Commercial Availability of Non-Invasive Prenatal Testing in Low- and Middle-Income Countries: Ethical and Policy Implications

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BACKGROUND

Non-Invasive Prenatal Genetic Testing (NIPT)

NIPT analyzes cell-free fetal DNA present in maternal serum to detect fetal chromosome aneuploidies [1] like Down syndrome (trisomy 21) or Turner syndrome (45,X). It is more accurate than serum screening or ultrasonography [2] and avoids the physical discomfort and risks of invasive testing methods [3]. However, NIPT is not diagnostic; positive results must be confirmed with amniocentesis or chorionic villus sampling [4]. Professional societies currently recommend NIPT only for women at increased risk of fetal aneuploidy (e.g., advanced maternal age, prior pregnancy with a trisomy) [5].

Commercial market for NIPT

NIPT was first introduced in Hong Kong in 2011 [6] and was commercially available in the United States soon after [7]. Four companies currently compete in the US prenatal testing market, and two Chinese and two European companies also sell tests internationally [7]. The global NIPT market will be an estimated $3.62 billion by 2019 [8].

NIPT in Low- and Middle-Income Countries (LMICs):

NIPT is being aggressively marketed worldwide and its availability is rapidly increasing. Yet it is not clear how NIPT will be integrated into clinical practice in LMICs, which have unique practical, ethical, and legal challenges for the introduction of new prenatal technologies.

GLOBAL AVAILABILITY OF NIPT

Countries where NIPT is currently marketed or in which marketing deals have been signed are presented [10]. Numbered countries are as follows: 1) Portugal, 2) Ireland, 3) United Kingdom, 4) Norway, 5) Sweden, 6) Finland, 7) Denmark, 8) the Netherlands, 9) Luxembourg, 10) Belgium, 11) Germany, 12) Switzerland, 13) Liechtenstein, 14) Italy, 15) Austria, 16) Czech Republic, 17) Slovakia, 18) Hungary, 19) Slovenia, 20) Croatia, 21) Romania, 22) Bulgaria, 23) Albania, 24) Greece, 25) Tunisia, 26) Cyprus, 27) Lebanon, 28) Israel, 29) Jordan, 30) Kuwait, 31) Bahrain, 32) Qatar, and 33) United Arab Emirates.

RESULTS

1. NIPT is available in over 60 countries. Tests are marketed to LMICs primarily in South America, the Middle East, South and Southeast Asia, and to a much lesser extent in Africa [9].
2. Access to NIPT is frequently limited to wealthier patients in urban areas who can pay for these tests out of pocket.
3. Clinical integration in many LMICs is complicated because prenatal genetic screening is not the standard of care, especially in underserved/low resource communities.
4. Currently, no genetic counseling for NIPT is provided by companies who market tests in LMICs.
5. While publicly funded hospitals/universities in LMICs may provide prenatal services for free or at low cost, few (if any) of these centers are integrating NIPT into routine clinical care. Barriers include the price of NIPT and the need to ship samples internationally for analysis by the testing company.
6. Only a handful of public sector institutions perform specialty prenatal genetic testing in most LMICs and have limited capacity for genomic sequencing.
7. Companies currently offering NIPT claim to be compliant with laws (e.g., India, China) prohibiting return of fetal sex information; however, more data on compliance procedures are needed.
8. Regulation of NIPT in LMICs is limited or non existent, with the notable exception of the Chinese Food and Drug Administration's recent approval of NIPT [10].

OBJECTIVES

1. Study the commercial availability of NIPT in LMICs.
2. Examine the potential effects of NIPT on standards of care, disparities in prenatal care, patient and provider education, and regulation of prenatal genetic testing and information.
3. Assess attitudes towards prenatal testing around the world.
4. Identify systemic factors affecting access to prenatal genetic testing.
5. Analyze the legal frameworks surrounding abortion and return of fetal sex information.
6. Examine social and cultural issues surrounding NIPT use in LMICs.

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MATERIALS & METHODS

Global availability of NIPT

We mapped the global availability of commercial NIPT (*Figure 1*) using publicly available information, Internet searches of press releases, company websites, industry trade reports, and newspapers/popular press articles between January 1, 2012 and April 30, 2014. The list is not exhaustive, as we relied only on publicly available information in English. Only commercial offerings of NIPT for chromosomal aneuploidies using cell free fetal DNA are included.

Implementation challenges

We used the following methods to examine the challenges associated with the implementation of NIPT in LMICs:

- Literature reviews
- Interviews with experts on NIPT and prenatal diagnosis
- Policy analyses
- Searches of popular press and social media
- Analyses of reproductive laws globally
- Surveys of stakeholders (patients and physicians)
- Online content analyses of patient experiences
- Country specific case-studies

CONCLUSIONS

1. Common themes resonate across the developing world, like limited capacity for genetic services, genetic counseling, poor genetics education, and inequitable access to prenatal care.
2. Legal structures and/or attitudes can vary widely, creating unique challenges and ethical dilemmas for implementation in different countries.
3. NIPT may increase access to safe and accurate prenatal genetic information, reduce disparities in prenatal care, and improve reproductive decision making for families in LMICs. However, many questions must be addressed:
   - Which technologies are most appropriate in LMICs?
   - How does public health infrastructure need to be strengthened?
   - How do we educate physicians, families, and policy makers?
   - What effect will national laws on termination of pregnancy have?
   - How will fetal sex information be regulated?
4. International, national, and local stakeholders must be engaged in order to guide NIPT implementation policies and to ensure the ethical and effective use of NIPT in improving prenatal care worldwide [9,11].

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FURTHER INFORMATION

http://sites.duke.edu/nipt/

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