communicable disease programs</p> <ul style="list-style-type: none"> - Programs may need to provide feedback and ongoing updates of surveillance data to maintain a high level of reporting and ascertainment going forward.
<p>Additional Information</p>	<p>Microcephaly itself is not a malformation but a sign that the brain is abnormally small. Congenital microcephaly can result from: 1) an abnormality in the very early formation of the brain, often with a genetic etiology, or 2) due to arrest or destruction of normally-forming brain tissue, such as by infection or vascular disruption.</p> <p>Brain abnormalities that can be present in a child with microcephaly include:</p> <ul style="list-style-type: none"> - Intracranial calcifications - Hydranencephaly - Pachygyria, lissencephaly, and other neuronal migration disorders - Ventriculomegaly - Hydrocephalus ex-vacuo – a condition where the damaged brain matter shrinks and is surrounded by fluid - Fetal Brain Disruption Sequence – brain destruction <i>in utero</i> resulting in collapse of the fetal skull, microcephaly, scalp rugae (excess folds) and neurologic impairment. <p><i>Note: This unusual condition has been described in some infants from Brazil thought to have congenital Zika virus infection.</i></p> <p>Microcephaly can occur alone or in combination with other major birth defects. Other defects for which microcephaly is often a feature are:</p>

	<ul style="list-style-type: none"> – Neural tube defects (anencephaly, spina bifida, encephalocele) – Holoprosencephaly – Craniosynostosis – Conjoined twins <p>Microcephaly can have multiple causes, and for many cases an exact cause cannot be identified. Known causes of congenital microcephaly are:</p> <ul style="list-style-type: none"> • <i>In utero</i> infections <ul style="list-style-type: none"> – Cytomegalovirus (CMV) – Rubella – <i>Toxoplasmosis gondii</i> – Herpes simplex – <i>Treponema pallidum</i> (syphilis) – Lymphocytic choriomeningitis virus (LCMV) – Zika virus (possibly) • Genetic causes <ul style="list-style-type: none"> – Chromosomal abnormalities – Single gene disorders (syndromes) – Mitochondrial mutations • Teratogens <ul style="list-style-type: none"> – Maternal alcohol use – Maternal medications (e.g., hydantoin or isotretinoin) – Toxins (e.g., mercury or radiation) • Maternal conditions (e.g., poorly controlled diabetes or hyperphenylalaninemia) • <i>In utero</i> ischemia or hypoxia (e.g., placental insufficiency or abruption) • Severe maternal malnutrition
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Assessing the Prevalence of Congenital Microcephaly

There can be substantial year-to-year variation in prevalence due to the rarity of congenital microcephaly overall and the population size.

When assessing prevalence, it is helpful to examine categories of congenital microcephaly based on severity (when known) and cause (when known/documented) in order to evaluate which may be changing over time.

- Severity of congenital microcephaly
 - HC < 3rd percentile for age and sex at birth or before 6 weeks of age
 - HC between 3rd and 5th percentiles for age and sex at birth or before 6 weeks of age
 - HC > 5th percentile for age and sex at birth or before 6 weeks of age

Note: Programs that ascertain “relative microcephaly” should include this as a subcategory of those with HC >5th percentile

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- HC values unavailable at birth or before 6 weeks of age
- Possible congenital microcephaly
- Congenital microcephaly attributable to known/documented causes
 - Microcephaly that occurs with coexisting neural tube defects, holoprosencephaly, craniosynostosis, or conjoined twinning
 - Chromosomal abnormalities

Note: Does not include copy number variants (microdeletions or microduplications) detected by microarray that are interpreted as nonpathogenic or of no or unknown clinical significance.
 - Clinical syndromes and single gene disorders (diagnosed or suspected)
 - *In utero* infections and type (diagnosed by culture or antibody titers)
 - Exposure to a known teratogen (e.g., alcohol, hydantoin, isotretinoin)
- No documented cause

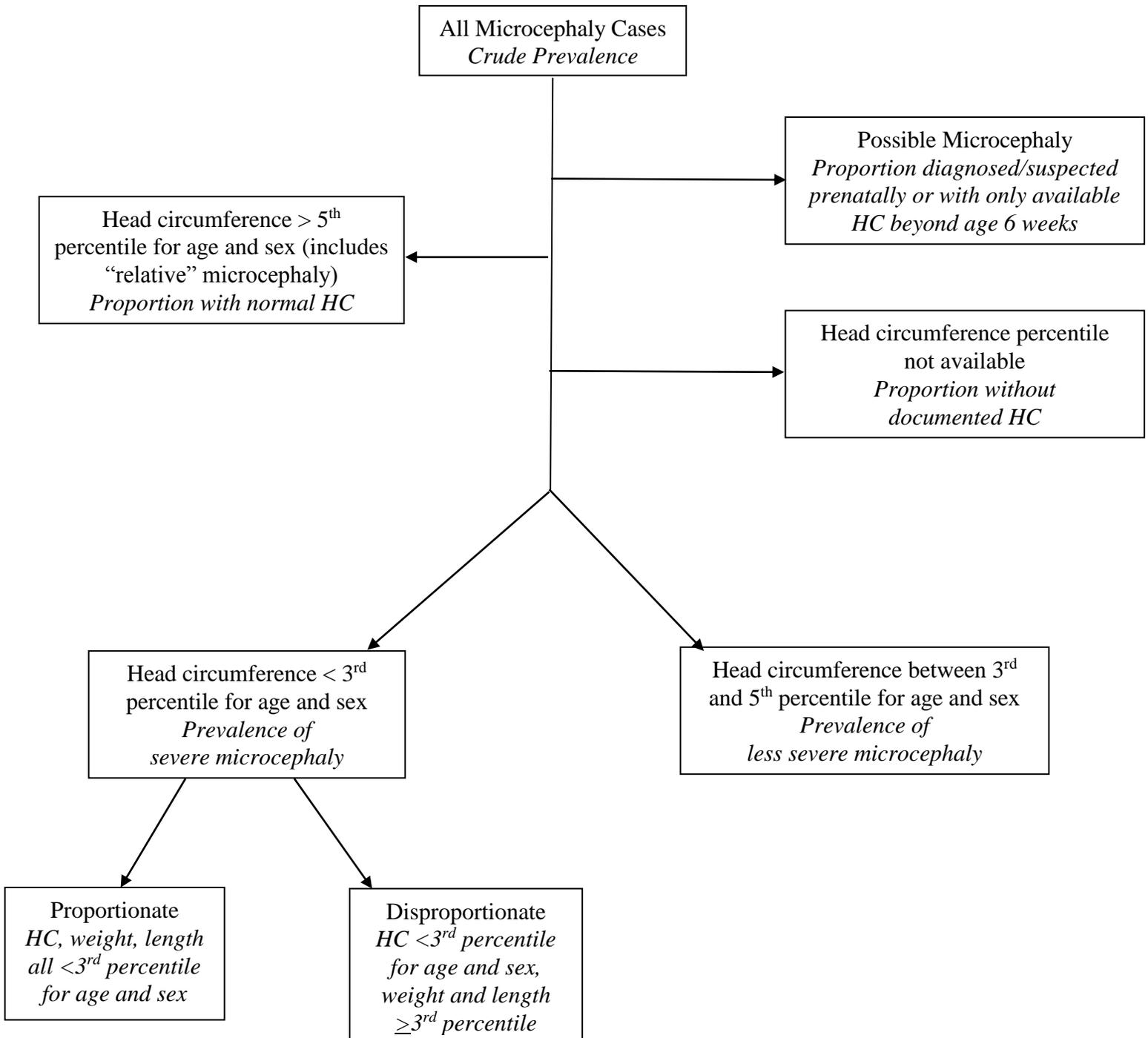
Note: It is in the category of no documented cause that an increase due to a new risk factor, such as Zika virus infection in utero, might be expected.

Suggested Reference Charts for Head Circumference at Birth by Gestational Age

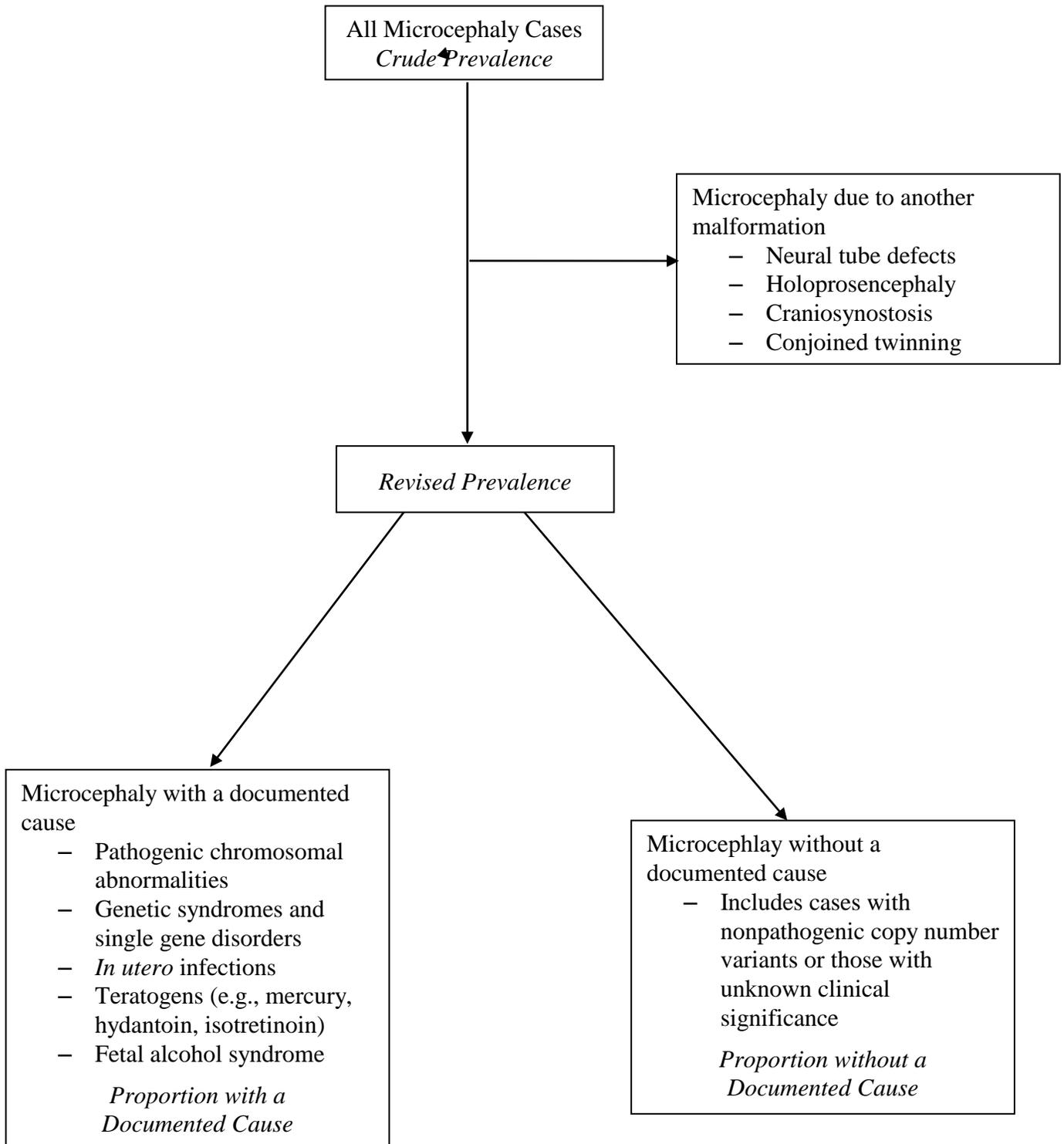
Gestational Age at Birth	Reference Chart	Web Link
33 to 43 Weeks	INTERGROWTH-21st Newborn Size at Birth Chart	https://intergrowth21.tghn.org/articles/intergrowth-21st-newborn-size-birth-chart/ A tool for calculating centiles for head circumference for infants 33-42 weeks is available at: https://intergrowth21.tghn.org/global-perinatal-package/intergrowth-21st-comparison-application/
24 to 32 Weeks	INTERGROWTH-21st Very Preterm Size at Birth References	https://intergrowth21.tghn.org/articles/intergrowth-21st-very-preterm-size-birth-references-and-z-scores-standard-deviations/ A tool for calculating centiles for head circumference for infants 24-32 weeks is also available from this site.
< 24 Weeks	INTERGROWTH-21st Fetal Growth Standards	https://intergrowth21.tghn.org/articles/intergrowth-21st-fetal-growth-standards/
<p>INTERGROWTH-21st Fetal Growth Standards are based on measurements <i>in utero</i> only. International standards for birth measurements in infants less than 24 weeks gestation are not available. For most elective pregnancy terminations and many stillbirths, accurate postnatal head circumference measurements are not possible.</p>		

For a study comparing head circumference measurements *in utero* to those obtained after birth, see: Melamed N, Yogev Y, Danon D, et al. Sonographic estimation of fetal head circumference: how accurate are we? *Ultrasound Obstet Gynecol* 2011;37:65-71.

Prevalence of Congenital Microcephaly Based on Severity



Prevalence of Microcephaly Based on Documented Cause



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CDC Resources

CDC Zika website: <http://www.cdc.gov/zika/index.html>

Fleming-Dutra KE, Nelson JM, Fischer M, et al. Update: Interim Guidelines for Health Care Providers Caring for Infants and Children with Possible Zika Virus Infection — United States, February 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:182–187. Available from: http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm?s_cid=mm6507e1.htm_w

Oduyebo T, Petersen EE, Rasmussen SA, et al. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016 *MMWR Morb Mortal Wkly Rep* 2016;65(05);122–127. Available from: http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2.htm?s_cid=mm6505e2.htm_w

Additional Resources for Growth Charts

Fenton TR and Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. *BMC Pediatrics* 2013;13:59-72.

Olsen IE, Groveman SA, Lawson L, et al. New Intrauterine Growth Curves Based on United States Data. *Pediatrics* 2010;125:e214-e224.

Papageorgiou AT, Ohuma EO, Altman DG, et al. International standards for fetal growth based on serial ultrasound measurements: the Fetal Growth Longitudinal Study of the INTERGROWTH-21st Project. *Lancet* 2014;384:869-879.

Villar J, Ismail LC, Victora CGV, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet* 2014;384:857-868.

Villar J, Giuliani F, Bhutta ZA, et al. Postnatal growth standards for preterm infants: the preterm postnatal follow-up study of the INTERGROWTH-21st Project. *Lancet Glob Health* 2015;3:e681-691. Charts available at: <https://intergrowth21.tghn.org/articles/new-intergrowth-21st-international-postnatal-growth-standards-charts-available>

Villar J, Giuliani F, Fenton TR, Ohuma EO, et al. INTERGROWTH-21st very preterm size at birth reference charts. *Lancet*. Published Online February 18, 2016. [http://dx.doi.org/10.1016/S0140-6736\(16\)00384-6](http://dx.doi.org/10.1016/S0140-6736(16)00384-6)

World Health Organization Child Growth Standards for birth to 5 years are available at: <http://www.who.int/childgrowth/standards/en/>

Note: Tools to calculate percentiles for weight, length, and head circumference by sex and gestational age or postnatal age based on several of these data are available at: <http://peditools.org/>