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Development and application of newborn screening information system of Zhejiang Province in China

Xiaoqiang Hao
Zhejiang University School of Medicine, National Clinical Research Center for Child Health
Qijiang Zhao
Affiliated Hospital of Shaoxing University
Huaqing Mao
Zhejiang University School of Medicine, National Clinical Research Center for Child Health
Minggang Li
Zhejiang Biosan Biochemical Technologies Co., Ltd
Qian Liu
Zhejiang Biosan Biochemical Technologies Co., Ltd
Yingying Zhou
Shaoxing Stomatological Hospital
Rulai Yang
Zhejiang University School of Medicine, National Clinical Research Center for Child Health
Xinwen Huang
Zhejiang University School of Medicine, National Clinical Research Center for Child Health
Xin Yang
Zhejiang University School of Medicine, National Clinical Research Center for Child Health
Zhengyan Zhao
zhaozy@zju.edu.cn

Zhejiang University School of Medicine, National Clinical Research Center for Child Health

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Abstract

Objective

The study aim was to leverage information technology for quality improvements to the newborn screening program (NBS) and to enable more comprehensive management data within Zhejiang Province, China.

Methods

Full utilization was made of the Internet, a data warehouse, artificial intelligence, and mobile Internet technology to construct a data management platform. Thes platform was designed for multiple diseases, terminals, and users, and has established the requisite digital infrastructure for NBS quality control. Continuous optimization of the platform is carried out based on user requirements.

Results

Through continuous upgrading and development of the NBS management system, remarkable achievements have been achieved. All core management indicators have significantly improved the screening rate has soared from 93.85% during the period of 2003–2013 to 99.91% in the period of 2014–2023; the recall rate of positive screening cases has risen from 95.71% to 98.38%; the rate of unsuitable blood samples has dropped from 0.24% to 0.09%; the re-sampling rate of unqualified blood Samples has increased from 93.42% to 98.50% and the number of samples delayed in delivery has decreased from 1.52% to 0.42%.

Conclusion

The application of the NBS management system has significantly enhanced the work efficiency of NBS and the screening process and the application has become standardized.

Introduction

NBS is the process of testing newborns for markers of certain congenital and hereditary diseases that may pose serious threats during the neonatal period or significantly affect growth and development in infancy and childhood. [1, 2]. It improves the quality of life of affected individuals and is one of the important measures to prevent birth defects [3]. The Zhejiang Neonatal Disease Screening Center was established in December 1998 and is one of the largest neonatal disease screening centers in China. In 1999, screening began for for congenital hypothyroidism (CH) and phenylketonuria (PKU). expanded to tandem mass spectrometry (MS/MS) in 2008, and later included congenital adrenal hyperplasia (CAH)

and glucose-6-phosphate dehydrogenase deficiency (G6PD) were added, gradually building a screening network that integrates "education, screening, diagnosis and treatment, follow-up, and program audit".

NBS involves multiple steps and institutions. In the early stages of this project, the management of patient information, screening data, diagnostic results, and follow-up information mainly relied on manual entry and paper records, leading to inefficiencies and data inaccuracies. To improve data sharing, efficiency, and process standardization, a comprehensive NBS information management system was essential [4–6]. We developed the first system(NBSS) in 2003 and upgraded it in 2014, continuously enhancing its functions. In recent years, WeChat is widely used in China because it has evolved from a simple instant messaging tool into an all-encompassing digital lifestyle platform that integrates services such as social networking, payment, content, government affairs, and mini-programs, deeply embedding itself into every aspect of people's daily lives. In 2018, we developed the WeChat official account and small programs of Zhejiang Newborn Disease Screening Center. the WeChat platform, we can provide professional precision education, information collection, online payment, report query, abnormal recall and other services, it allows parents to deeply participate in the program of NBS. We have summarized the development and accumulated screening data and reported it here to informational and international screening programs.

Methods

The NBSS of Zhejiang Province was jointly developed with the Zhejiang Provincial NBS Center in collaboration with Zhejiang Biosan Biochemical Technologies Co., Ltd. and Shanghai Xinghe Software Co., Ltd. Currently, this system has been granted the Computer Software Copyright by the National Copyright Administration of the People's Republic of China (2008SR28460, 2009SR061026).Many different healthcare professionals are involved in the system, including 335 maternity institutions and 90 county level management institutions. The operation procedures of NBS are strictly followed in accordance with the "Technical Specification Requirements for NBS" [7]. Capillary blood from a heel stick is dropped onto blood collection paper after babies are 48 hours of age. The samples are naturally dried, sent to county level management institutions, and then delivered to the Zhejiang Provincial NBS Center for testing as shown in Fig. 1.

1.1 System architecture

The NBSS uses the B/S architecture [8–10]. It was developed based on Java, and a relational database was selected to ensure the high efficiency and stability of data storage [11]. The system adopts a six-layer modular architecture (user terminal layer, application gateway layer, business service layer, data management layer, infrastructure layer, and architecture enhancement layer), which achieves medical data security control and distributed transaction guarantee through terminal multi terminal access, an API security gateway, a core business cluster and configuration center decoupling, multi-level data storage, and dual track data flow design. It supports seamless integration with third-party systems and meets the high concurrency and scalability requirements of the regional level screening business. In

terms of data security, the system utilizes the MD5 irreversible encryption algorithm to encrypt key information such as user passwords [12]. To further enhance the security of sensitive data, it is strengthened through the encryption algorithm package built into the database to ensure data security during storage and transmission. To prevent data loss, the system has regularly automated database backups. The server and storage adopt the dual-computer hot standby mode to comprehensively ensure the absolute data safety. The main function module of NBSS system is as shown in Fig. 2.

1.1.1 Basic information maintenance

The maintenance of basic information is a crucial step in ensuring the normal operation of the system, mainly covering aspects such as organization, user, and privilege management.

1.1.2 User identity authentication

There are various types of users in the system, the user identity authentication module function is to verify the legitimacy of users and prevent unauthorized users from accessing the system, obtaining sensitive information or conducting malicious operations. When logging into the system, users are required to enter both their usernames and passwords. Only after passing strict verification, they are allowed to enter the system to perform corresponding operations.

1.1.3 WeChat platform

The WeChat platform, we can publish various tweets through WeChat official account, which can be displayed in text, pictures, videos and other forms, to accurately educate parents of newborn babies about the significance of the newborn disease screening project, disease introduction, screening process and other popular science knowledge, so as to promote the improvement of screening rate. In terms of information collection, due to the increasing number of screening projects, blood collection personnel in grassroots hospitals are often busy with work. They not only need to manually fill out blood cards, but also need to enter the blood card information into the newborn screening information management system, which is labor-intensive and prone to errors. After the application of WeChat mini program, parents can independently enter newborn information, and the information is automatically synchronized to the NBBS. Blood collection personnel only need to print and paste the information on the blood card in the system, which significantly reduces the probability of errors and greatly reduces the pressure on grassroots work. For some government free screening programs, parents can obtain online fee reductions through real name authentication on WeChat mini programs. For fee items, parents can also make online payments for easier fund management. After the laboratory issues a screening report, parents can quickly access the report online, eliminating the need for multi-level unit level phone notifications. For reports of abnormal results, the system will prompt parents to take their children for re-examination as soon as possible, greatly reducing the recall time for suspected children.

1.1.4 Information entry Module

Information entry can be completed by the blood collection units or the newborn screening center through the NBSS, or by parents via the WeChat platform. The information entry module function is to enter the basic information of neonates, including such important contents as the mother's name, the neonate's gender, date of birth, blood collection date, home address, contact phone number, and sample barcode number. The NBBS and the WetChat platform are equipped with an information verification function, such as verifying the number of digits of phone numbers and the number of digits of blood spot collection card barcodes, which ensures the accuracy of information. Such an approach can effectively reduce the information error rate of medical staff and improve the entry efficiency.

1.1.5 Sample delivery Module

The sample delivery module focuses on managing the logistics distribution information of samples, covering three important links: items to be submitted, batch delivery, and laboratory acceptance. After the sample submission from a blood collection unit, the system generates a logistics QR code, which is affixed to the blood sample package. At each stage of sample delivery, scanning the QR code on the delivery form enables real-time tracking of the package logistics, including monitoring the cold chain temperature, location, and responsible personnel. This significantly enhances the quality control of logistics delivery and ensures the safety of samples and vehicles.

1.1.6 Laboratory test and report Module

Once the samples are received by the NBS center, the staff scan the sample barcode for acceptance and conduct quality assessments. If the quality fails to meet the standards, the sample will be defined as unqualified and returned for resampling. Qualified samples will be transferred to the laboratory. The laboratory examination module function is to manage the specimen testing, result uploading, quality control review, data review, report review, queries, printing, and abnormal notifications. Different cutoff values and interpretation rules are set for different assays, and the system automatically interprets the results. It also supports manual modification of report conclusions.

1.1.7 Quality control management Module

The quality control module is used for internal quality control analysis and management. The details are as follows: (1) Internal Quality Control Management: Supports self-selection of quality control rules, allowing flexible setting of appropriate quality control standards based on different screening assays and actual conditions. Real-time viewing of intuitive Z-score internal quality control charts and out-of-control markers enables quick identification of anomalies. The system also supports the establishment of internal quality control target values and automatically generates internal quality control reports. (2) Internal Quality Control Indicator Analysis: By analyzing indicators such as the mean, standard deviation, standard deviation index, and coefficient of variation, the stability and reliability of the testing data are thoroughly evaluated, providing a scientific basis for quality control.

1.1.8 Result query Module

Parents can check four statuses of the sample: name entered, blood collected, tested, and report issued, through the WeChat mini-program. After the report is issued, parents can query the report through various channels such as websites, SMS, and the WeChat mini-program. Blood collection units can query and print reports in real-time through the system, enabling them to provide parents with accurate explanations and professional suggestions. The Zhejiang Provincial NBS Center began to add genetic screening in the NBSS in 2021. In the report review process, the system page can simultaneously display the biochemical and sequencing results, and the reviewers make a comprehensive judgment based on the results of genetic screening and tandem mass spectrometry tests.

1.1.9 Recall and reinspection management Module

This module effectively manages samples with positive initial screening results. Staff can query the list of samples requiring recall in real-time, notify parents via SMS, and promptly update the recall status to ensure timely diagnosis and treatment of suspected positive cases.

1.1.10 Diagnosis and treatment management Module

The diagnosis and treatment management module provides treating clinicians with patient management and treatment-related recording functions. It establishes standardized electronic medical records for genetic metabolic specialties, freeing doctors from the cumbersome task of handwritten records. Specific functions include: (1) Adding New Patients. (2) SMS Notification Management. (3) Correlation with past medical history. (4) Non-text Data Management: Supports the upload and management of non-text data such as CT, MRI, ultrasound, ECG, audio, and video recordings. (5) Electronic Medical Record Storage and Printing. (6) Data Analysis: Processes data such as height, weight, and head circumference to generate growth curves, helping doctors detect growth deviations early and intervene promptly to ensure healthy child development. Additionally, the system is connected in real-time to the Zhejiang Maternal and Child Health Information Network, enabling doctors to access patients' medical records from other hospitals during diagnosis and treatment. This helps doctors gain a comprehensive understanding of the patient's condition and treatment history, avoid redundant tests and treatments, make more accurate diagnoses, and develop the most suitable treatment plans.

1.1.11 Statistical report

The system has numerous statistical report modules: Blood Spot Delivery Statistics, Confirmed Case Statistics, Rejected Blood Spot Data Query and Recalled Statistics.

1.1.12 Statistical Methods

The chi-square test was performed using SPSS software to compare the screening rate, follow up of positive tests, rate of unsuitable blood samples, follow up of unsuitable blood samples, and rate of delayed blood sample delivery before and after using the system. A P-value < 0.05 was considered statistically significant.

Results

To verify the effectiveness of this study in improving the quality and management level of newborn screening, we evaluated the neonatal screening work in Zhejiang Province using a series of management indicators, including the screening rate, recall rate of infants with positive tests, follow up of unsuitable samples, and transit time of the samples to the laboratory. It was found that data for only two core management indicators were complete for the years 1999 to 2002, while other core management indicators were missing. There were two reasons for this: firstly, during this period, data were recorded in paper or Excel formats and highly prone to data loss. Secondly, these data lacked a unified format and standard, making effective statistical analysis difficult. However, since 2003, with the application of the NBSS, the data is complete This fully demonstrates that when managing a large amount of data, information-system-based means are essential to avoid data loss and damage.

We conducted a comparative analysis of the core management indicators after 2003 (Table 1). The comparison time periods were divided into NBSS Version 1(2003–2013) and NBSS Version 2(2014–2023). The results show that significant changes occurred in all core management indicators. The screening rate rose from 92.84% to 99.95%, which means that more neonates can received newborn screening. The WeChat platform has played a very important role in public education and awareness campaigns in this process, since 2018, our online education has reached more than 4.5 million people. The recall rate of infants with positive screen results increased from 95.71% to 98.38%, indicating that the management of these infants is more efficient. The rate of unsuitable blood samples decreased from 0.24% to 0.09%, and the re-sampling rate of unsuitable blood samples increased from 93.42% to 98.50%, a significant improvement in the quality of blood collection and follow up. During the period of the study the standard for late delivery has been adjusted from 30 days after birth before 2009, 20 days from 2009–2013 and 10 days from 2013. Nevertheless, the rate of samples delayed in transit improved from 1.5% (2002–2013) to 0.4% (2014–2023), which is attributed to the information-based management of logistics. All the above quality indicators have a significant improvement effect after system use, and the differences are statistically significant(P<0.01).

Table 1
The core management indicators of NBS in Zhejiang Province from 1999 to 2023.

Year	the number of babies screened	screening rate (%)	Follow up of positive tests (%)	Rate of unsuitable blood samples (%)	Follow up of Unsuitable blood samples (%)	Rate of delayed blood sample delivery (%)
2003	313089	78.04	95.00	0.81	85.00	1.00
2004	387101	80.93	92.65	0.62	99.95	3.24
2005	467471	87.33	93.44	0.49	99.97	3.75
2006	482991	90.71	93.91	0.48	99.98	1.31
2007	549427	94.55	95.52	0.56	99.99	0.62
2008	589416	97.17	95.27	0.23	99.99	0.58
2009	594647	97.75	95.64	0.08	99.99	1.92
2010	606751	98.43	95.80	0.12	99.99	1.54
2011	646570	98.36	96.44	0.08	99.99	1.00
2012	700752	98.97	97.64	0.08	99.99	0.28
2013	666235	98.98	97.33	0.09	99.99	4.48
Subtotal	6004450	93.85	95.71	0.24	93.42	1.52
Year	**the number of babies screened**	**screening rate (%)**	**Follow up of positive tests (%)**	**Rate of unsuitable blood samples (%)**	**Follow up of Unsuitable blood samples (%)**	**Rate of delayed blood sample delivery (%)**
2014	673046	99.64	97.01	0.22	99.99	2.31
2015	654105	99.54	97.03	0.06	99.99	0.74
2016	654241	99.02	97.95	0.10	99.99	0.20
2017	746486	100.07	98.74	0.17	99.99	0.02
2018	611835	100.62	98.67	0.06	99.99	0.19
2019	587601	99.87	98.72	0.08	99.99	0.18
2020	480109	100.72	98.83	0.03	99.99	0.05
2021	434088	99.92	98.95	0.03	99.99	0.10

Note: Screening rate=Number of infants receiving effective screening within 20 days of birth/number of live births in the same period×100%. The standard for late delivery has been adjusted from 30 days after birth before 2009, 20 days from 2009–2013 and 10 days from 2013.

Year	the number of babies screened	screening rate (%)	Follow up of positive tests (%)	Rate of unsuitable blood samples (%)	Follow up of Unsuitable blood samples (%)	Rate of delayed blood sample delivery (%)
2022	403681	100.02	98.88	0.05	99.99	0.06
2023	381782	100.05	98.82	0.03	100.00	0.03
Subtotal	5626974	99.91	98.38	0.09	98.50	0.42
X^2		5780.96	14.88	3828.35	5.17	35271.15
P		<0.01	<0.01	<0.01	<0.01	<0.01

Note: Screening rate=Number of infants receiving effective screening within 20 days of birth/number of live births in the same period×100%. The standard for late delivery has been adjusted from 30 days after birth before 2009, 20 days from 2009–2013 and 10 days from 2013.

Discussion

The traditional screening model has numerous drawbacks. To address this, the Zhejiang Provincial NBS Center developed a NBSS to enhance efficiency and quality. Key improvements include: First, information digitalization has improved data accuracy and efficiency. Replacing manual entry with a networked system enables real-time quality evaluation, statistical analysis, and report generation. Second, cold chain logistics integration ensures sample traceability via GPS tracking and continuous temperature monitoring, preventing loss or delays. Third, WeChat mini programs facilitate education, streamline workflows, and enhance user experience. Parents can self-enter information, access reports online, and make payments, reducing staff workload and shortening recall times for suspected cases.

Through continuous optimization from 2014 to 2023, the NBSS has achieved remarkable quality improvements, effectively coordinating health administrative departments, medical institutions, and families throughout the entire screening process. For health authorities, it provides precise data for decision-making. For medical staff, it offers convenient access to patient information. For families, it delivers essential education and follow-up services, ensuring more complete screening and care. The system's ability to establish complete electronic files and disease cohorts further supports in-depth data analysis and early health problem prediction.

Currently, the system has achieved interconnectivity with pre-pregnancy and prenatal data, promoting the integration of birth defect prevention efforts. It also features embedded algorithms for online risk interpretation and personalized service pushes. The system's value has been recognized, having been selected for the National "13th Five-Year" Science and Technology Innovation Achievements Exhibition and securing six related software copyrights.

However, with the continuous increase in screening volume and rising service expectations, further improvements are needed. These include strengthening data security, optimizing the user interface, expanding functional modules (e.g., incorporating AI for automatic interpretation), and enhancing integration with other medical information systems to improve service synergy and resource allocation.

Conclusion

We have developed and implemented a highly innovative NBBS that integrates community engagement, sample transport management, and the entire process of laboratory testing and reporting. The implementation of this system has significantly improved all project quality indicators, promoted the standardization of the technical application and processes, and made the management more scientific, fully embodying the principles of being fast, accurate and orderly. In conclusion, during its continuous development, the NBSS should keep focusing on the actual needs, continuously carry out improvements and innovations, to provide even higher-quality services for the health of neonates.

Declarations

Institutional Review Board Statement

The study was approved by the Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine (NO.2018-IRB-076). The study was conducted according to the Declaration of Helsinki.

Informed Consent

Statement: Written informed consent was obtained from all participants' parents and/or guardians.**Data Availability Statement**: The datasets generated and analyzed during the current study are not publicly available due to participant privacy concerns but are available from the corresponding author upon reasonable request.

Consent for publication:

Consent for publication: Written informed consent was obtained from the parents/guardians of all participating neonates. No individual patient data are presented, so additional consent for publication of identifiable information was not required.

Conflicts of Interest:

The authors declare no conflicts of interest.

Abbreviations:

IMD inherited metabolic disorders

NBS newborn screening

NBSS newborn screening system

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This research received no external funding.

Author Contribution

Conceptualization, Q.J.Z.; methodology, Q.J.Z.; formal analysis, X.Q.H., H.Q.M.; data curation, X.Q.H., H.Q.M.; software development, M.G.L. and Q.L.; investigation, Y.Y.Z.; writing-original draft preparation, X.Q.H., Q.J.Z.; writing-review and editing, X.Q.H., Y.Y.Z., R.L.Y., X.W.H. and X.Y.; supervision, R.L.Y., X.W.H., X.Y. and Z.Y.Z.; project administration, R.L.Y., X.W.H. and X.Y.; resources, Z.Y.Z. All authors have read and agreed to the published version of the manuscript.

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Data Availability

The datasets generated and analyzed during the current study are not publicly available due to participant privacy concerns but are available from the corresponding author upon reasonable request.

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Figures

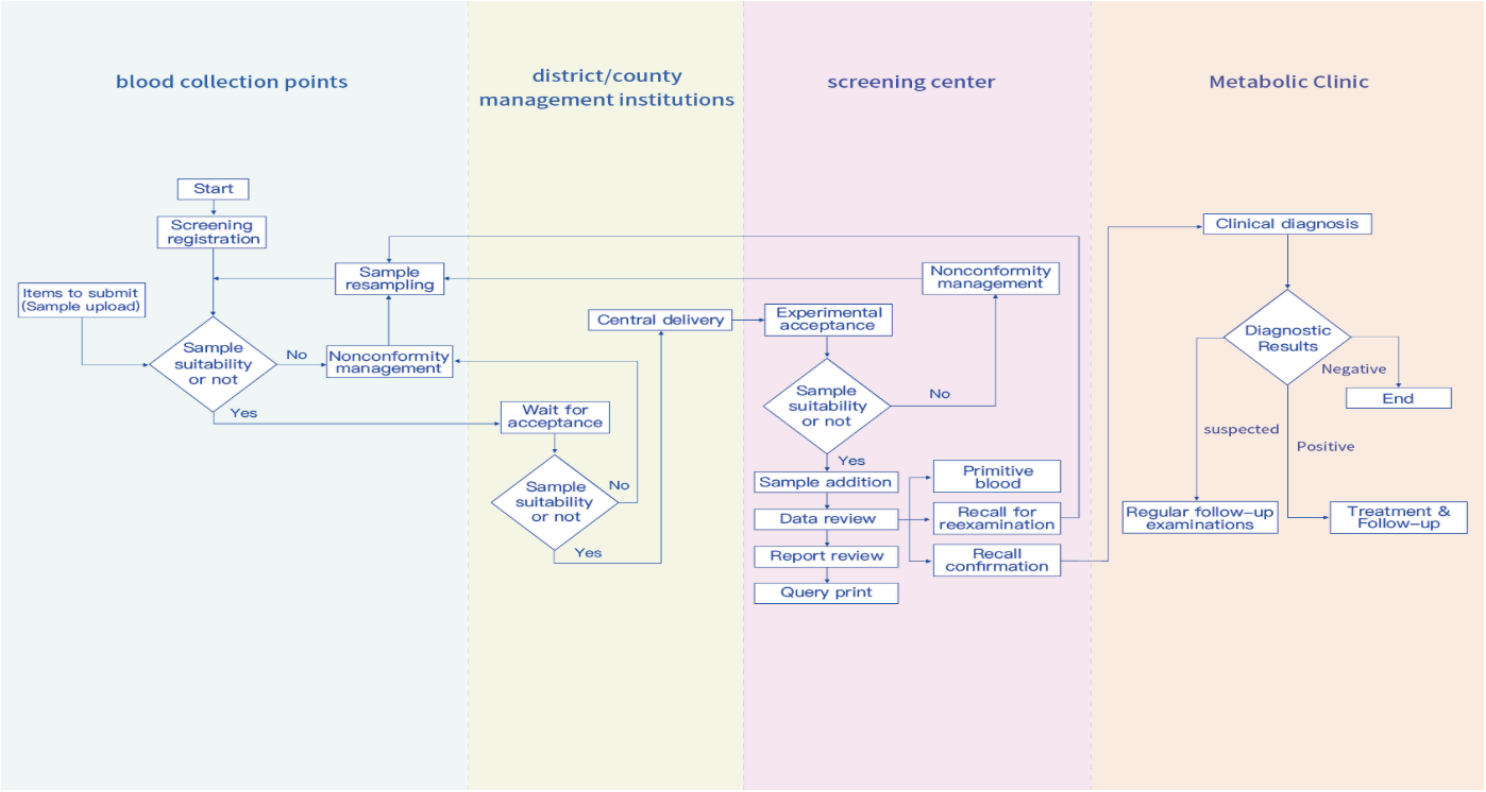


Figure 1

The technical route of NBS nice but please change sample qualification to suitability or acceptability or just say sample acceptable yes/no

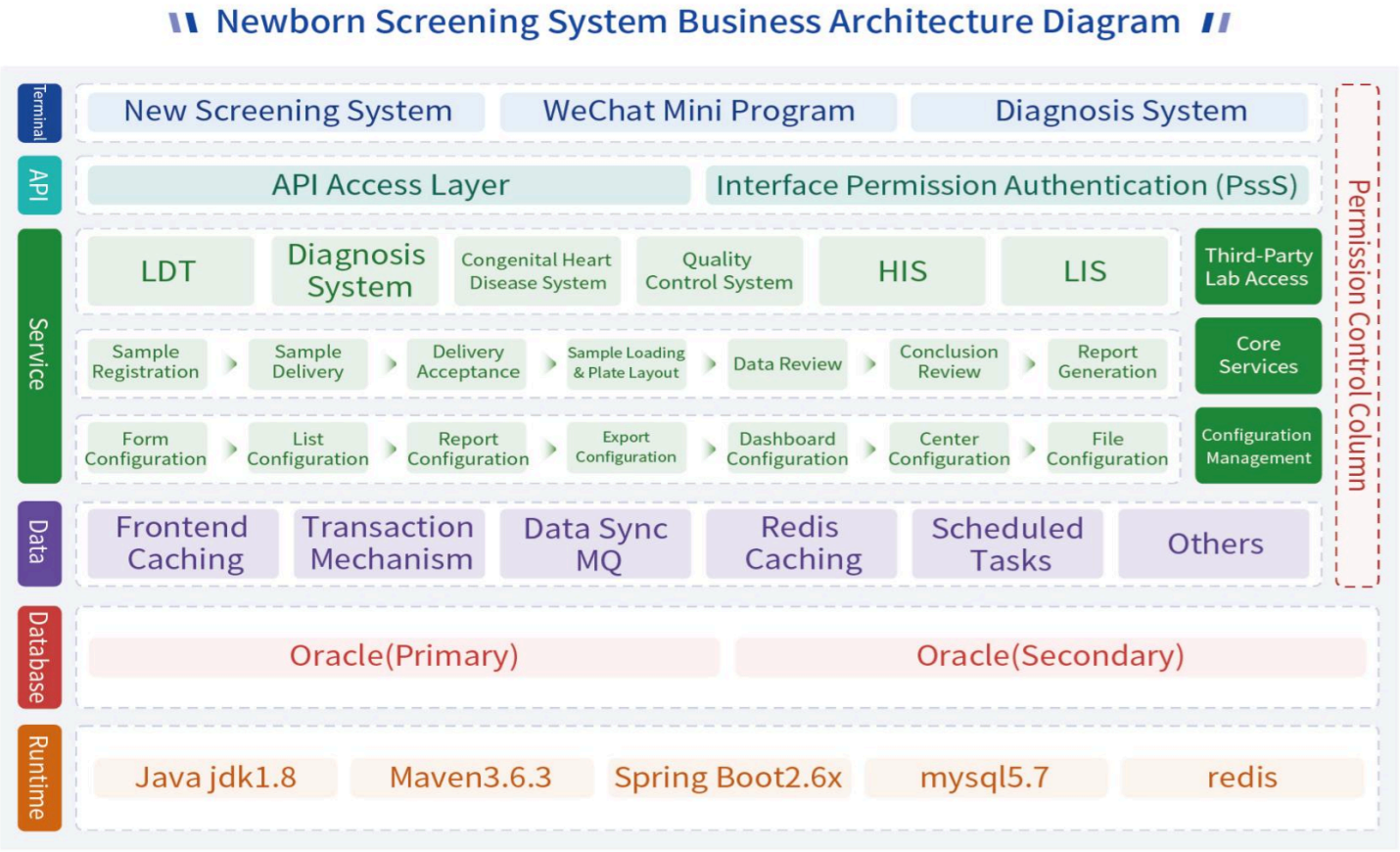


Figure 2

The architecture diagram of NBSS