Making Sausage

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Disclosures and Limitations

- Officer and shareholder in Invitae, a publicly traded company covered by SEC rules
- National Advisory Council for NHGRI
- Involved in negotiations with medical insurance companies to bring Invitae “in network”
- Can only speak in generalities about a heterogeneous and complex ecosystem
- Anecdotal evidence based on many hours of conversations with various payers and payer groups

"You were right—I really didn't want to know how it's made, because that was incredibly boring."

Anecdotes and Data

"The plural of anecdote is data"

- Raymond Wolfinger , Stanford Graduate Seminar (1969-1970)

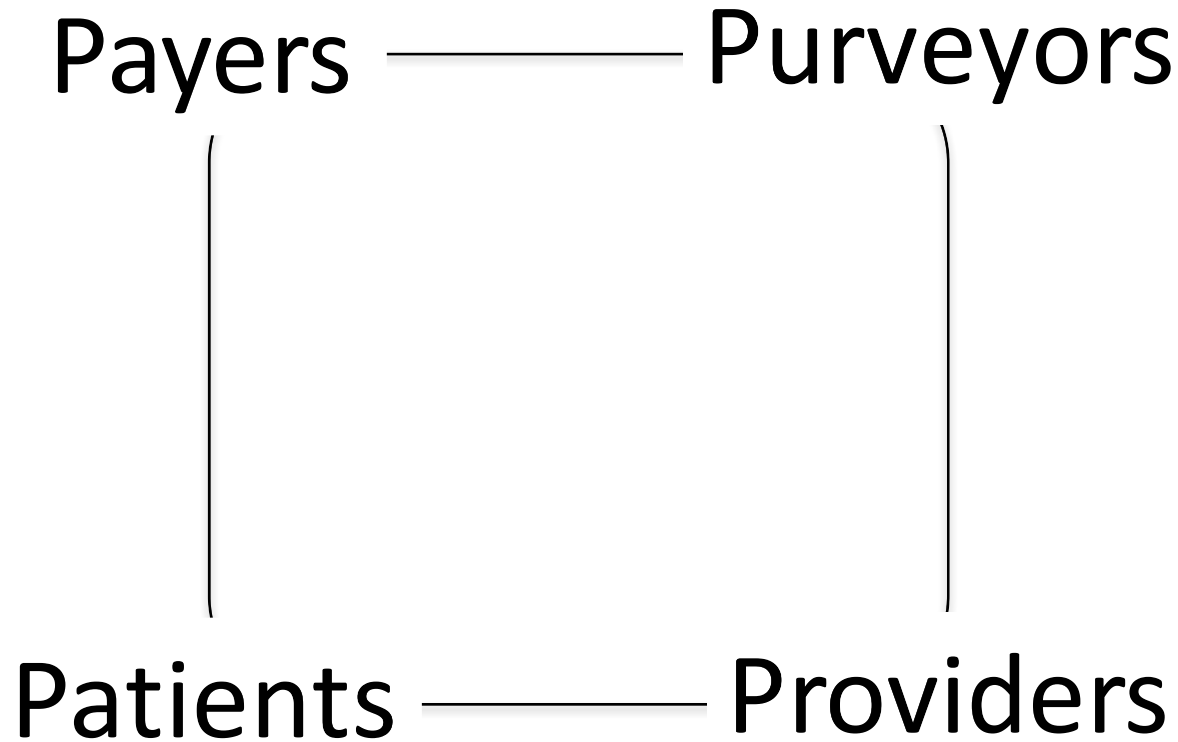
"The plural of anecdote is not data"

- Roger Brinner, reference?
- Bernstein, I. S. Metaphor, cognitive belief, and science. Behavioral and Brain Sciences 11:247-24 (1988).
- Frank Kotsonis, Clinical Evaluation of a Food Additive (1996)

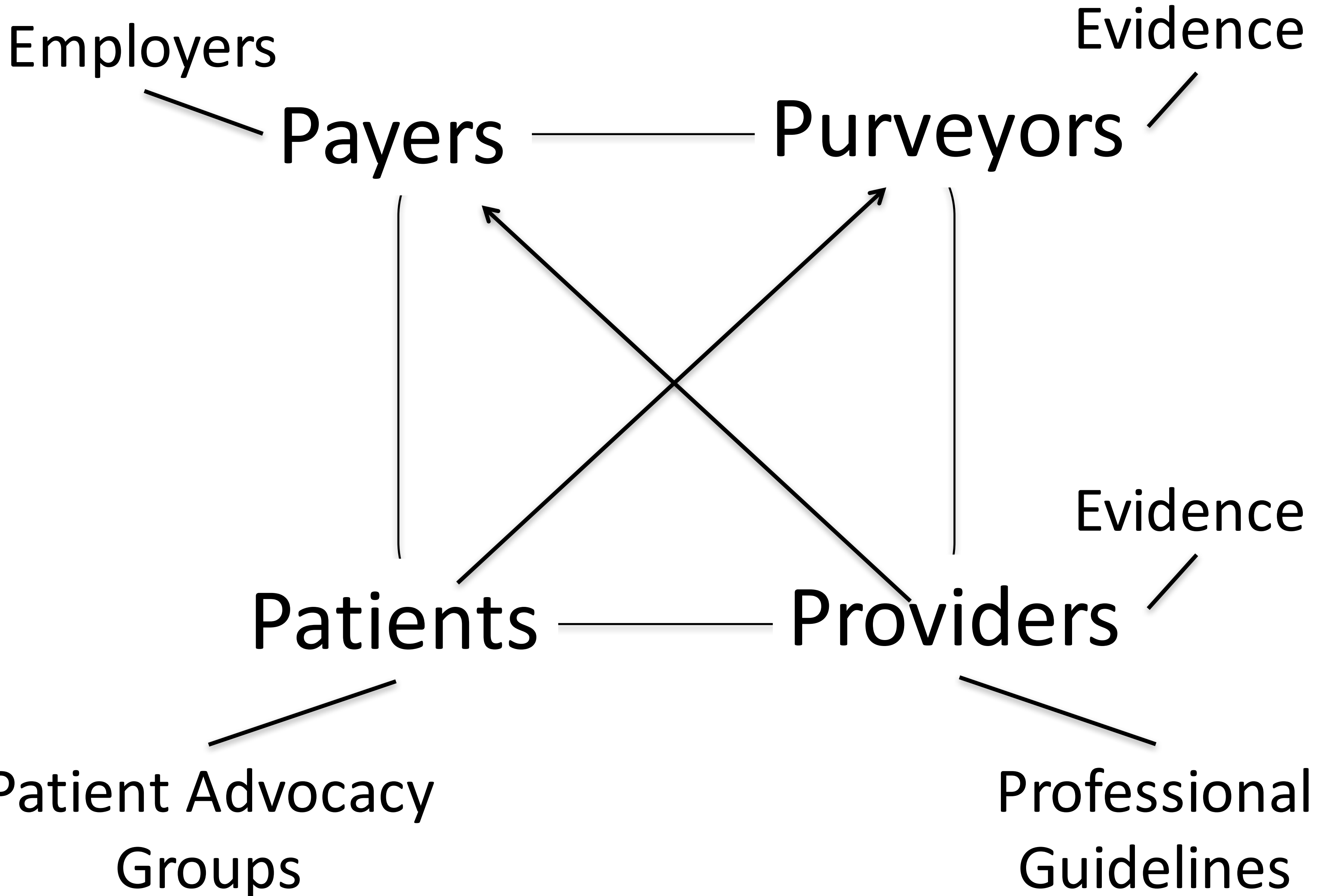
Who Ultimately Decides?

Payers

Complex Ecosystem (“Four P’s”)



Complex Ecosystem ("Four P's")



Payers

- Very heterogeneous in their level of knowledge and sophistication
- May use Palmetto MolDx or private insurance Tech Assessment groups…or not
- Feel they have been “had” or “burned” in the past by new technology and by code stacking
- Worried about cost of testing but even more so on misuse of test results (e.g. VUS’s) to trigger unnecessary and expensive downstream testing and procedures

Payers (2)

- Respond to Professional Guidelines and pressure of a tsunami of unpaid claims
- Under financial pressure from employers who wish to keep health premiums down
- Looking to partner with Labs and others to provide “Utilization Management”
- Experiencing financial stress from Affordable Care Act, with mandate to reduce administrative costs-→ recent M&A

Payer Coverage with Evidence Development:

“Not our job to finance your business development”

Purveyors (Labs)

- Survive by selling tests – financial incentive to develop evidence but limited resources to do so
- Perverse benefit of patent protection for testing is to incentivize evidence development (May the ACLU forgive me!)
- Unfortunate tendency to claim "low VUS rates" either from hubris or for marketing -> overcalling feeds Payer paranoia

Van Driese et al. in JAMA

- Discordance between LQTS genotypes and the EHR-based phenotype in an unaffected cohort from EMR, designed to simulate incidental findings
- Could be interpreted as very low predictive value of genotype in unaffected individuals due to lack of penetrance
- However, could also mean
  - Misclassification of variants by the 3 labs
  - False negative phenotyping based on medical record

Providers (Academic Researchers)

- Very important role in evidence development and assessment
- Partnerships with labs have and can be fruitful, particularly in clinical utility and medical economic studies that labs are in no position to carry out themselves
- Alphabet soup of NHGRI and NIH initiatives: CSER, IGNITE, eMERGE, NSIGHT are valuable but…

Carry the “Taint” of the Ivory Tower

Providers (Community)

- Generally too busy and decentralized to play an important role in evidence development and assessment
- Have similar difficulties assessing what they hear from laboratory sales teams as they do with pharmaceutical company “drug reps”
- Undescores the special role of integrated systems in evidence development

Providers

- Professional Guidelines that are up-to-date and speak with one voice are very important
- Compare NCCN versus the cacophony of guidelines in cardiology genetics, some of which are >5 years old

Patients

- Often have an adversarial relationship they may experience substantial bureaucratic procedures and a string of denials despite paying substantial premiums
- Fundamentally, I believe much of this arises from a lack of agreement on what constitutes Clinical Utility

Complex Ecosystem ("Four P's")