Translating cfDNA Screening:
Ethical and Social Issues Along the Pathway

Marsha Michie, PhD[1]; Ruth M. Farrell, MD, MA[2]; Megan Allyse, PhD[3]

[1]University of California, San Francisco; [2]Cleveland Clinic; [3]Mayo Clinic

Background

The recent development and worldwide implementation of prenatal cell-free DNA screening (cfDNA) has provided a compelling case study of the many ethical, social, and legal implications of genomic translation. In an era of rapid change in genomics, cfDNA has emerged quickly, propelled by advances in high throughput technology and multimillion-dollar marketing campaigns in a startlingly short time frame. In the process, cfDNA has leap-frogged over standard regulatory structures, and become readily routinized in prenatal care, raising a number of issues for patients, providers, and society about the scope of this technology.

Here we present an overview of the translational pathway of cfDNA, bringing attention to particular points of change and/or conflict in stakeholders' goals, social priorities, and ethical principles. These observations point to ways in which ELSI scholars have intervened, and should continue to do so, particularly through collaborative efforts with other stakeholders.

Methodologies

This overview of the still-progressing translational pathway of cfDNA emerges from over six years of empirical (qualitative, quantitative, and mixed-methods) research—beginning prior to its clinical introduction in 2011—with relevant stakeholders, including test developers, health care providers, patients, parents, and advocates for women, reproductive health, medically underserved populations, and people with disabilities.

With many collaborators, we have also brought together diverse stakeholders at three international symposia to discuss the impact and possible futures of cfDNA here in the US and around the world, with a particular focus on patients and families in diverse socioeconomic contexts. (See **Further Information** below for more on our research.)

Stakeholders in cfDNA: Competing interests

Test Developers	Public/private insurers	Genetic specialists	Generalist providers	Patients/ families	Patient advocates
Rapid translation	Slower translation	Slower translation	Slower translation	varies	Slower translation
No/limited FDA oversight	FDA oversight	FDA oversight	FDA oversight	FDA oversight	FDA oversight
Media hype, market messaging	Peer-reviewed research	Peer-reviewed research	Review articles, CMEs	Patient-centered education	Patient-centered education
Positive recommendation from professional societies	Consensus from professional societies	Consensus from professional societies	Clear guidance from my own professional society	varies	Input into professional society recommendations
Full insurer coverage	Coverage only for recommended indications	Full coverage for acceptable indications	Full coverage for acceptable indications	Equitable access	varies

Stakeholders have shaped the translation of prenatal cfDNA screening from its discovery and laboratory validation, through its clinical translation and current impact on health care systems and public health. The interests of stakeholders compete/conflict in several key areas, as shown above.

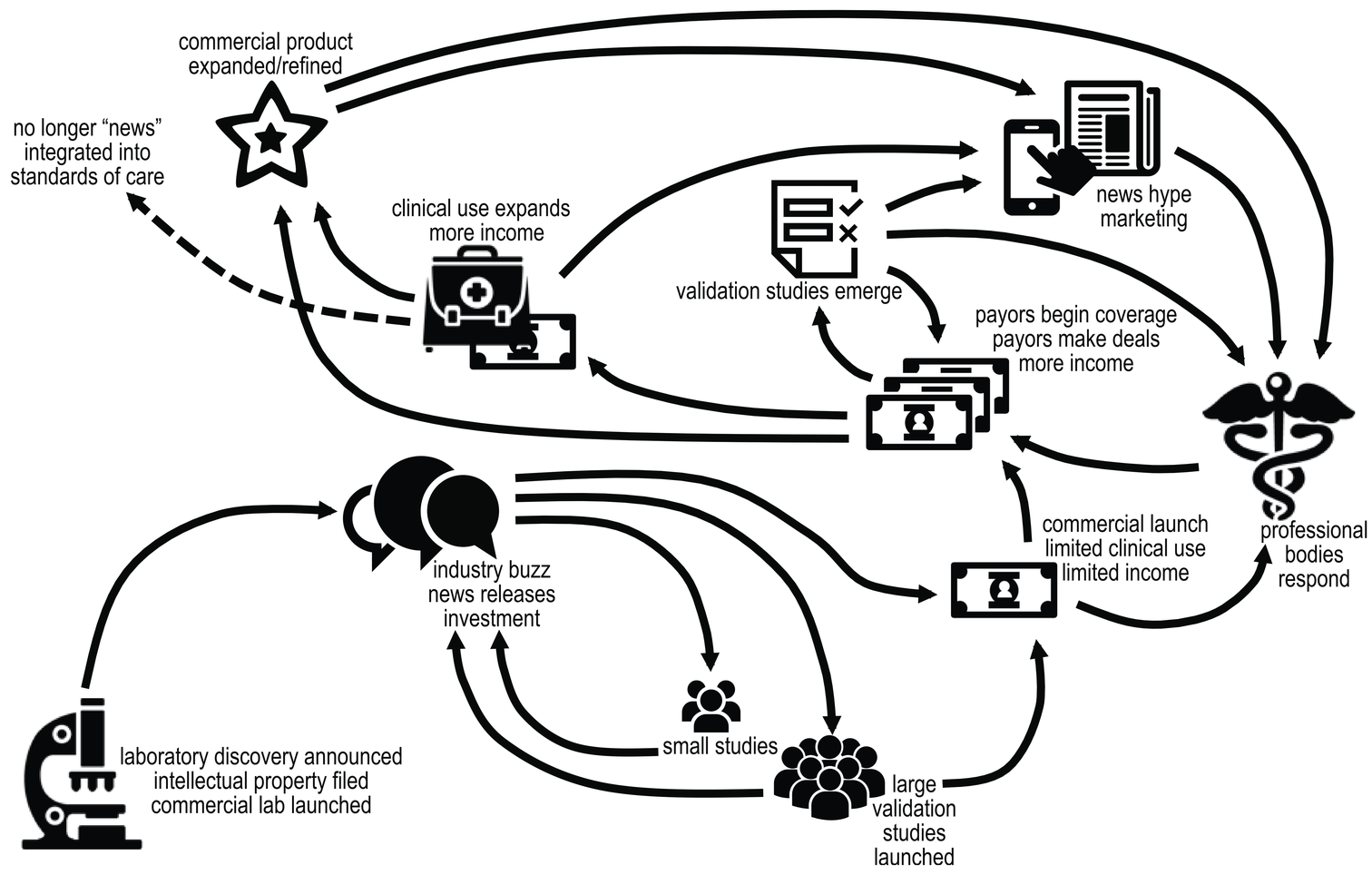
The interests of commercial test developers, tied as they are to profit motives and competition with other commercial entities for market shares, are often misaligned with those of patients, health care providers, and even payors. Yet these commercial laboratories have been the primary force behind the rapid translation of cfDNA, and have been a major source of information about these tests for both patients and providers (particularly generalist providers such as OB/GYNs, nurse midwives, and general practice physicians).

However, while every stakeholder group has unique interests, those interests often align, or can be made congruent, in key areas such as education and professional society recommendations. Recent efforts to bring all stakeholders to the table have found surprising points of agreement, and lent new energy to collaborative efforts at socially and ethically appropriate cfDNA implementation.

Acknowledgements

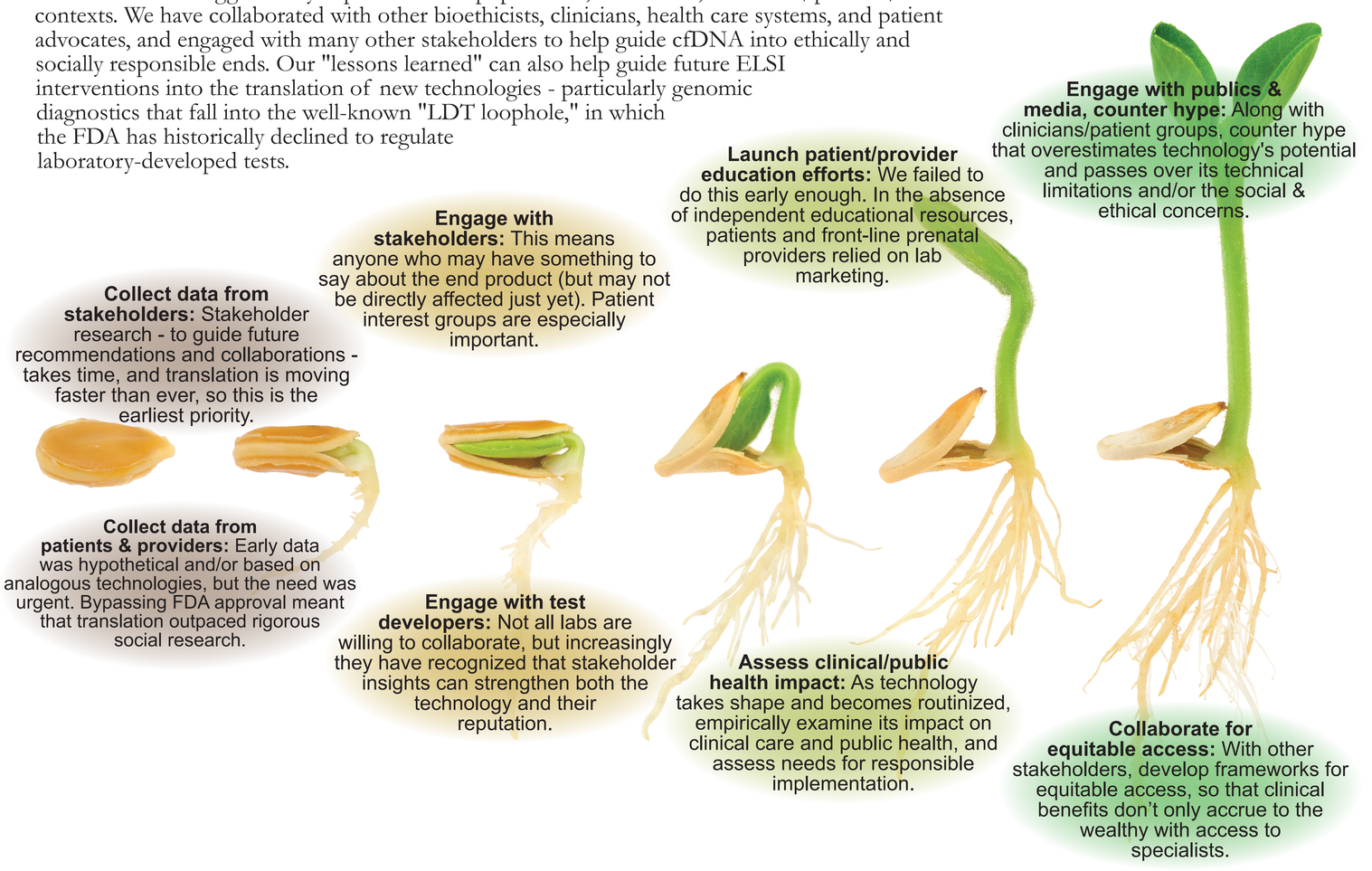
We gratefully acknowledge financial support from NIH grants R00HG006452 and R21HG008511, and organizational support from: UCSF Institute for Health & Aging and UCSF Bioethics; Cleveland Clinic Department of Bioethics; Mayo Clinic Department of Bioethics; and PIRC, the Prenatal Information Research Consortium.

A translational pathway for prenatal cfDNA screening



ELSI guidance along the translational pathway

Efforts to build ELSI guidance into the translational pathway for prenatal cfDNA screening began as soon as the proof of concept was demonstrated in 2010, and continue today as this technology continues to evolve and its use aggressively expands to new populations, indications, and social/political/economic contexts. We have collaborated with other bioethicists, clinicians, health care systems, and patient advocates, and engaged with many other stakeholders to help guide cfDNA into ethically and socially responsible ends. Our "lessons learned" can also help guide future ELSI interventions into the translation of new technologies - particularly genomic diagnostics that fall into the well-known "LDT loophole," in which the FDA has historically declined to regulate laboratory-developed tests.



Further information

For more information about this study and related research, visit the Prenatal Information Research Consortium (PIRC) at http://prenatalinformation.org, email us at pirc@prenatalinformation.org, or scan this QR code with your smartphone.