Medical Device Development Roadmap

A/Prof Tan Sze Wee
BMRC

Agenda

1. Medical Device Development Roadmap
2. Local Development Roadmap Challenges
3. Financing Requirement
4. Personal Experience
5. Global Healthcare Challenges
6. Summary

A Basic Roadmap

Medical Device Development

From Prototype to Regulatory Approval

Aaron V. Kaplan, MD; Donald S Baim, MD; John J Smith, MD, JD; David A Feigal, MD; Michael Simons, MD; David Jefferys, MD; Thomas J Fogatry, MD; Richard E Kuntz, MD, MSc; Martin B. Leon, MD

Circulation. 2004; 109:3068-3072

Based on the first Dartmouth Drug and Device Development Workshop - Woodstock VT. October 2003

Idea Generation, Invention

Very few new ideas come out of large medical device companies

More typically orginated with *physician* and*/or engineer inventor*

They initiate the patent process

- Provisional (must be converted after 1 year)
- Utility
- International

Build (or commission building) of prototypes

Invention and Development

Small Engineering team

Preliminary bench testing

Build-test-fail-redesign (multiple cycles)

Establish close collaboration with small number of leading physicians in the field

Develop basic market analysis, business plan

Initial Clinical Testing

Design concept frozen

Larger engineering team assembled (10-20)

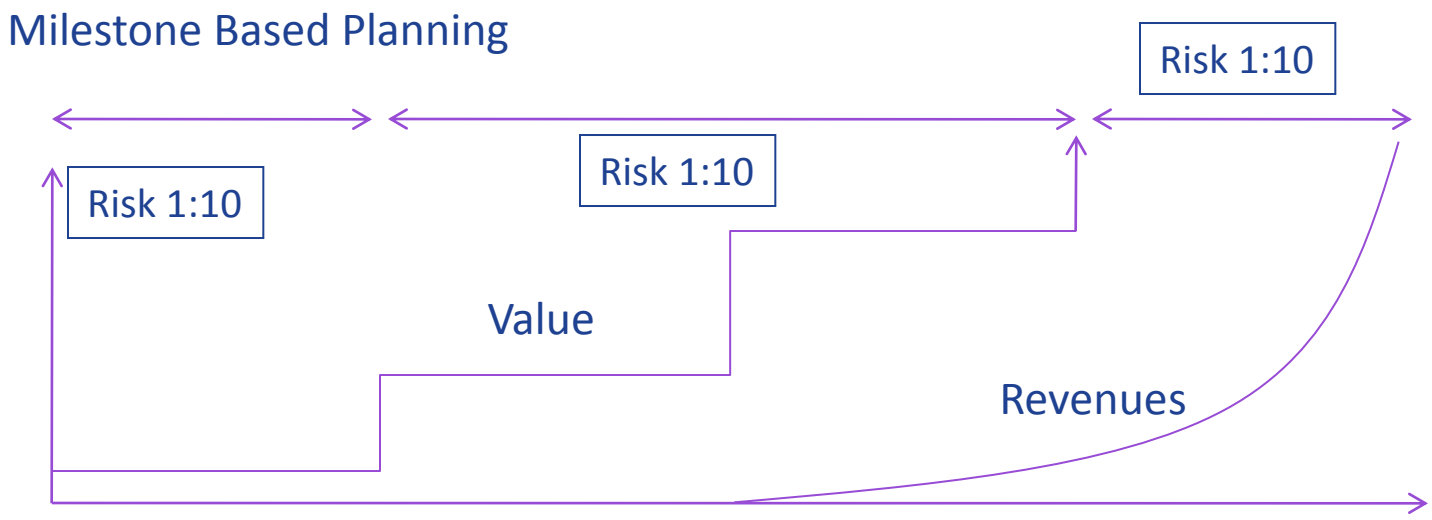
Broader set of GLP tests performed

Clinical and regulatory consultants brought in

Initial *clinical* strategy formulated

- IDE (PMA vs 510k clearance) vs HDE
- Location of FIM and pilot testing (usually OUS) set
- Preliminary discussion of pivotal trial design
  - Superiority vs Non-inferiority, control groups, endpoint

Start-Up Value Creation Process



MILESTONE	Seed CONCEPT 6-12 months	First Round PRODUCT 12-18 months	Second Round REGULATORY 12-36 months	Third Round DISTRIBUTION 12 – 36 months
MANAGEMENT	Project Leader	CEO	CEO w/Full Team	CEO w/Full Team
MARKETING /SALES	Assessment	Market Entry Strategy Define	OUS Distribution Underway	Launch US Distribution
PRODUCT DEVELOPMENT	Proof of Concept	Product Complete	Next Generation Underway	*Major Company Acquisition, Quality work, Commericalisation Risks*
CLINICAL	Thought Leaders Identified	Study Underway	Study Completed	
REGULATORY	Path Outlined	Clear Regulatory Path	FDA Approval	

COMMERCIALISATION OF EARLY STAGE INNOVATION: ENTITIES INVOLVED

Ideation >>> POC >>> POV >>> Early series funding >>>Late series funding >> Exit

1 **Ideation team**

Typically in public sector research performers (PSRPs) including RIs/IHLs, clinical institutes

2 **Early Stage Start ups**

3 **Late stage start ups & SMEs**

Examples:

Project teams within

NUS National University of Singapore

National Heart Centre Singapore

M.E.R.C.I

NANYANG TECHNOLOGICAL UNIVERSITY

SERI

A*STAR SINGAPORE

Singapore General Hospital SingHealth

D.D.O.

amaranth medical

EndoMaster

IVANTIS

CHOCOLATE PTA Balloon Catheter

AIT biotech Advanced • Innovative • Trusted

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COMMERCIALISATION OF EARLY STAGE INNOVATION: EXPERTISE INVOLVED

*Adapted from Biodesign theory

Ideation >>> POC >>> POV >>> Early series funding >>> Late series funding >> Exit

Commercial | Clinical | Productisation

1 Ideation team

Typically in RIs/IHLs, Clinical institutes

Deliverable: Develop business plan and model, project plan and timeline for start up stage
- Start clinical and market validation,
- Conduct IP landscape review and strategy
- Initiate reg & reimbursement, sales & distribution strategy

Deliverable: Identify clinical pathway
- Articulate clinical needs
- Validate clinical needs

Deliverable: Develop working prototype
- Develop working prototype & engineering specs
- Conduct design risk analysis
- Initiate design for manufacturing & QMS strategy

2 Early stage start up

Deliverable: Execute project plan for early stage of biz and fund raising
- Complete clinical and market validation,
- Do fund raising
- Do patent reviews
- Finalise reg & reimbursement strategy
- Finalise sales & distribution strategy

Deliverable: Finalise clinical validation plan, and determine end points
- Assemble Scientific & Medical Advisory Board
- Conduct pre-clinical and clinical coordination work

Deliverable: Reach design freeze stage, (design for manufacturing and assembleability)
- Conduct design risk analysis
- Reiterate working prototypes
- Design for manufacturing processes and engineering
- Begin QMS work

3 Late stage start ups & SMEs

Deliverable: Demonstrate effective biz ramp up
- Do fund raising
- Conduct IP filing & management
- File for reg submission & post-market surveillance
- Pursue & update reimbursement strategy
- Execute product branding, market launch & extend market reach
- Ramp up sales & distribution channels.

Deliverable: Continue clinical validation

Deliverable: Scale up manufacturing & improve product pipeline
- Sustain engineering for existing products and manufacturing processes
- Improve product pipeline
- Update design control & quality audits

COMMERCIALISATION OF EARLY STAGE INNOVATION: JOB FUNCTIONS INVOLVED

Ideation >>> POC >>> POV >>> Early series funding >>> Late series funding >> Exit

Commercial | Clinical | Productisation

1 Ideation team

Typically in RIs/IHLs, Clinical institutes

Deliverable: Develop business plan and model, and project plan and timeline for start up stage

- Project manager (Supported by 1-2 men team)

Deliverable: Identify clinical pathway

(typically outsourced)
- Clinical PI
- Clinical development specialist

Deliverable: Develop working protoype

- Core team of technical/ productization engineers

2 Early Stage Start ups

Deliverable: Execute project plan for early stage of business & fund raising

- Early stage CEO

(Supported by 1-2 men team)

- Fund raising manager
- IP filing & mgmt specialist (typically
- Pricing & Reimbursement specialist (typically outsourced)

* In Singapore: Functions typically done by early stage CEO

Deliverable: Finalise clinical validation plan, and determine end points

(typically outsourced)
- Clinical development specialist
- Clinical trial coordinator

Deliverable: Reach design freeze stage, (design for mfg and assembly)

- Core team of technical/ productization engineers
- QMS specialists (typically outsourced)

3 Late stage start ups & SMEs

Deliverable: Demonstrate effective biz ramp up

- Late stage CEO
- Business Dir to execute reimbursement strategy, pdt branding, & ramp up sales & distribution
- CFO for fund raising

* In Singapore: Functions typically done by one individual

Deliverable: Continue clinical validation

- Clinical development specialist
- Clinical trial coordinator

Deliverable: Scale up manufacturing & improve product pipeline

- QMS specialists
- Core team of technical/ productization engineers
- Manufacturing Operations personnels

PROPOSED INTERVENTIONS:
"QUALITY" OF PROJECT MANAGERS & EARLY STAGE CEOs

THEORY +

EXPERIENCE +

MENTORSHIP

Existing programs such as Singapore-Stanford Biodesign program, NUS LLP

Existing incubators & accelerators as potential receptacles to offer local on-the job training.

Various agencies have their own set of advisors/ expert panels.

Intervention #1

Entrepreneurship Fellowship

Support for candidates to undergo on-the-job training in overseas locations (e.g. leading incubators, start-ups)

Intervention #2

Panel of mentors

Group of local and overseas experts to serve as a common resource to mentor local project managers and early stage CEOs

Typical MedTech Enterprise Funding Model in the U.S

	Pre-Seed	Seed	Early-Stage	Mid-Stage	Growth	Pre-IPO
Class II Devices - US FDA 510(K) Clearance / CE MDD Pathway						
Key Characteristics	•Develop & evaluate prototype •Engineering Specification	•Design verification & validation •Design risk analysis (dFMEA) •Design for manufacturing & assembly (DFMA)	•Clinical validation •Design freeze •Design history file (DHF) completed •Pilot manufacturing	•QMS certification •CE and FDA certification •Manufacturing scaling-up •Form sales team and appoint distributors •Product branding		•Expansion of sales force and distribution network •Reimbursement Success
Round	-	Series A	Series B	Series C	Series D	Series E
~ Quantum	500k – 1mil	< 5mil	5-10mil	10-15mil	20-30mil	30-50mil
Revenue	Pre-Revenue / 1-2mil				<10mil	
Time	Year 1-3		Year 3 - 6		Year 6 - 9	
Valuation	Value less than ~25mil since clinical impact and ability to commercialise or license has not yet been established			Value of ~25 -100mil due to traction in commercialisation and a vision of sustainability, synergy and licensing		Value of ~100mil – 2bil

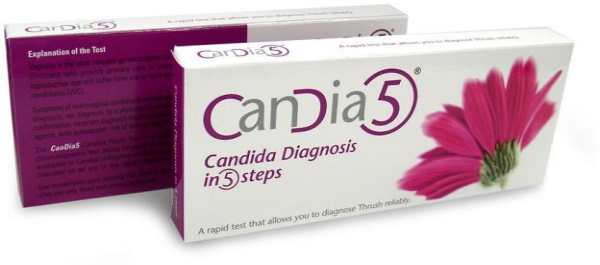
- **Focus on Class II devices (broadest spectrum of devices) where MedTech SMEs can compete.**
- **Class I devices are usually exempted from product registration; and**
- **Class III devices are usually MNCs' play.**

Case Studies: Successful MedTech Companies – Proxy Companies for reference

Company	Description of Business Activities	Regulatory Pathway	First Funding Date	Date of IPO	Total Funding	IPO Market Cap
Cardiac Inc	Proprietary automated anastomotic systems used by Surgeons during coronary artery bypass surgery	510k	1997	2006	50mil	98mil
			~9 yrs to IPO		ROI = X 1.96	
Conor Medsystems Inc	Drug-eluting stents for the treatment of restenosis	510k	2000	2004	78mil	409mil
			~4 yrs to IPO		ROI = X 5.24	
Mircus Endovascular Corporation	Implantable and disposable medical devices for the treatment of cerebral vascular diseases	510k	1996	2005	59mil	151mil
			~9 yrs to IPO		ROI = X 2.56	
SenoRx Inc	Minimally-Invasive devices for the diagnosis and treatment of breast cancer	510k	1998	2007	55mil	123mil
			~9 yrs to IPO		ROI = X 2.24	
Xtent Inc	Customizable Drug-Eluting Stent (DES) systems for the treatment of coronary artery disease	510k	2002	2007	46mil	376mil
			~5 yrs to IPO		ROI = X 8.17	

Sources: Stanford Biodesign, VentureXpert, VentureSource

Personal Experience - CanDia 5



CanDia5 is the World's first and only "point of care" rapid test kit to detect Vulvo Vaginal Candidiasis , commonly known as thrush

The worldwide market is estimated in excess of US$220 million in Ethical and Retail sectors

CanDia5 is CE approval

80% of worldwide IVD sales reside within US, Europe (Top 5) and Japan

CanDia5- Product Positioning

CanDia5® will be promoted as a screening test for VVC during Pregnancy.

- This is because pregnant women are at high risk of developing VVC during their pregnancy (13% prevalence)
- 10-20% of pregnant women are asymptomatic
- VVC during pregnancy is significantly associated with intrauterine growth retardation[1].
- Recent evidence has also shown that screening and treatment of VVC during pregnancy significantly reduces the prevalence of preterm labour[2].

[1] Polk et al. (1989) Association of Chlamydia Trachomatis and Mycoplasma Hominis with Intrauterine Growth Retardation and Preterm Delivery. Am J Epidemiol. 129 (6):1247-1257
[2] Kiss H. et al BMJ 2004, 329:371
[3] Sobel, J.D. (1997). Review Article: Vaginitis, The New England Journal of Medicine, 337(26), 1896-1903.

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CanDia5- Product Positioning

CanDia5® can be used as an accurate test aiding doctors in the diagnosis of Recurrent VVC

- **Most women of reproductive age will suffer from one or more episodes of VVC**
- **Up to 5% of healthy women of reproductive age may suffer from recurrent VVC, which is defined as 4 or more episodes per year[3].**
- **Symptoms of VVC are non-specific and neither self-diagnosis, nor diagnosis by a physician is reliable without laboratory confirmation.**

[1] Polk et al. (1989) Association of Chlamydia Trachomatis and Mycoplasma Hominis with Intrauterine Growth Retardation and Preterm Delivery. Am J Epidemiol. 129 (6):1247-1257
[2] Kiss H. et al BMJ 2004, 329:371
[3] Sobel, J.D. (1997). Review Article: Vaginitis, The New England Journal of Medicine, 337(26), 1896-1903.

Realty : Product Development Challenges

Patenting

Technology Development

Basic Research Discovery

Valley of Death 1

Clinical Trials

Product Design

Regulatory

Product Development

Valley of Death 2

Re-imbursement

Market Creation

Technology Development

Product Development

Commercialization

Healthcare trends

Patient-centric care
- Better health for more people at lower cost

Towards wellness and prevention
- From post-symptomatic diagnosis to pre-symptomatic screening
- Improved access through telehealth

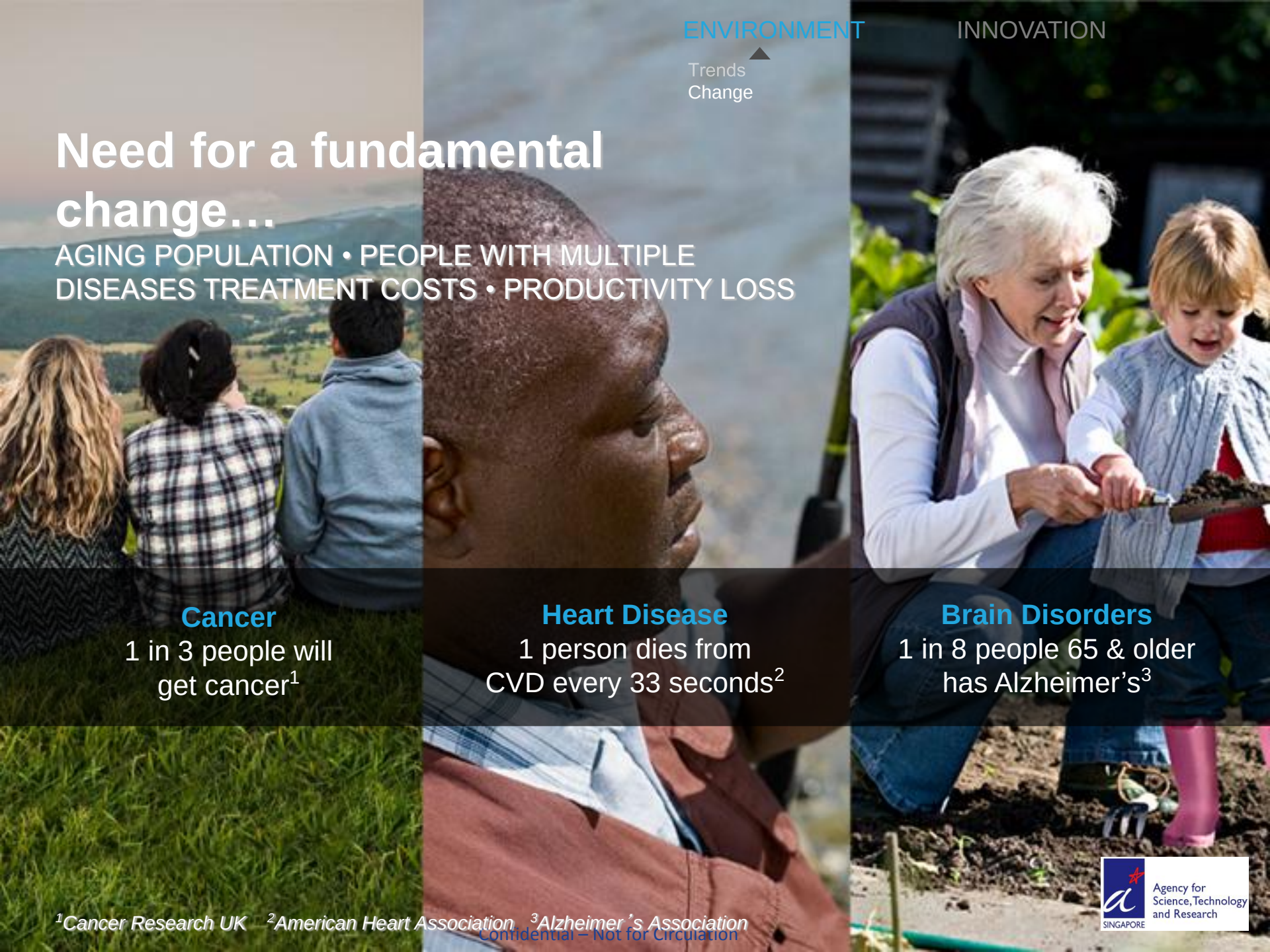
Clinical convergence
- Diagnostic tests (in vivo and in vitro)
- Diagnosis linked to therapy
- Convergence of pharma / diagnostic industries

Productivity and 'cost-out' driven
- Reimbursement pressure on providers

Information driven
- Payors demand rigorous cost/benefit analysis
- Accessible and actionable patient information

Need for a fundamental change…

AGING POPULATION • PEOPLE WITH MULTIPLE DISEASES TREATMENT COSTS • PRODUCTIVITY LOSS



Cancer
1 in 3 people will get cancer[1]

Heart Disease
1 person dies from CVD every 33 seconds[2]

Brain Disorders
1 in 8 people 65 & older has Alzheimer's[3]

[1]*Cancer Research UK* [2]*American Heart Association* [3]*Alzheimer's Association*

Top challenges in developed markets

Drivers and issues




	Revenue	Cost	Quality	Access
USA	Declining revenues and shift from fee for service to Population Health Management, accountable care	More insured and aging population/ chronic disease on rise	Care is not coordinated and fragmented. Seamless IT/digital requirements escalate	Shortage of Primary care and other specialties. Multidisciplinary teams form
Nordics	Constrained by limited availability of public funds	Cost containment thru increased efficiency of resources	Incentives to better integrate different levels of care and IT requirements increase	Reforms to increase accessibility

Reference: Nordic Health Care Systems Recent Reform & Current Policy Challenges – WHO 2009 on behalf of European Observatory on Health Systems & Policies Health Innovation in the Nordic Countries – Nordic Council of Ministers, Copenhagen 2010
American College of Healthcare Executives (ACHE) Top Issues Confronting US Hospitals: Jan 2012
HIMSS Leadership Survey, Senior IT Executive Results, February 21, 2012

Top challenges in emerging markets

Drivers and issues




	Revenue	Cost	Quality	Access
Brazil	Growing private, state/fed health insurance, medical tourism: 28% CAGR	Critical need to update/expand HC technology & infrastructure	26 states & one federal district with varying economics and regulations	Access is improving, demand increasing with need for staff, technology, IT
India	Inefficiencies limit patient throughput and revenue, driving high prices	Patients spend significant portion of income on private healthcare for advanced disease	Informatics, analytics solutions for population management	Expansion of small-to mid size hospitals, care centers , provider training
Middle East	Need regulatory, informatics, payment framework for private sector $, private insurance	Rapidly increasing costs due to exploding volume of expensive chronic patients	Lack of skilled providers at all levels; High turnover rate due to expats	Lack capacity to provide services to rapidly increasing multi-/complex chronic disease patients

Reference: E. Mediterranean Health J "Need for Building capacity to prevent chronic diseases in North Africa and The Middle East"; Booz & co "Getting a handle on Chronic Disease Health Management Services in the GCC Region"; Harvard J. of Middle East politics & Policy "Emerging trends in Middle Eastern Health Policy"

Reference: Pan American Health Organization/World Health Organization "Health Situation in the Americas. Basic Indicators 2012"
Frost & Sullivan – "Healthcare Growth Opportunities in Brazil ",Aug 2012

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Questions:

- Would a device designed & manufactured in Singapore be applicable to the rest of the world?
- If not, where do we develop local products?
- How do we develop local products?
- Will local products have utilization elsewhere?

Summary

- Medical Device Development is a long journey
- Starting with focusing on medical needs, but also need to understand market demand
- Challenges in commericalization talent and financing
- Need strategic locations for product definition, development, and commercialization
- Products developed in one location can be applicable to many other locations