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Neonatal Informatics: Transforming Neonatal Care Through Translational Bioinformatics

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Abstract

The future of neonatal informatics will be driven by the availability of increasingly vast amounts of clinical and genetic data. The field of translational bioinformatics is concerned with linking and learning from these data and applying new findings to clinical care to transform the data into proactive, predictive, preventive, and participatory health. As a result of advances in translational informatics, the care of neonates will become more data driven, evidence based, and personalized.

Introduction

The first three articles in this series examined the current state of neonatal informatics as it pertains to topics such as computerized order entry, clinical decision support, handoff communication, and data entry and review. The goal of this final installment was to illustrate a realistic vision for the future of neonatal informatics by citing examples in which translational bioinformatics are transforming patient care.

The Abundance of Data

Health care, like many modern industries, is in the midst of a “data deluge.” (1) The computerization of the medical record has resulted in the storage of a wealth of clinical data, including clinical documents, vital signs, laboratory results, pharmacy records, and diagnosis codes. In addition, with the cost of whole genome sequencing approaching \$1,000 and the availability of less expensive direct-to-consumer genotyping services, the amount of genetic data being generated is enormous. (2)(3)

This abundance of data creates many challenges, from nonclinical issues such as storage, security, and integration, to clinical ones such as the effective display of information to providers. (4)(5) Beyond these challenges exists an even greater opportunity: generating

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new knowledge by mining the data and using it to improve patient care. (6) The field of translational bioinformatics is concerned with the bridging of biological and clinical knowledge and discovery to “link innovations from bench to bedside.” (7)(8)

According to the American Medical Informatics Association, an end product of translational bioinformatics is “the transformation of increasingly voluminous biomedical data, and genomic data, into proactive, predictive, preventive, and participatory health.” (9)(10) Although some overlap exists among the concepts of these “4 Ps” that describe the application of new biomedical knowledge, they serve as a useful framework for the ways in which neonatal care will be transformed through translational bioinformatics.

Proactive Care

Proactive: Acting in advance to deal with an expected change or difficulty—

Earlier recognition of a patient’s deteriorating status allows for intervention that may alter the clinical course toward an improved outcome. Indeed, rapid response team (RRT) intervention has been shown to decrease mortality in pediatric inpatients. (11) Initiating an RRT call has traditionally relied on manual acknowledgment of a change in patient status, but mining clinical data for patterns that exist before an RRT call offers promise in the ability to automatically identify at-risk patients in real time. (12) Similar methods could be applied to clinical events that represent worsening status in neonatology, such as hypoglycemia, (13) emergent intubation, the initiation of a vasoactive drip, or a code event. For instance, the real-time analysis of streaming vital signs data is being piloted in the NICU at The Hospital for Sick Children (SickKids) in Toronto, Ontario, Canada. (14)

Another opportunity to personalize care using a proactive approach arises when insufficient evidence exists to guide specific clinical decisions. Frankovich et al (15) at Stanford University recently described the use of a research data warehouse comprising de-identified data captured from the electronic medical record (EMR) to aid in a clinical decision: whether to anticoagulate a patient with rheumatologic disease. Analysis of a cohort of similar patients from the research data repository yielded relative risk values for thrombosis, which were central to the decision to anticoagulate. Certainly this approach could be useful for decision-making in neonatal care.

Predictive Care

Predict: To state, or make something known in advance, especially using inference or special knowledge—

In addition to the proactive use of clinical data to signal a change in patient acuity or to help answer a clinical question, patterns mined from clinical data will be useful for predicting diagnoses and outcomes. For example, research examining patterns in the clinical data that precede a diagnosis of necrotizing enterocolitis is underway at Stanford. This work could inform a predictive model that suggests the diagnosis before it manifests clinically; features of the model itself may contribute to a better understanding of necrotizing enterocolitis pathogenesis or help identify harmful practices that play a role. In other work specific to neonatology, patterns in vital signs data have been shown to predict both short- and long-term morbidity in preterm infants (16) and are useful in predicting imminent sepsis. (17) Finally, modeling lung mechanics using real-time data from ventilator measurements could inform selection of ventilation strategies and adjustments.

The availability of genetic information will add to the ability to make predictions in the context of clinical data. The eMERGE (Electronic Medical Records and Genomics) Network is a group of institutions linking genetic data to EMRs to advance scientific discovery; their ultimate goal is to personalize medicine by incorporating new findings into

clinical care. (18) Pharmacogenomics knowledge integrated with an EMR, for instance, could guide the decision to initiate pharmacotherapy, as well as selection of the ideal therapeutic agent and dose. (18)(19) The challenges in management of patent ductus arteriosus represent a salient opportunity. (20) Models based on genetic and clinical data could aid in predicting which infants are at risk for persistent patent ductus arteriosus and cardiorespiratory complications. Similar models could generate risk/benefit profiles for different medications, suggesting which are most likely to achieve ductal closure and which are least likely to cause adverse effects.

Preventive Care

Preventive: Preventing, hindering, or acting as an obstacle to; slowing the development of an illness; prophylactic—One clear promise of personal genome sequencing is in guiding preventive care. The genome sequence of “Patient Zero” led to specific recommendations, including the initiation of statins due to predicted future heart disease. (21) A more recent analysis of the genomes of a family of four (including two teenagers) led to predictions of blood-clotting abnormalities in the children and resulted in changes to their anticoagulation regimen to prevent adverse events. (22) Although some overlap exists in care that is considered proactive, predictive, and preventive, perhaps the ultimate example of preventive care in the field of neonatology is the prevention of preterm birth. To that end, the March of Dimes and Stanford University School of Medicine established a research center to identify the causes of prematurity in an effort to prevent it. (23)(24) The center brings together researchers from multiple disciplines, including biomedical informatics. Early contributions resulting from translational bioinformatics approaches include the identification of candidate serum biomarkers for earlier diagnosis of preeclampsia and identification of maternal environmental factors that may influence preterm birth. The transdisciplinary environment of the center, including its informatics expertise, will continue to enhance our understanding of preterm birth. Similar efforts are underway at Seattle Children’s Hospital and the University of Washington as part of the GAPPS (Global Alliance to Prevent Prematurity and Stillbirth) initiative. (25)

Participatory Care

Participation: The process during which individuals, groups, and organizations are consulted about or have the opportunity to become actively involved in a project or program of activity—Electronic tools can be used to engage parents of infants in the NICU, improve family satisfaction, and may facilitate earlier discharge from the hospital. (26) Multiple NICUs have developed automated daily updates for parents that are generated by using the EMR. These updates include information such as the provider caring for an infant, change in weight, feeding tolerance, number of diapers, apnea/bradycardia/desaturation events, medications, a summary of key laboratory results, diagnoses, and the plan of care. At Lucile Packard Children’s Hospital, the EMR-generated daily parent update improved parent engagement by increasing the ability to identify the care team, knowledge of an infant’s clinical status and plan of care, and satisfaction with the NICU experience.

Beyond the NICU, the participatory role of families can be supported by using electronic personal health records (PHRs). (27)(28) PHRs encourage information self-management by families, enable health information exchange between providers, enhance continuity of care, and have the potential to improve shared decision-making. (28) The families of NICU patients with complicated inpatient stays certainly could benefit from a PHR, as could families of infants with more routine newborn courses, who would be able to manage information such as immunizations, bilirubin values, and sepsis screens. Lucile Packard

Children's Hospital recently piloted development of a bidirectional link between a pediatric EMR and a commercially available, interoperable PHR. (29)(30)

Summary

Translational bioinformatics approaches already are generating new biomedical knowledge relevant to neonatal care. Incorporation of this new knowledge into clinical practice via integration within EMRs will allow for prospective evaluation of its impact on patient outcomes and ultimately lead to the delivery of personalized, precision medicine: "diagnostic, prognostic, and therapeutic strategies precisely tailored to each patient's requirements." (31)

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Objectives

After completing this article, readers should be able to:

1. Appreciate the opportunity related to the abundance of biomedical data being generated.
2. Understand the concept of translational bioinformatics.
3. Describe examples of the application of new knowledge from translational bioinformatics.