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Newborn Screening Follow-up; Approved Guideline—Second Edition

This guideline describes the basic principles, scope, and range of follow-up activities within the newborn screening system.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.

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Newborn Screening Follow-up; Approved Guideline—Second Edition

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Abstract

Newborn screening for congenital conditions is a public health system composed of testing, follow-up, diagnosis, management, evaluation, and education. As part of the system, follow-up activities play an essential role in facilitating early detection, diagnosis, and intervention for affected newborns. Clinical and Laboratory Standards Institute document NBS02-A2—*Newborn Screening Follow-up; Approved Guideline—Second Edition* describes the basic principles, scope, and range of follow-up activities within the newborn screening system. It is intended for use by those involved in any aspect of follow-up, including health care providers, parents, and others concerned with the health and welfare of newborns.

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Foreword

Newborn screening is an essential public health activity focused on testing every newborn for certain congenital conditions which, without early management, can result in significant morbidity and mortality. Screening tests separate newborns at higher risk of having a condition from those who are at low risk. Screening is not diagnostic, and newborns identified with presumptive findings require further testing and clinical evaluation to confirm their status as affected or unaffected. Newborn screening for many congenital conditions is now routine throughout much of the world and traditionally uses a dried blood specimen—blood applied to purpose-manufactured collection paper sent to specialized screening laboratories. In addition, birthing facility point-of-care screening for newborn hearing loss has been performed for several years, and birthing facility screening for critical congenital heart defects and various other conditions has recently been introduced into newborn care.

Effective newborn screening systems (NSS) provide the infrastructure for universal access and rapid follow-up for affected newborns whose lives and health may be at risk. A complete system for screening comprises six parts: testing, follow-up, diagnosis, intervention and/or management, evaluation, and education.[1] Parents/legal guardians, all health care providers, and the newborn screening program (NSP) involved in the care of the newborn should collaborate to ensure that the NSS functions effectively to provide maximum benefit.

It is estimated that approximately one newborn in 600 will be affected with a congenital condition detectable by dried blood spot screening, and three newborns in 1000 will be affected with hearing loss.[2] Birth incidences of conditions may vary greatly among different populations, but if congenital heart defects are included, then in most parts of the world around 1% of newborns will be identified as being at risk for physical and/or developmental disabilities, or even death, as a result of a condition that can currently be identified by a newborn screening test. Technological advances will, in the future, enable programs to screen for increasing numbers of conditions.

Follow-up activities can be divided into two broad categories: short-term follow-up (STFU) and long-term follow-up (LTFU). Within newborn screening, simply reporting "screen positive," "out-of-range," or "invalid" results does not ensure appropriate or timely treatment for affected newborns.[3-5] Rapid, efficient, and effective *short-term follow-up* is critical to ensure that newborns needing further testing are evaluated quickly, and receive the testing indicated and prompt and appropriate referral for subspecialty care and support services.[6-8] Active STFU responsibility ends when the infant is proven either not to be affected or has been verified to be under appropriate care, including treatment.

The primary aim of newborn screening is to provide intervention to affected babies. LTFU is the means by which accountability of NSS and NSPs can be ensured. It determines if they are sustaining their primary aims of preventing mortality and mitigating morbidity. Such follow-up is vital to the evaluation of newborn screening benefits throughout the life of an individual, as well as to the family and society.[9] NSPs may not be directly involved in long-term outcome assessment, but if they do not play a central coordinating role, then they need to facilitate LTFU and be aware of the results.

The quality of follow-up services directly affects the lives of families with babies. This document outlines the role of follow-up services within an NSS, and provides guidance for developing, ensuring, and maintaining effective follow-up services. NBS02 has been updated, and sections dealing with LTFU have been expanded to include discussion of assessment of health outcomes from newborn screening. Additions include a section about the development of condition definitions, which are essential for assessing health outcomes, and expansion of the section on education. Also, the terms "in-range" and "out-of-range" have been updated to be consistent with other CLSI documents and global usage. Efforts have been made to reach consensus among an internationally representative group of newborn screening stakeholders to describe best practices for newborn screening follow-up.

Key Words

Community/public health resources, congenital heart defects, dried blood spot screening, endocrinology, hearing loss, long-term follow-up, metabolic disorders, newborn hearing screening, newborn screening, point-of-care test, population screening, quality assurance, short-term follow-up

Newborn Screening Follow-up; Approved Guideline—Second Edition

1 Scope

The primary goal of this guideline is to enhance the quality of follow-up services for newborns screened through public health or other newborn screening programs (NSPs). The quality of these services has a direct impact on the health of newborns and families, and on the effectiveness of newborn screening as a system.

Short-term follow-up (STFU), in the first days and weeks of life, is essential to ensure that all newborns receive a valid screening test, and that those with screen positive results receive a definitive diagnosis, in the most expedient manner possible, and appropriate clinical management if confirmed.

Long-term follow-up (LTFU) comprises all of the activities that should occur after a patient is diagnosed and subsequently confirmed with a condition. It includes care coordination, assuring the availability of evidence-based treatment, continuous quality improvement, new knowledge discovery, and, importantly, periodic assessment of the clinical outcomes in affected individuals without which there can be no assurance that newborn screening goals are being met. It should also include efforts to document cases diagnosed clinically or outside the newborn screening system (NSS).

This guideline outlines STFU and LTFU activities that should be included in an NSS. It does not address other components of the overall NSS, such as laboratory methods, intervention protocols, or administrative organization. It is intended for global use by public health officials, policy makers, and all involved in any aspect of follow-up within NSS, including confirmatory laboratory personnel, health care providers, parents, and families.

2 Standard Precautions

Because it is often impossible to know what isolates or specimens might be infectious, all patient and laboratory specimens should be treated as infectious and handled according to "standard precautions." Standard precautions are guidelines that combine the major features of "universal precautions and body substance isolation" practices. Standard precautions cover the transmission of all known infectious agents and thus are more comprehensive than universal precautions, which are intended to apply only to transmission of blood-borne pathogens. The Centers for Disease Control and Prevention address this topic in published guidelines that focus on the daily operations of diagnostic medicine while encouraging a culture of safety in the laboratory.[10] For specific precautions for preventing the laboratory transmission of all known infectious agents from laboratory instruments and materials and for recommendations for the management of exposure to all known infectious diseases, refer to CLSI document M29.[11]

3 Terminology

3.1 A Note on Terminology

CLSI, as a global leader in standardization, is firmly committed to achieving global harmonization wherever possible. Harmonization is a process of recognizing, understanding, and explaining differences while taking steps to achieve worldwide uniformity. CLSI recognizes that medical conventions in the global metrological community have evolved differently in the United States, Europe, and elsewhere; that these differences are reflected in CLSI, International Organization for Standardization, and European Committee for Standardization (CEN) documents; and that legally required use of terms, regional usage, and different consensus timelines are all important considerations in the harmonization process. In light of