High Impact Diagnostics

Halteres Associates

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Halteres from Ancient Greece
National Archaeological Museum in Athens

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What are some examples of high impact diagnostics?

- PSA
- Cholesterol
- HIV viral load
- HCV viral load
- Breast cancer prognosis (BRCA, Oncotype)
- Vitamin D testing
- HbA1c
- TB DNA
- Many others

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How can we predict what is likely to be a high impact diagnostic?

- How can we identify new potential high impact diagnostics?
- How can we determine how well they need to perform?
- How can we actually plan to create a high impact diagnostic?

Many New Diagnostics Don't Make the Grade

- Many diagnostic tests are developed every year
- Few ever become "high impact" products
- Why? There are many reasons
- They just don't perform well enough
  - Sensitivity
  - Specificity
  - Reproducibility
- The clinical evidence base just isn't sufficient
  - Too few published clinical studies
  - Studies too small
- There is poor reimbursement
- Poor attempts to educate physicians

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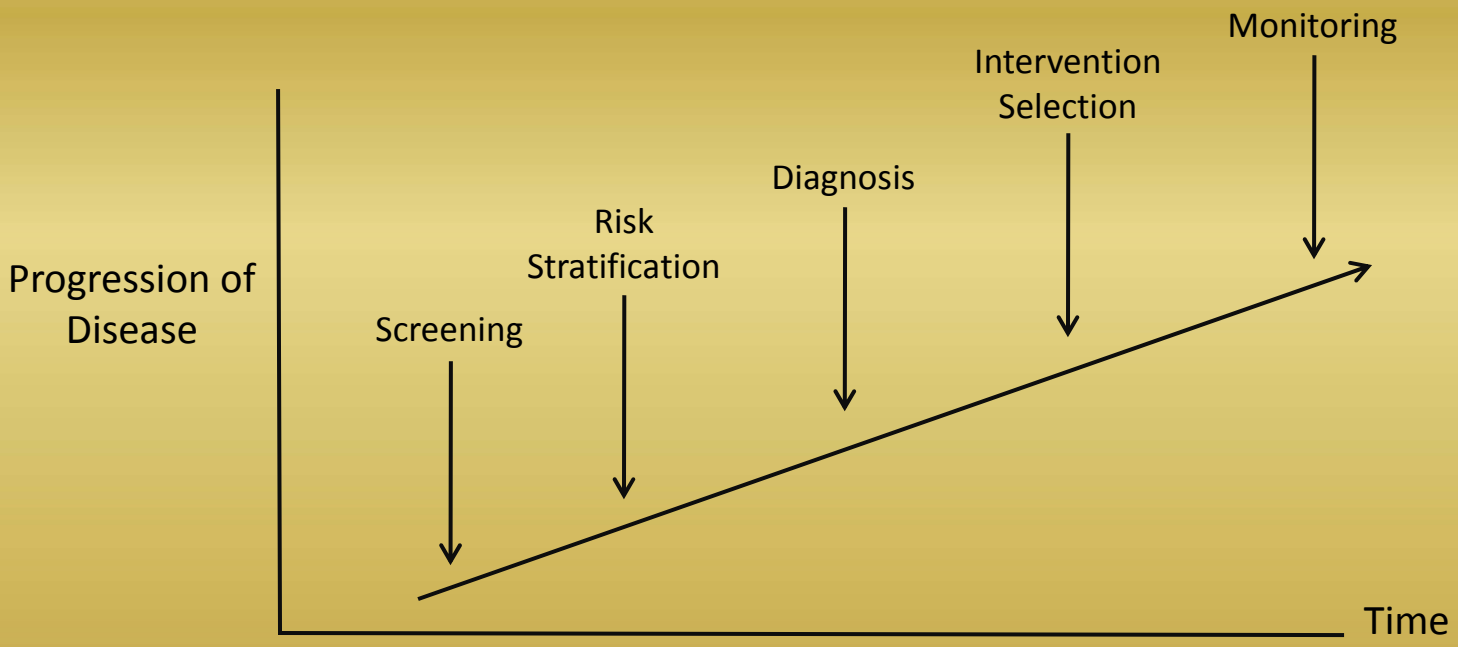
Diagnostics Tests Can Be Grouped Based Upon Progression of Disease

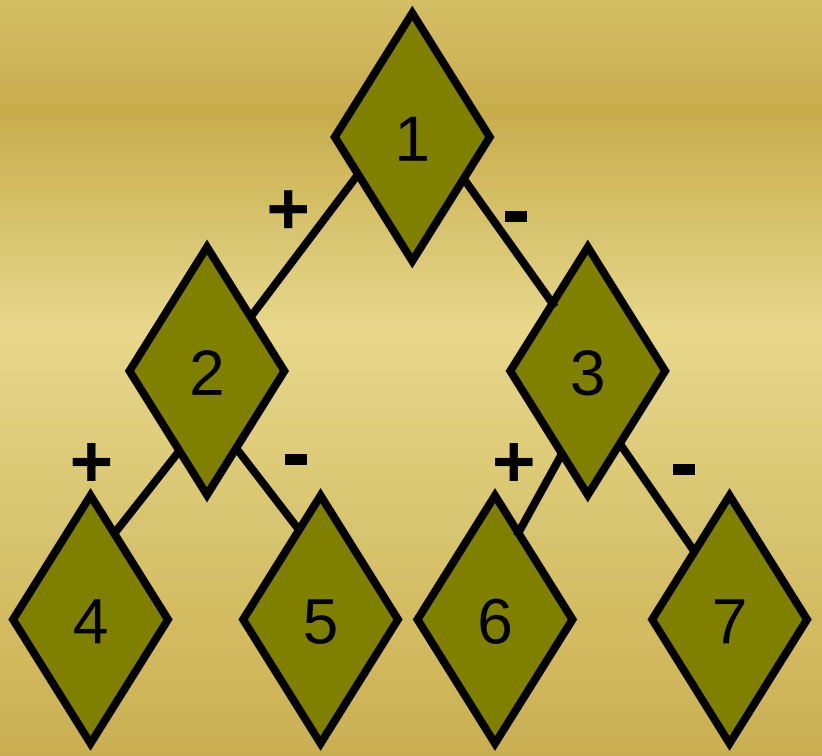
New diagnostics are needed in all categories



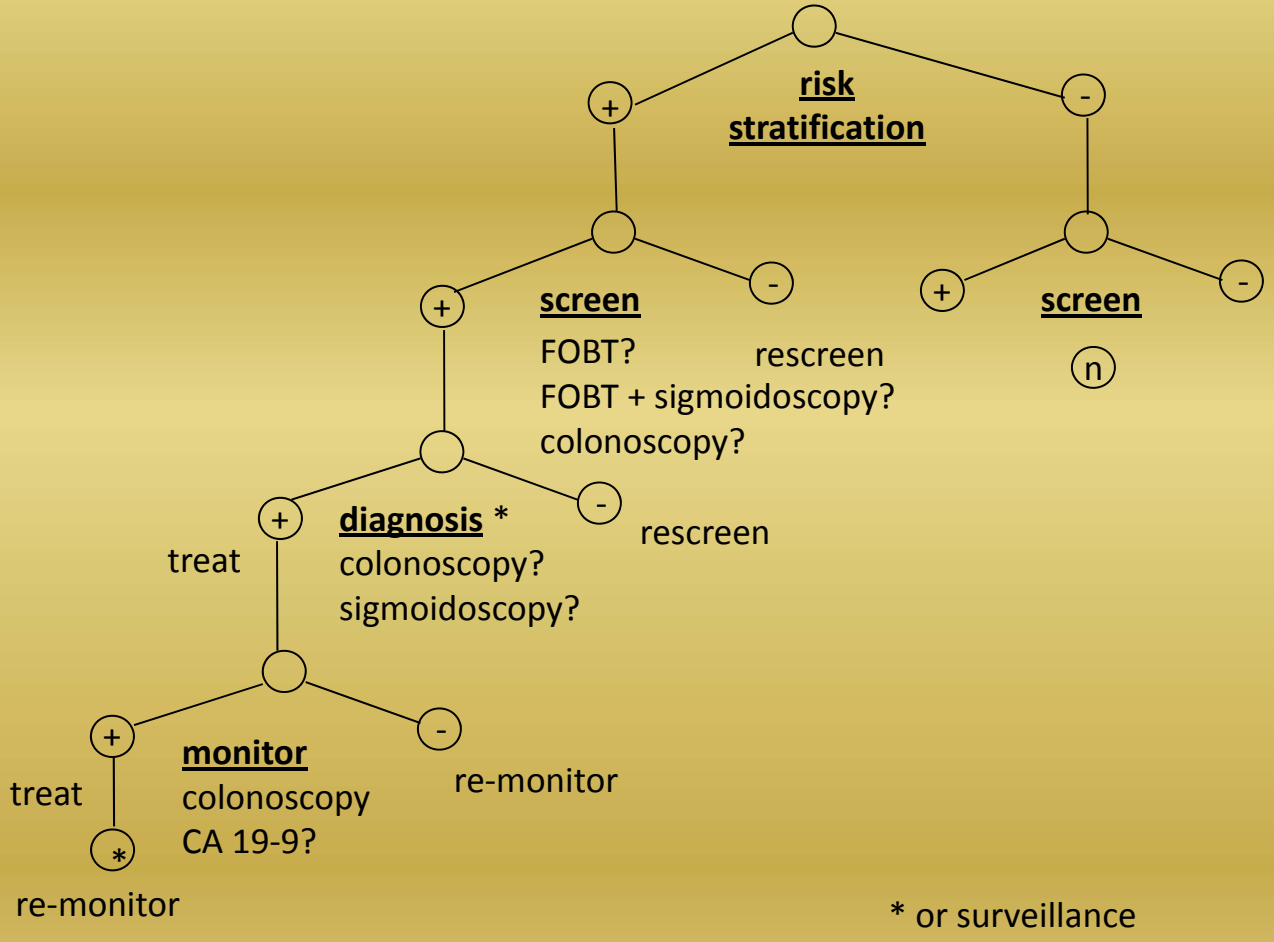
Searching for Diagnostics Opportunities: Disease Decision Trees

At each decision point:

- What is the quality of the decision today?
- What is the clinical impact of the decision?
- What is the economic impact of the decision?



CRC Decision Tree Summary



Measure of a New Test Value: CER

Cost Effectiveness Ratio calculated by applying the formula below to two model estimates (one with and one without the new test)

$$\frac{\Delta \text{ \$ Disease Cost}}{\Delta \text{ Life Years Saved}}$$

Rule of Thumb for CERs (US Perspective)

- Ideal would be cost saving (save money)
- Second best would be cost effective
- CER of $20,000/LY ~ great value
- CER less than $50,000/LY ~ acceptable value for most US interventions
- CER between $50,000 and $100,000/LY is expensive
- CER greater than $100,000/LY is unacceptable

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Example Cost Effectiveness Ratios (CERs)

Intervention	Cost/LY Saved
Angiography for MI	$21,831
Mammography	$25,000
Coronary Bypass	$40,000
HAART for HIV Disease	$15,000
Blood pressure medications	$5,000 - $72,000
Screen for Hemochromatosis	$9,900
NICU for babies <1000g	$5,100
Seatbelts in school buses	>$1,000,000

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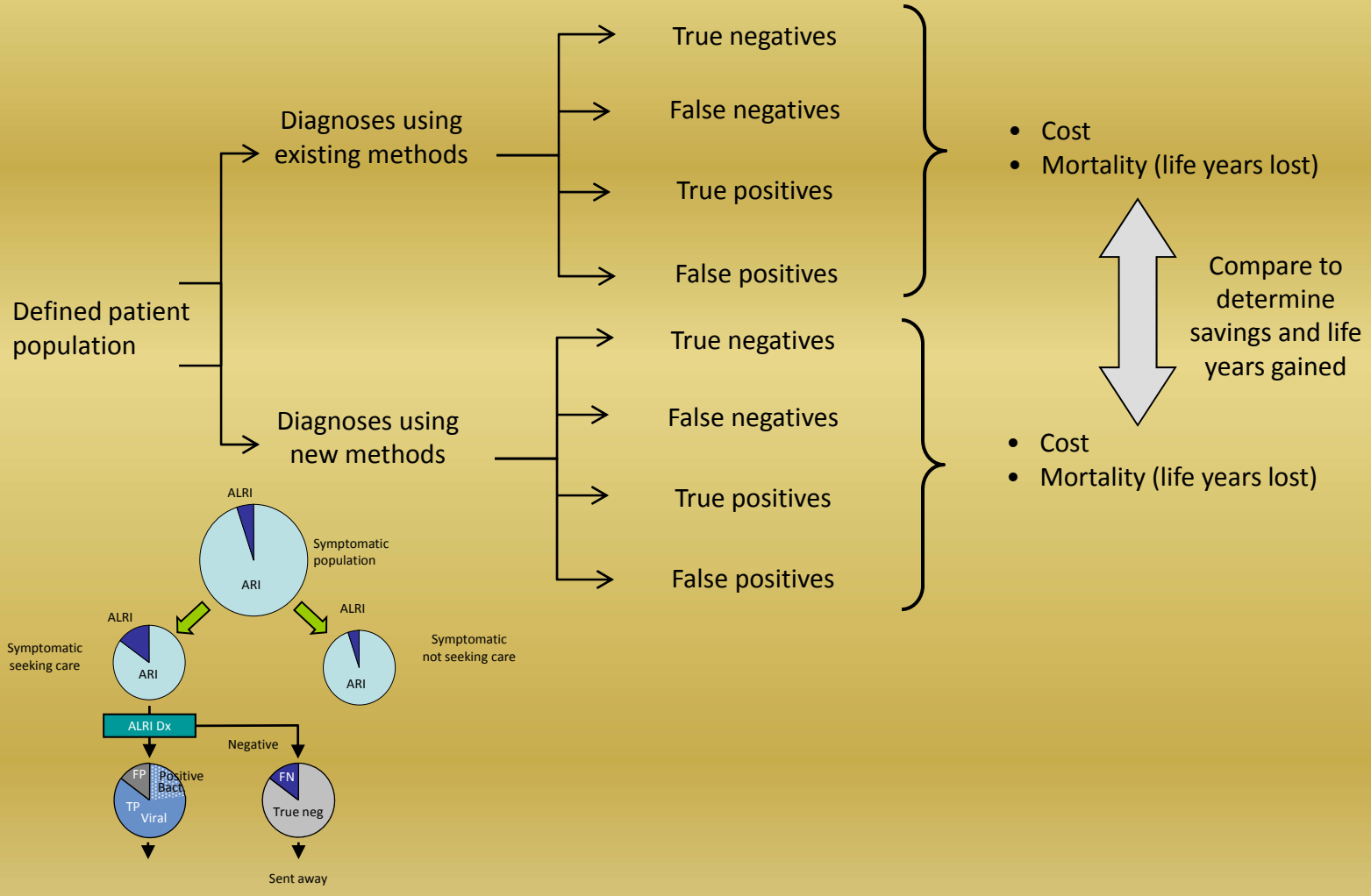
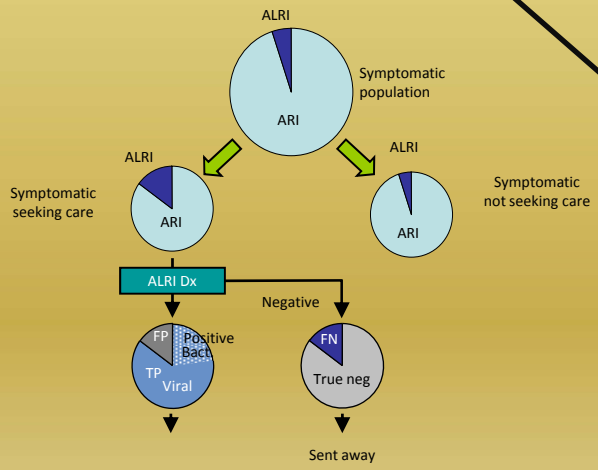
Calculating the Performance Needed: Health Economic Modeling



Calculating the Performance Needed: Health Economic Modeling

Clinical

Cost evaluation/patient = $0.35
Total cost evaluation = $970.00



True negatives	
% patients	65.5%
Number patients	1,800
Cost per patient	$0
Total cost	$0
Mortality rate	0%
Deaths	-

False negatives	
% patients	3.6%
False negatives	100
Cost per patient	$0
Total cost	$0
Mortality rate	30%
Deaths	30

True positives	
% patients	14.5%
Number patients	400
Cost per patient	$66
Total cost	$26,500
Mortality rate	10%
Deaths	40

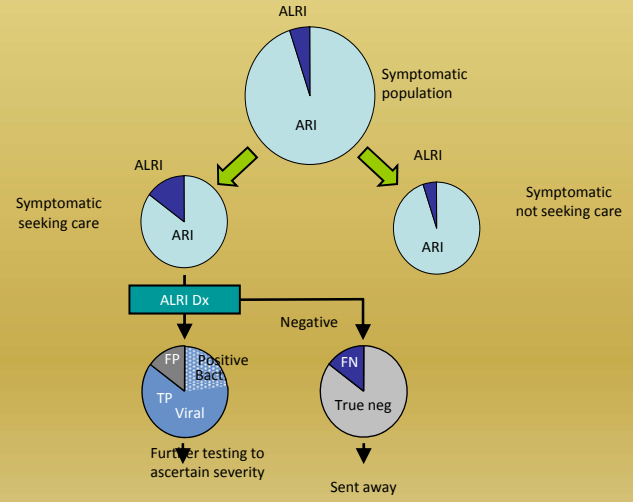
False positives	
% patients	16%
Number patients	450
Cost per patient	$66
Total cost	$29,813
Mortality rate	0%
Deaths	-

Calculating the Performance Needed: Health Economic Modeling

		ALRI test specificity					
		75%	80%	85%	90%	95%	100%
ALRI test sensitivity	75%	-$2.1	$0.6	$3.3	$6.0	$8.7	$11.4
	80%	-$2.7	$0.0	$2.7	$5.4	$8.1	$10.8
	85%	-$3.3	-$0.6	$2.1	$4.8	$7.5	$10.2
	90%	-$3.9	-$1.2	$1.5	$4.2	$6.9	$9.6
	95%	-$4.5	-$1.8	$0.9	$3.6	$6.3	$9.0
	100%	-$5.1	-$2.4	$0.3	$3.0	$5.7	$8.4

Per 1% improvement result in savings per patient diagnosed:

- Sensitivity = $0.12
- Specificity = $0.54



High Impact Diagnostics

- New tests will be successful if they:
  - Help to improve a decision in the decision tree
  - Are clinical meaningful
  - Are cost effective or cost saving

How do people develop new high impact diagnostics?

- We'll look at a fictitious company that wants to develop a new HIV viral load diagnostics product
- We'll follow the decision process for this company

Fictitious Example: RetroViraTech (RVT)

- RVT wants to develop an HIV viral load diagnostic testing device
- RVT is investigating prototype methods and devices
- RVT needs to determine its path to commercialization

Commercial Opportunity Attractiveness: RVT's Homework

- Size of potential market
- The clinical question to be answered using their test
- Performance requirements based upon economics
  - Cost of false positive? (for instance, treat healthy people) Implies specificity requirement (70%? 99%?)
  - Cost of false negative? (for instance, don't treat those who need it) Implies sensitivity requirements (70%? 99%?)
- Competition and IP (this can be a significant issue)
- Regulatory hurdles (FDA)
- Potential value (justifiable and affordable selling price)
- Time to meaningful sales (this can take longer than you think)

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Commercial Opportunity Attractiveness

Criteria	Weighting Factor	Score	Definition
Unmet Medical Need	**3**	**0**	Little impact on outcomes. Current diagnostic methods are sufficient. Difficult to change current medical practice
		1	Favorable impact on outcomes, although current methods exist. Iconix product would have a definable "value proposition"
		2	High unmet medical need. Major impact on quality of life. High cost disease.
Time to Meaningful Sales	**2**	**0**	>5 years after initial revenue
		1	2 - 5 years after initial revenue
		2	<2 years after initial revenue.
Economic Value	**3**	**0**	Niche market. Less than $500 million per year sales
		1	Market potential of $50 - $200 million per year sales.
		2	Market potential in excess of $200 million; investor "pizazz"
Market Size	**1**	**0**	<50,000 tests per year expected
		1	Population requiring testing is 50,000 to 200,000 tests per year
		2	Large population requiring >200,000 tests per year
Competition	**1**	**0**	Little differentiation; highly competitive
		1	Some competition but arguable that Iconix has a better solution
		2	Well suited for methodology. Less than or equal to two competitors
Special Interest Groups	**2**	**0**	Forgotten diseases; little evidence of special interest groups. Incoherent support.
		1	Some special interest groups but limited funding available
		2	Well supported by special interest groups
Partnership	**2**	**0**	Synergy with Rx or Dx unlikely
		1	Synergy with Rx or Dx likely but no Rx partner has yet been identified
		2	Clear synergy with Rx or Dx likely and potential partners exist

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Steps in the Creation of New Diagnostics Products

- Determine unmet medical need
- Determine user requirements
- Set product specifications
- Acquire or discover biomarkers
- Find or develop a testing platform that fulfills the user requirement
- Demonstrate the required performance
- Develop the commercial test or system
- Seek appropriate regulatory approvals
- Educate those who will benefit and those who will use it

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User Requirements: What are they?

- An understanding of the needs and limitations of the customer including
  - Sample and implications
  - System performance
  - System characteristics
  - Cost of ownership

Examples of User Requirements

- Sample type (collection issues, sample volume, storage temp, contamination issues, etc.)
- System performance (sensitivity, specificity, multiplex level, reproducibility, etc.)
- System characteristics (electricity, temperature control, user skill, quality control, waste issues, size, etc.)
- Cost of ownership (purchase, operating, maintenance, etc.)

Technical Likelihood of Success: What RVT Needs to Consider

- Do biomarkers already exist?
- If not:
  - What is the chance that there is a marker at high enough concentration to detect?
- Are there clinical samples available to prove the clinical utility?
- What are the clinical proof issues?
- Does a commercial testing system already exist that would work? (always faster)
- If not:
  - Is someone working on one that can be used in the near future?
  - How will a new system be developed?
- What are the product development hurdles?
- What is the timeline to product introduction?
- How difficult will it be to manufacture?
- From all of this, what are the product specifications?

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Clinical Studies are Critical to Success

- The size of the sample bank is very important
  - Need 50 or more “events” for 1 marker
  - Need 100-250 “events” for 10 markers
  - “Normal” samples should be 2-3X the number of disease samples
- Clinical annotations are often poor
- Samples are often stored improperly
- Enough samples will be needed for research, development and regulatory approval (clinical validation)
- Need to have an untouched cohort for FDA approval
- Acquisition of samples is usually the toughest part of diagnostics research
- You must publish papers that support reimbursement

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Technology Probability of Success

Criteria	Weighting Factor	Score	Definition
Availability of Samples	**3**	**0**	There are no sample banks yet identified and collecting samples will take > 9 months
		1	There are no sample banks yet identified or sample banks exist for discovery only and collecting samples will take < 9 months
		2	Banked samples exist for both discovery and validation and it is likely that we will be able to gain access to them without sacrificing too much
Time to Market	**3**	0	>5 years to initial revenue with high risk
		1	2 - 5 years required for initial revenue with moderate risk
		2	<2 years to initial revenue with a high probability of success
Technological Fit	**3**	**0**	Difficult sample type Other technological approach will likely prevail. Highly complex disease and difficult to collect/interpret data and samples.
		1	Specialized samples required for testing (tissue or CSF). Possible competitive approaches.
		2	Well suited for methodology. Measurement is on accessible sample type (plasma, urine, stool)
Regulatory Hurdles	**2**	**0**	Major regulatory hurdles; long, involved proof of principle and value support
		1	Some regulatory hurdles but achievable within two years of submission
		2	Few regulatory issues; existing diagnostics predicate of sufficient value
Intellectual Property	**1**	0	No or weak patent protection
		1	Patents submitted but not yet issued
		2	Strong patent portfolio; patents already issued; high likelihood of licensing revenue

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Product Design Specification

- Developed by a Product Development Team from the User Requirements
  - Team should have representatives from research, development, manufacturing, engineering, software, quality, regulatory, marketing, and a team leader
- Specifications for all system components
  - Size, color, user interface, composition, materials, number of containers, shipping requirements, storage, labeling, rare reagents, detection system, stability needs, weight, volumes, vendors, software specifications, final costs, etc., etc.
- Trade off of time to market, cost and performance
- Product specification document signed off by entire team, then management
- Complete a budget and project plan

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Phases of Product Development: Research

- Research goals:
  - Academic research goal: discover something new
  - Industrial product research goal: determine the feasibility of a new product concept
- At the end, no new inventions are needed
- Performance is almost good enough
- Risks are identified and acceptable
- Now it's time for development…

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Phases of Product Development: Development

- Development involves:
  - Meeting product specifications
  - Optimization of performance
  - Optimization for manufacturing

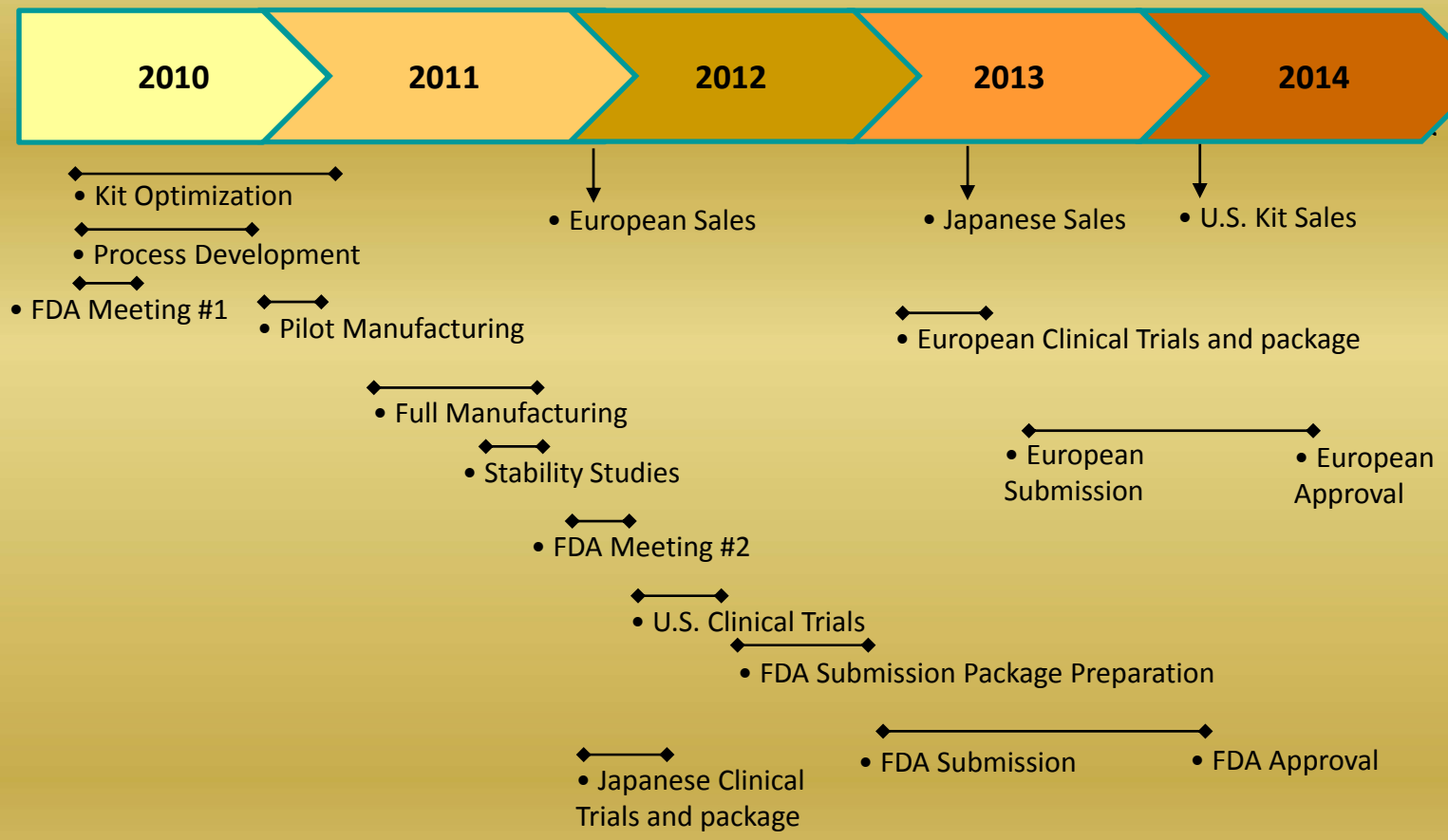
Sometimes these two things are in conflict

  - Prepare for manufacturing…

Phases of Product Development: Manufacturing

- Manufacturing involves:
  - Development of production methods
  - Production
  - Quality Control
  - Shipping
  - Storage
  - Supply chain

Global Diagnostic Company's Activities



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OK, RVT Has a Plan

- Now comes the hard part…making it happen
  - Money
  - The right people
  - Execution of plan
  - Market the product

Creation of New High Impact Diagnostics Products

- Understand the unmet need
- Determine user requirements
- Set product specifications
- Acquire or discover biomarkers
- Find or develop a testing platform
- Demonstrate the required performance
- Develop the commercial test or system
- Seek appropriate approvals
- Educate those who will use it

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What does a new diagnostic opportunity look like?

- Quality of decision is poor today (perhaps it is not made at all)
- Clinical impact is high
- Economic impact is high
- Commercial attractiveness is good
- Technical probability of success is high
- Regulatory path is clear
- Clear definition of customers
- Clear route to payment
- Acceptance is likely in a reasonable time frame
- Freedom to operate (IP)
- Development is affordable
- Organization has a competitive edge
- The investment makes sense

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What are some examples of high impact diagnostics?

- PSA
- Cholesterol
- HIV viral load
- HCV viral load
- Breast cancer prognosis (BRCA, Oncotype Dx)
- Vitamin D testing
- HbA1c
- TB DNA
- Your test here

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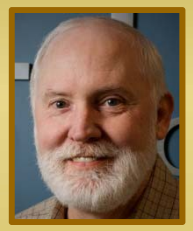

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