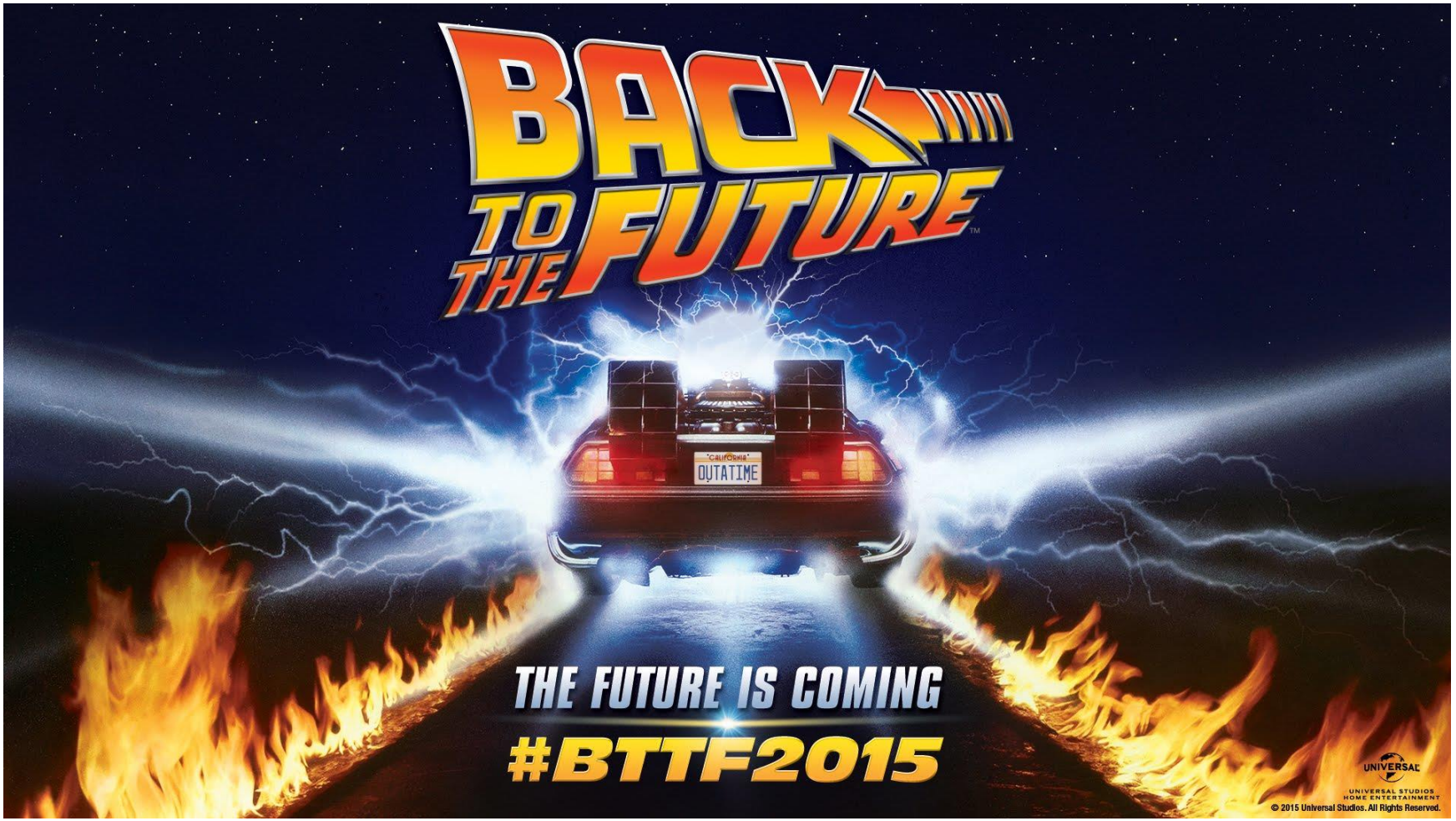
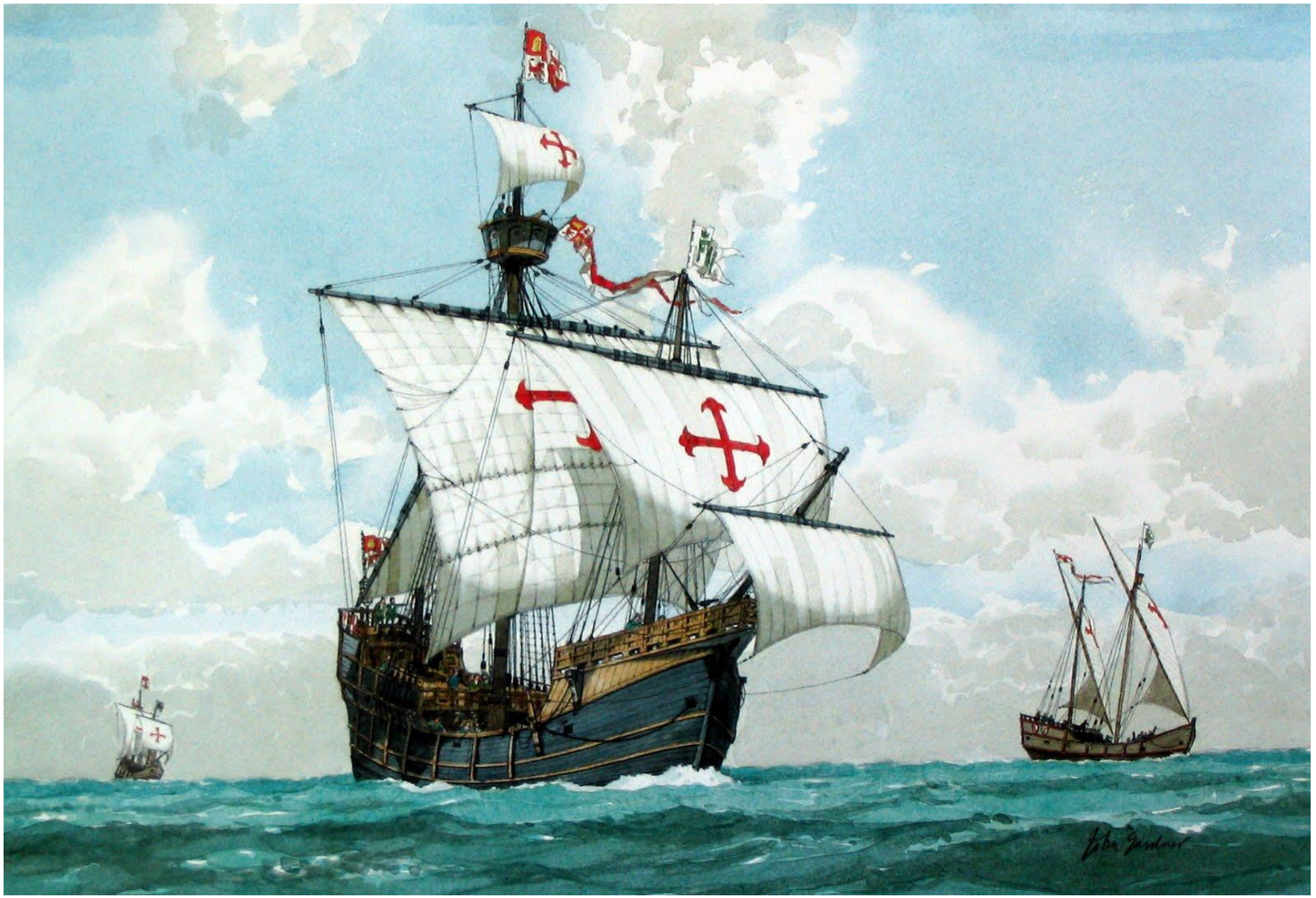


Marty McFly & Dr. Emmett Brown

Geniale geest en ondernemer

Pionieren

America



Mars

Geniale geest en ondernemer

Integratie van Kennis

- Universiteiten
- Gildes in de Gouden Eeuw
- Kamerlingh-Onnes (“door meten tot weten”)
- Pressure cooker

The quest!

“Je gaat het pas zien als je het door hebt!”

Q & A

- Jack is looking at Ann, but Ann is looking at George. Jack is married, but George is not.
- Is a married person looking at an unmarried person?

- A: yes
- B: No
- C: can not be determined

Q & A

- Jack is looking at Ann, but Ann is looking at George. Jack is married, but George is not.
- Is a married person looking at an unmarried person?

- **A: yes**
- B: No
- C: can not be determined

Solution

Jack	Ann	George
married	???	Not married

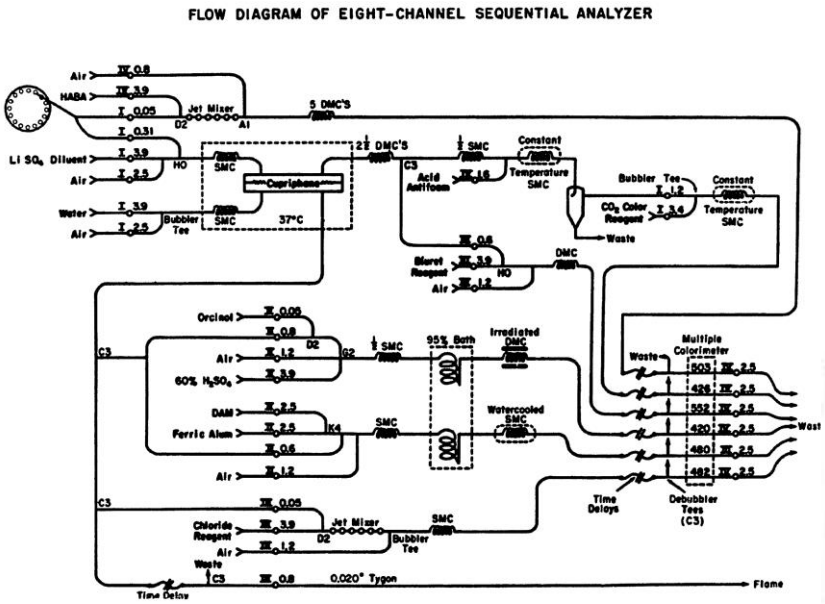
Optie 1: Not married

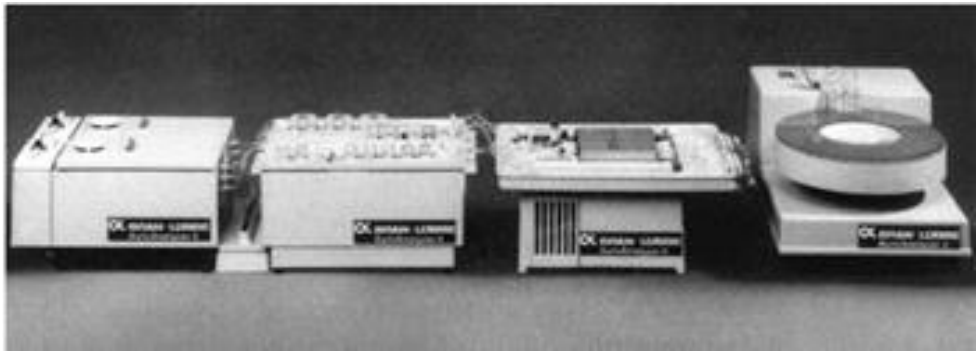
Optie 2: married

Pionieren

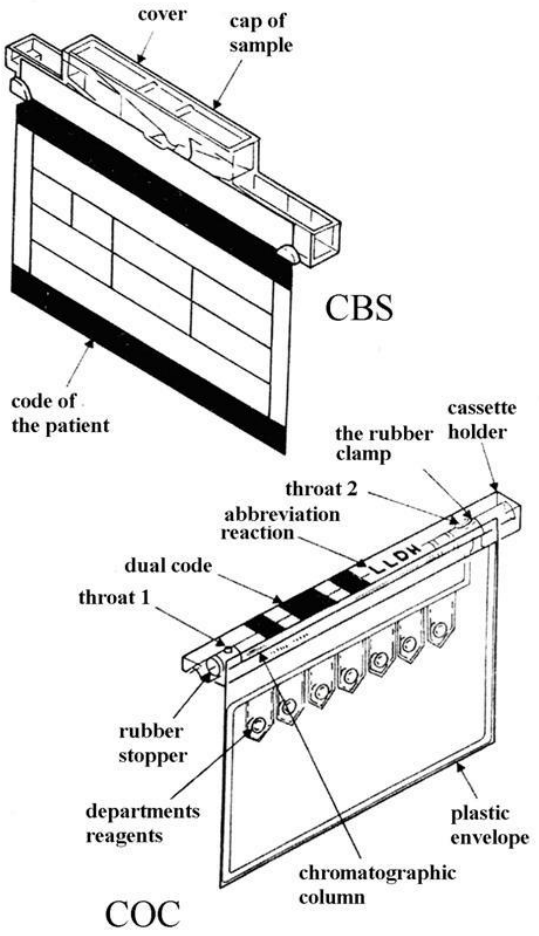
- Enkelvoudige reacties
  - Fehling, Bang, Fredrikson, Abell-Kendall, Lieberman-Burchard, Jaffé, Zijlstra-Van Kampen
- Technieken
  - Simultanous determinations, continuous flow, impedantie meting
- Ontwikkeling van nieuwe vakgebieden
  - (organische) chemie, biochemie, (patho-)fysiologie
- Automatiseren, computeriseren
  - Astra (B), Cobas-Bio (R), Ektachem (K), SMAC (T)

Technicon Autoanalyzers

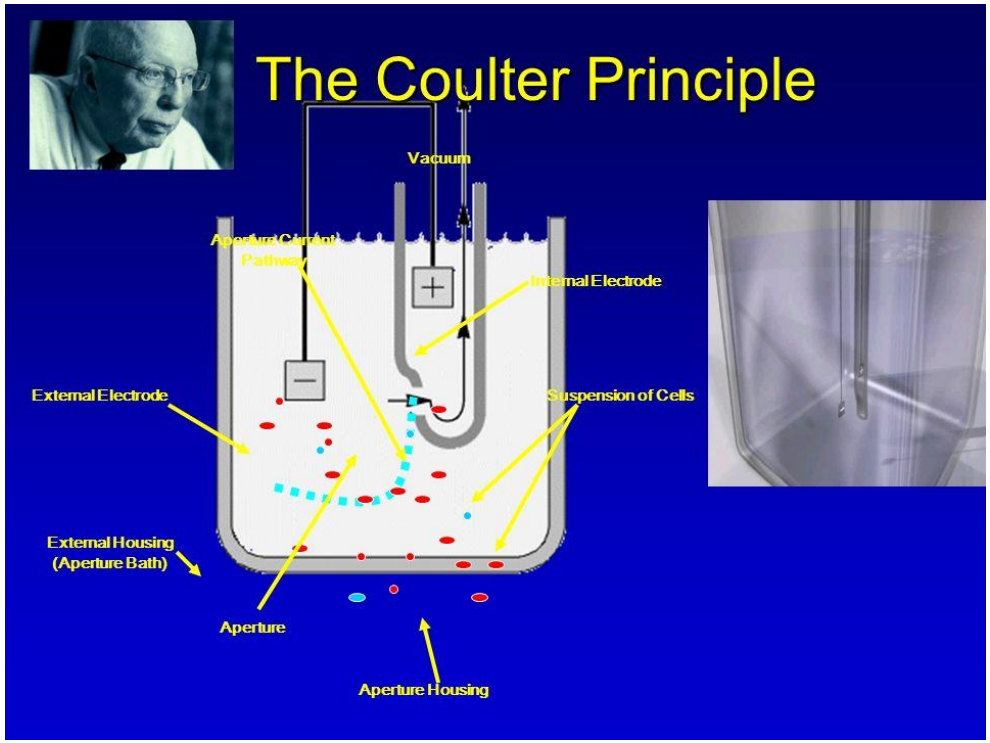


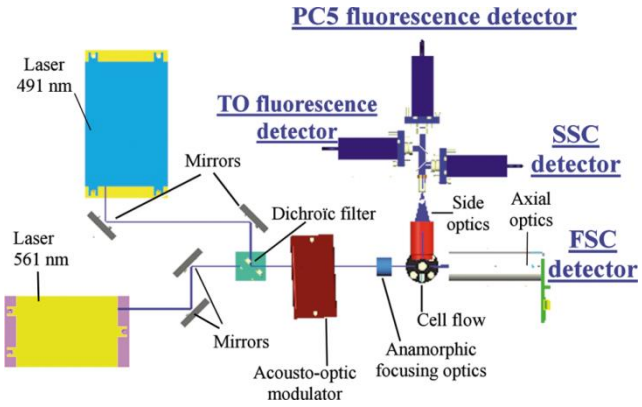


ACA DuPont

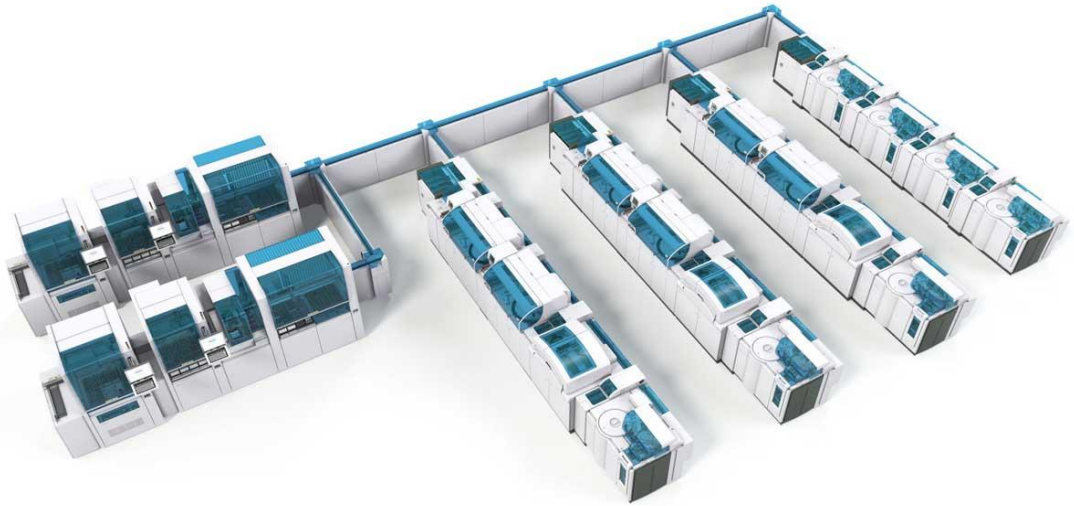

cover
cap of sample
CBS
code of the patient
cassette holder
the rubber clamp
throat 2
abbreviation reaction
dual code
throat 1
rubber stopper
departments reagents
plastic envelope
chromatographic column
COC

Hematologie





Random Access/consolidatie



Step by Step

- Enkelvoudige testen: reageerbuis
- Mechanisering: de schroevendraaier
- Automatisering: QC-plotjes
- Consolidering: service engineer
- Systeem kwaliteit: RvA, ISO 18159

Nieuwe pioniersfase

thuis

Ziekenhuisverplaatste zorg

zelfzorg

Hulp

Self management

Nieuwe pioniersfase

Ziekenhuisverplaatste zorg

zelfzorg

thuis

Self management

ketenondersteuning

main frame
centraal
inrichting
ICT
ZIS

POCT/POS
op locatie
logistiek
dataverkeer
KIS

Nieuwe pioniersfase

Sturing?

- Vraag
  - Patient
  - Client
- Overheid
- Zorgverzekeraar
- Technologie (diagnostiek)
- Technologie (care cure)
- Technologie (IT)

POC in 2025!

If you think you are in control, you don’t go fast enough!

(Mario Andretti)

ISALA LABORATORY

HbA1c

European Reference Laboratory (**ERL**):

Gold Standard HbA1c

IFCC-network Laboratories for standardization of HbA1c
IFCC Integrated Project (Implementation & Education)

POCT

Reference Laboratory for POCT

All Major Diagnostic Manufacturers
EFLM Workinggroup for POCT

DIABETES/CARDIOLOGY/POC

Glucose

Reference Laboratory for Glucose Meters

ISO workinggroup TC 212
IFCC Workinggroup for glucose meters in IC
International Diabetes Education (**IDE**) Center
TUV Rheinland **Certification** Glucose Meters

Economic Modelling

Decision Group: Committee Implementation

Economic modeling and decisions

in health care
(Boston University, Washington University Nijerode,
Geneva University, Isala)

Content

- Changes in Healthcare
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10 Prospects

1. Individualized reference values
2. Satellite connection diagnostics
3. Authentication/Telemedicine
4. Artificial Intelligence
5. Decision Support Software
6. Risk profiling
7. Screening
8. Preventive testing
9. Non-invasive testing
10. Mindset testing/Behaviour change

Point-of-care Testen

POCT

- Bed-side test
- Near patient
- Mobile, handheld or smaller
- *Professionals: 1 device, more patients, monitoring*

Home-use Testing

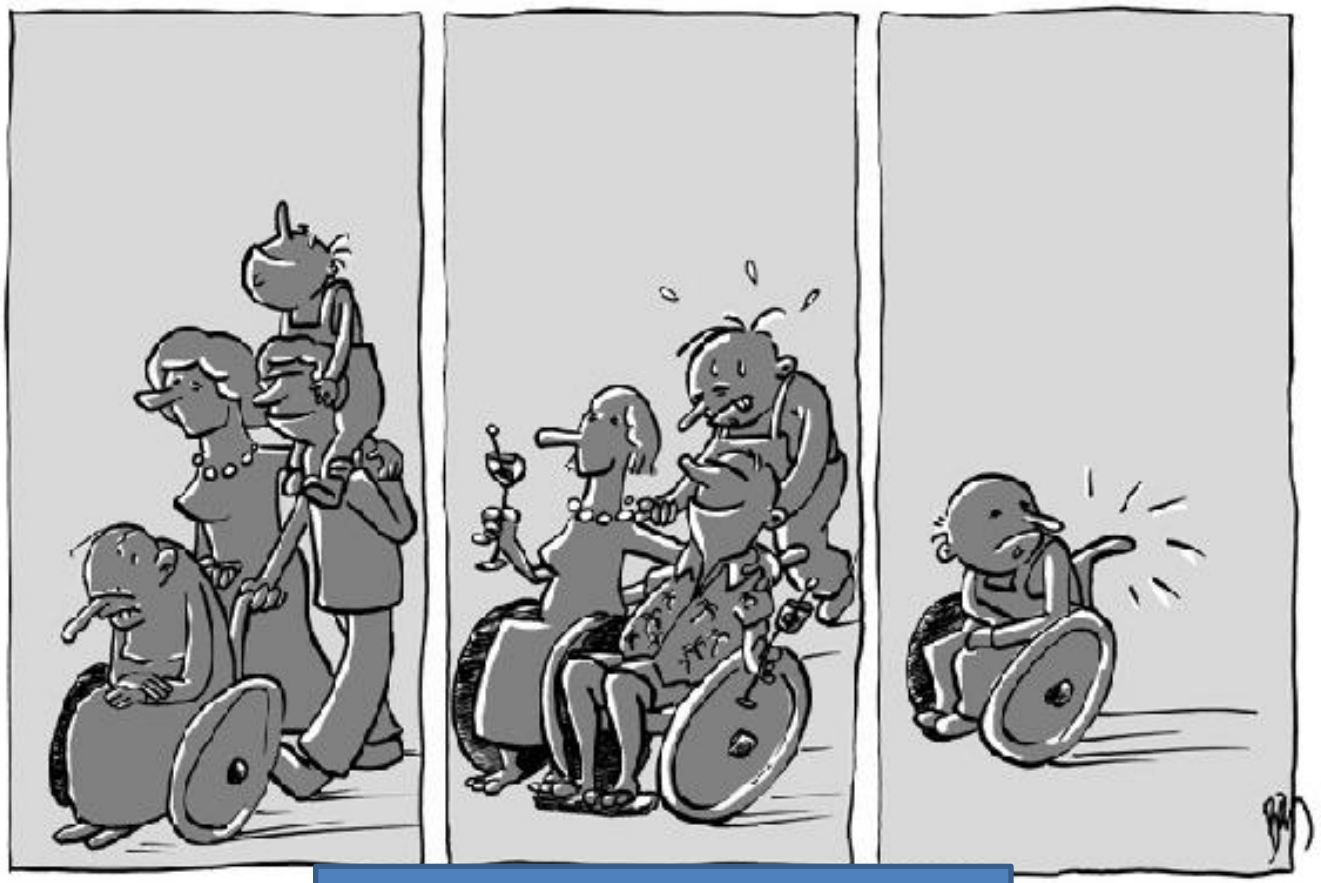
- *Patients: 1 device, 1 patient, monitoring*

Preventive Medical Testing

- *Clients, Professionals, Commercial Parties:*

  1 device, 1 or more clients, monitoring and diagnosis

Certainties

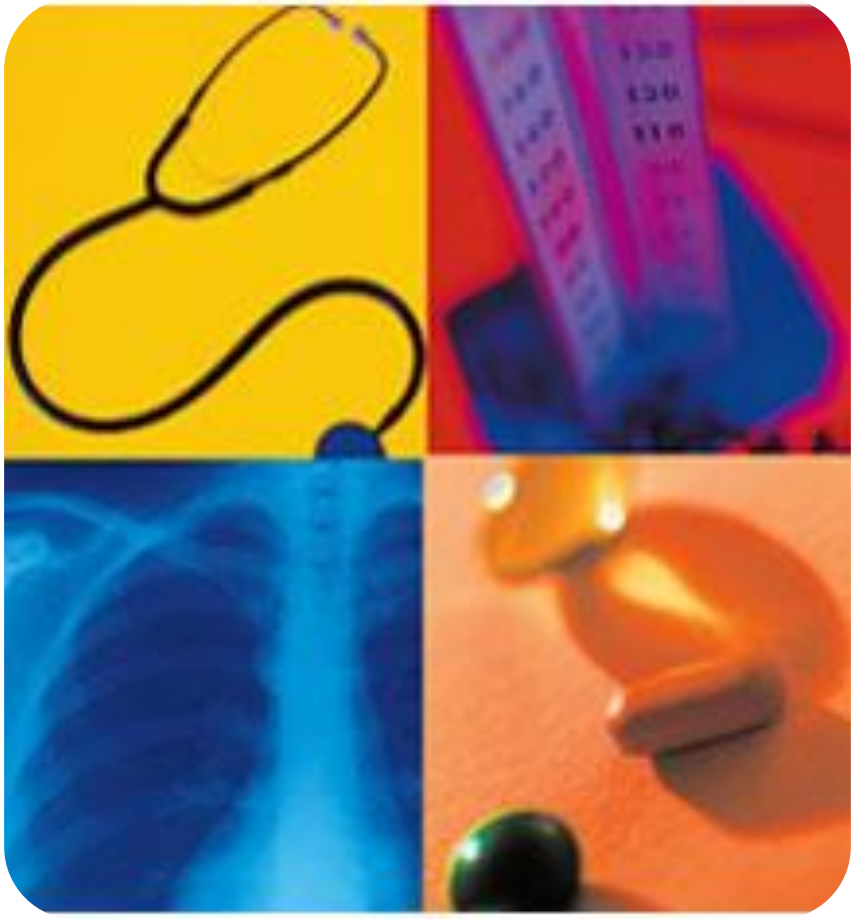


Demography

Uncertainties

Who pushes healthcare changes?

Professional/Insurance Companies or patient?



Uncertainties

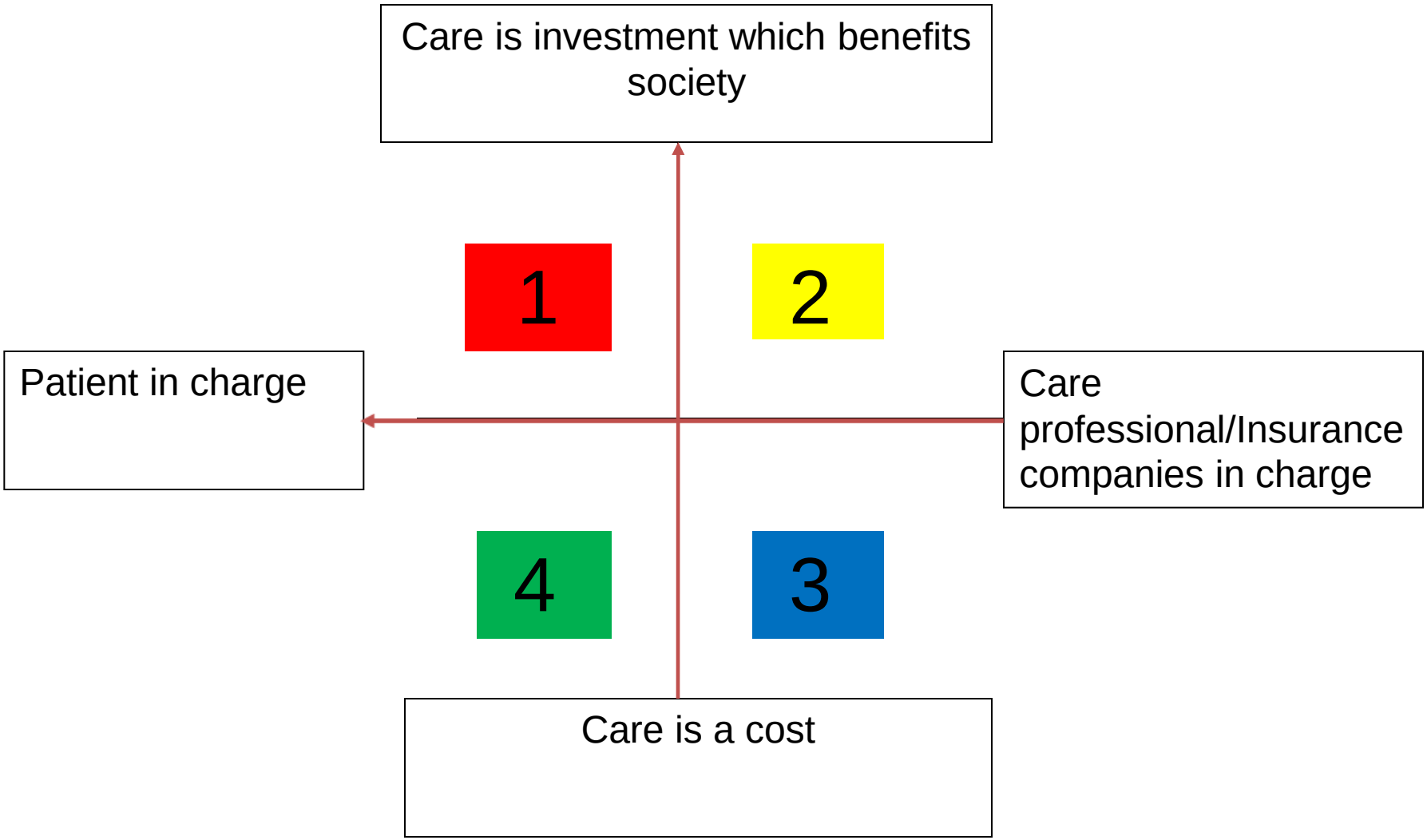
How do we think about healthcare in the future?

Is healthcare only a cost or provides it also benefits to society?

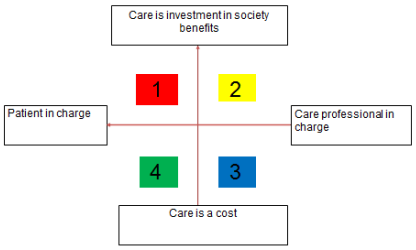
Uncertainties and tensions

Patiënt empowerment or professional in charge

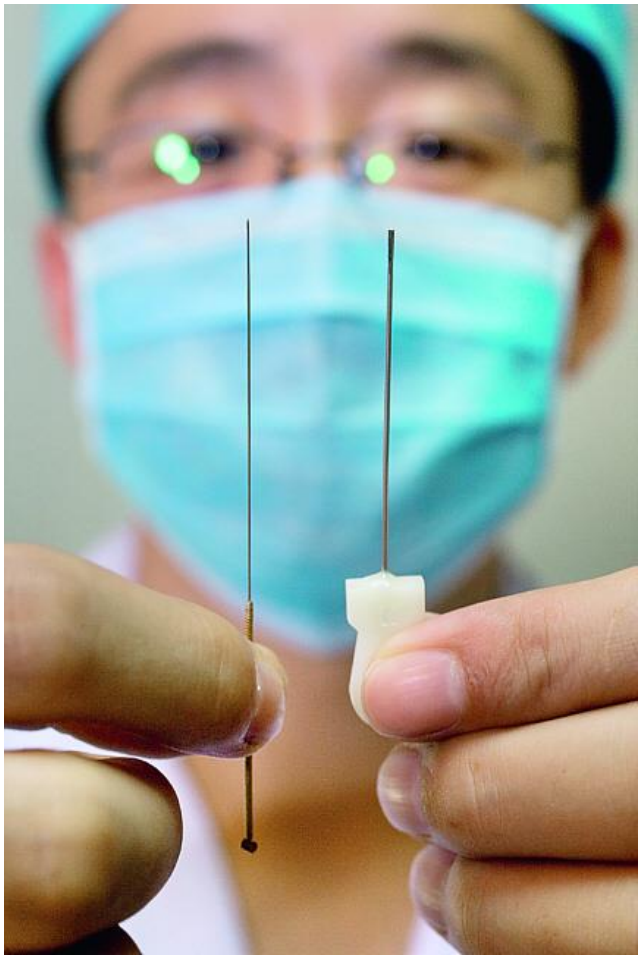
Care is a cost or an investment with benefits for society


Care is investment which benefits society
1
2
Patient in charge
Care professional/Insurance companies in charge
4
3
Care is a cost

Kind of blue

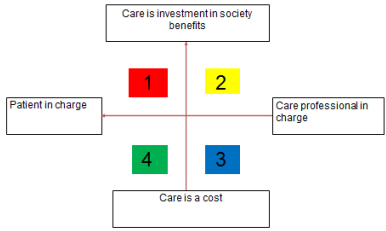


- Care will be limited to medical and nurse services (Central lab out of hospital → POCT)
- Limit pull by patients; limit access for new patients (POCT)
- Focus professional handling: medical evidence based at minimum quality standard (POCT)



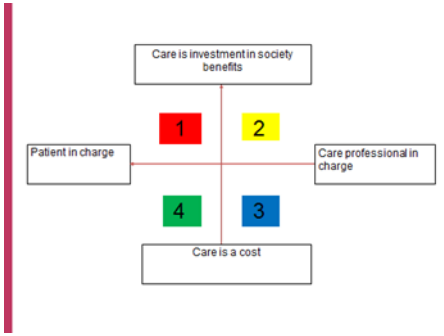
Slingerland, Dubrovnick, 2013

In the yellow pages



- Professionals care services:high patient health benefit / quick commencement of labor
  POCT/Home-use testing
- Focus handlings: preventing relaps and permanent malfunction in other life domains
  Home-use testing

Get ready for red



- Patients search services for quality of live (balancing work, education, family live, participation in society) Home-use testing
- Focus professional: fast access and services to other sectors
- Innovations: support healthy and unhealty citizens in participation in society 24/7, health and behaviour Home-use testing

Evergreens

- Care limited to medical and nurse services
  (Central lab out of hospital → POCT)
- Focus professional: maximize therapy adherence (POCT/Home-use testing)
- Cut back overhead costs and costs of care providers. More patiënts served for less costs (POCT/Home-use testing)

Home-use testing to improve quality of life

	Traditional	*Home-use testing*
Analysis:	> 1 hour	few minutes
Where:	Hospital	Home
Hardware:	Complex	KISS
User:	Highly educated	Patient
Sample:	Tube of blood (Serum)	1 droplet of blood
Patient Empowerment:	No	Yes

Slingerland, Dubrovnick, 2013

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POCT/home-use Testing

POCT (**Cost**/Professional)

- Diabetes (glucose/HbA1c)
- MI (troponins)
- Heart failure (pro)BNP
- Kidney function (creatinin)
- Bipolar disorders: monitoring toxicity (Lithium)
- Anti-coag monitoring (INR, D-dimer)
- Hypertension (Salt balance)
- Other diagnostics (total cholesterol, HDL-chol etc.)

Home-use Testing (**Wellness**/Patient)

- Diabetes
- Heart failure monitoring
- Kidney monitoring (creatinin)
- Anti-coag monitoring (INR)
- Hypertension (Salt balance)
- Other compendium diagnostics (total cholesterol, HDL-chol etc.)

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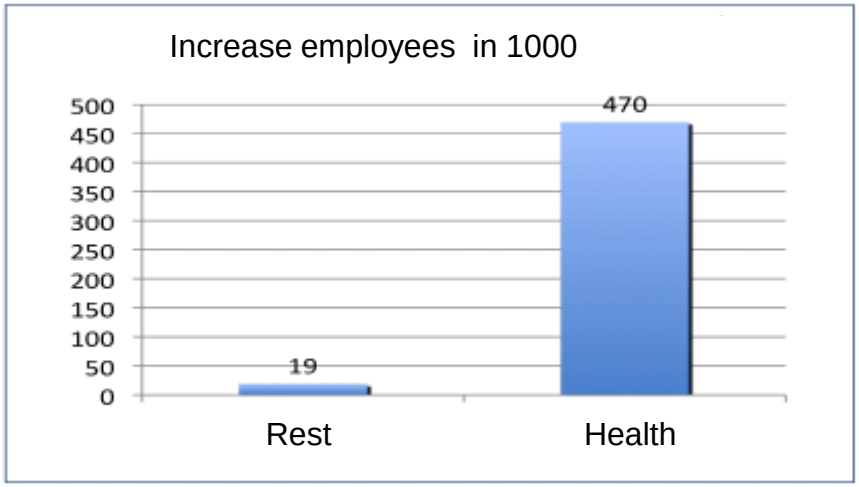
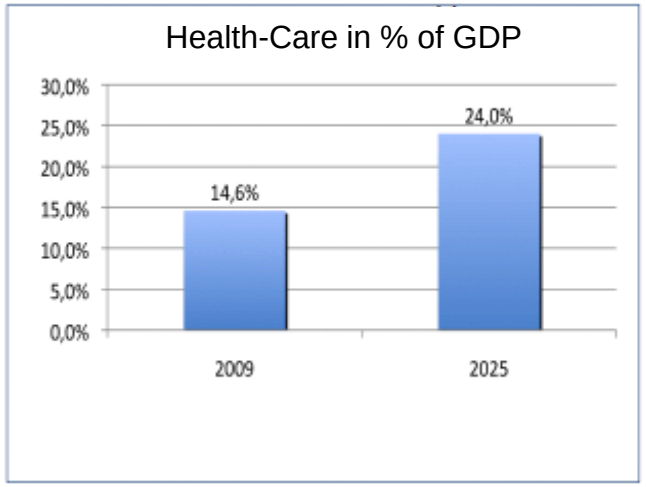
Changes health-care market

- Diabetes and other chronic diseases increase
- Hospital → GP→ patient
- Financial transparancy
- Competitor market
- Raise of costs

More Health-Care People Needed!





- In 2025 60% increase health-care employees
- Raise tax or increase self-contribution!
- Do we have these employees?

Hopeless Health Care?

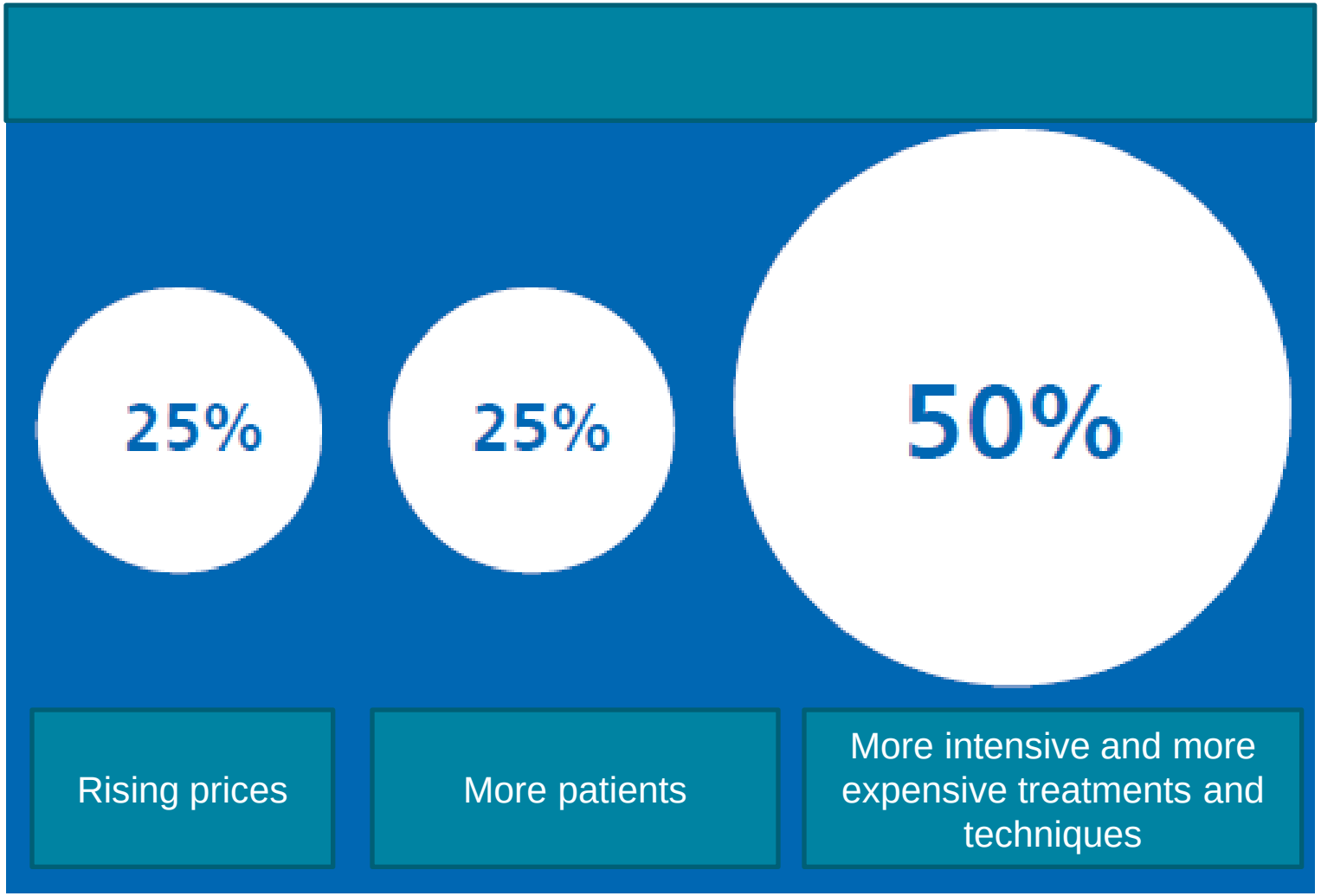
- Unhealthy habits: food, alcohol, smoking*
- Insufficient prevention + perverse incentives leading to fragmented health-care**
- Marginal increase productivity in health care***
- Coronairy disease, stroke, heart fail[illegible] diabetes

- ** RIVM, van gezond naar beter, 2010*
- *** gemeten naar verloren levensjaren, RIVM, van gezond naar beter, 2010*
- ****Probleemanalyse Innovatie in de zorg , Innovatie Platform en departementen, 2008, eigen analyse*

More Granny's!

- Number elderly increase fast
- Diseases associated too!

Causes of cost increases in curative specialistic care



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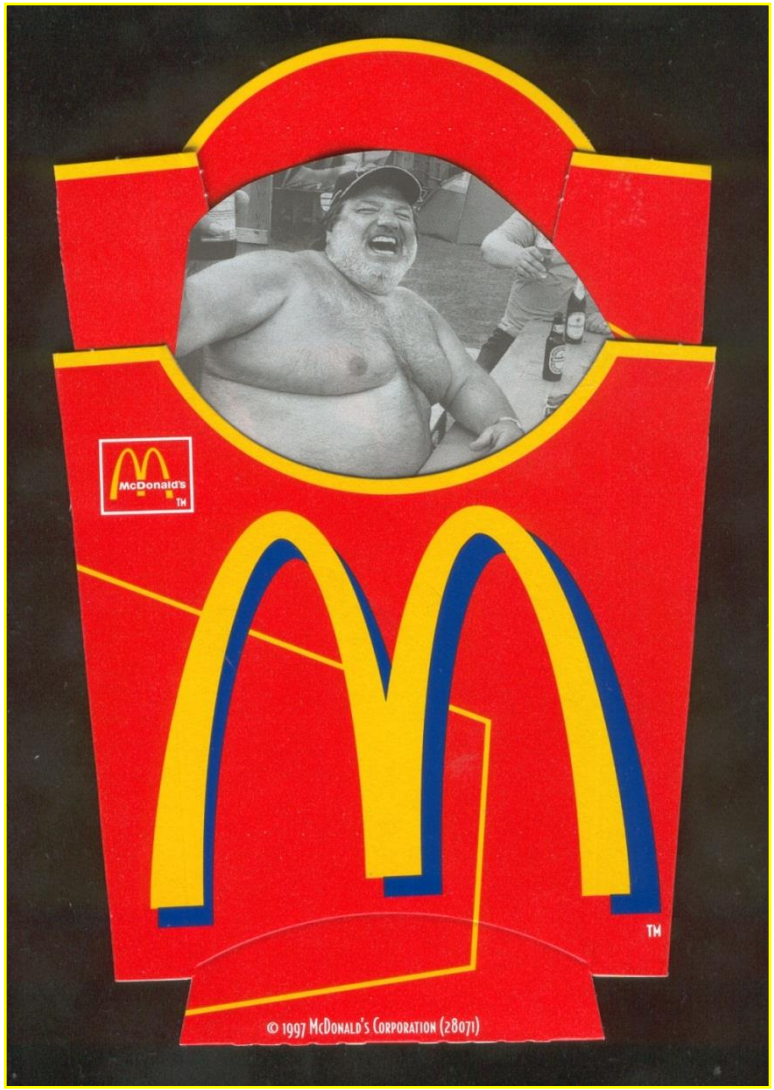
Hopeless Health Care?

- Eat more
- Exercise less
- Grow fatter
- Diabetes (II) and CVR increases dramatically
- Need efficient diagnosis
- Need efficient therapy



Redefine Health Care?

- Cost
- Demographics
- Access
- Variation in Clinical Practice
- Inefficient use of Information
  - Data-Management/Loss of Data
  - No Translating Data in Health Information
  - Inefficient Warning Signals
  - Insufficient Integrated Care
  - No Use of Artificial Intelligence to combine data
  - Insufficient Risk Profiling

From Past to Future

- 80’s Building Computers
- 90’s Network Computing
- 00’s Internet, Social Media
- 10’s Connecting Everywhere
- 20’s From Cure To Well Being and prevention?

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Changes

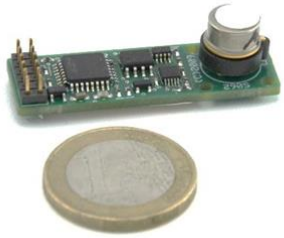
- Genomics, Proteomics, Metabolomics
  (prices have dropped dramatically)
- Mobile Diagnostics
- Digitalization of Information
- High Speed Microfluidics (Lab-on-a-chip)
- Personal Care everywhere
- Who-owns-data debate
- Artificial Intelligence (Smart Diagnostics; computer power doubles every 18 months!)
- Connected Health Information


A Step Closer
There is only so much one can see.
Discover more from a different point of view

Changes in Diagnostics

- Diagnostics move closer to or into patient!
- POCT, POST or In-Patient Testing (IPT)
- Non-invasive Diagnostics
- Multi-purpose POCT
- Tele-diagnostics
- Nano-scale

Electronic-nose



- Dysruptive technology
- Non invasive
- Pattern recognition instead of Biomarkers
- Self learning system in case of internet based screening (Artificial Intelligence)

- TBC
- Cow mastitis
- Head/Neck tumor
- COPD/Asthma

The eNose company

WWW.ENOSE.NL

Glucotrack

- Ultrasound, electromagnetic, and thermal technologies to obtain blood glucose readings

Integrity Applications, an Israeli company

Non-invasive Diagnostic POCT (*Pendragon*)

Slingerland, 21st centennial diagnostixs, 2011

Non-invasive glucometers

Paralia
Interim & Consultancy Health

Expert in medische laboratoria

Home | Diensten | Expertise | Contact | Nieuws | Links | Voorwaarden

Volg Paralia op:

C8 MediSensors brengt eerste non-invasieve glucosemeter naar Europa

C8 MediSensors focust zich op glucose monitoring. Voor ernstige diabetici is het noodzakelijk om vaak de glucosewaarde te meten. Tot op heden gaat dit met zogenaamde invasieve glucosemeters, meters die werken door middel van een naald. C8 MediSensors heeft zich tot doel gesteld om een non-invasieve meter te ontwikkelen. Hiervoor heeft men een meter ontwikkeld, welke op basis van licht in staat is om door de huid de glucosemoleculen te meten. Men maakt daarbij gebruik van het zg. Raman-spectrum van de glucosemolecuul. Het systeem wordt via een band gedragen op het middel. Uitlezen van het systeem gaat door middel van de mobiele telefoon.

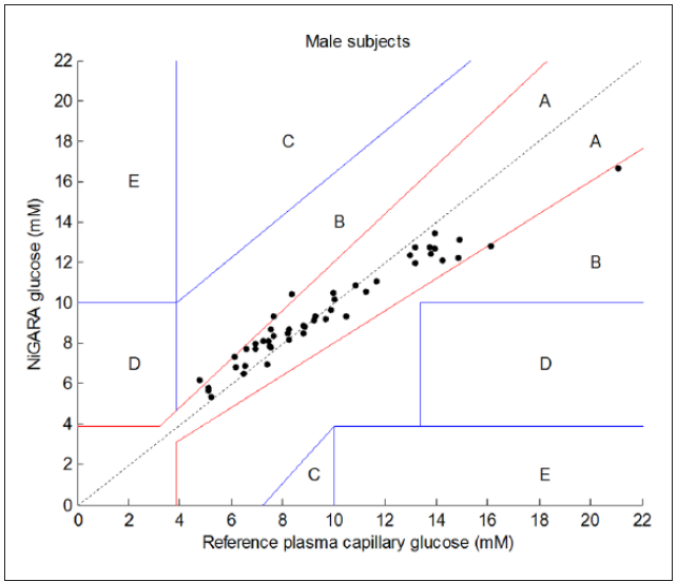
De "C8 MediSensors Optical Glucose MonitorTM" System is eind oktober 2012 CE-gemarkeerd. In 2012 is voor $24 miljoen aan preferente aandelen uitgegeven om verdere financiering van de uitrol mogelijk te maken. Het "healtymagination Fund" van GE is een van de majeure financiers.

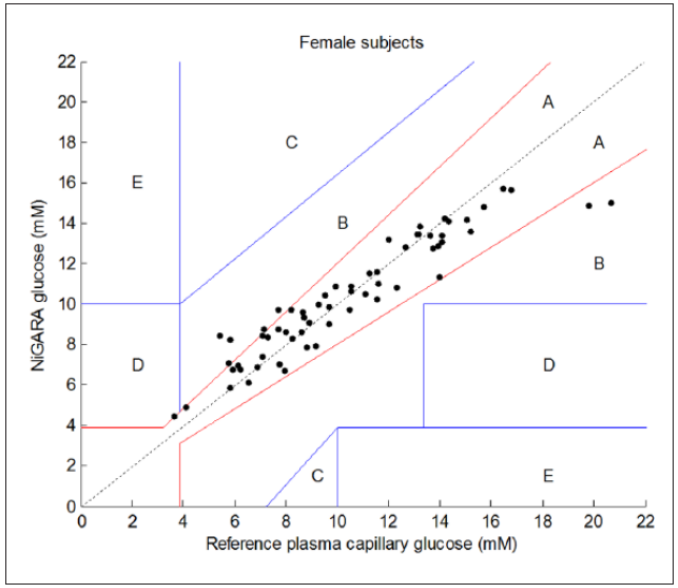
Een verbeterpunt is met name nog de levensduur van de batterij. Het systeem kost $4.000 en wordt alleen via de website van C8 MediSensors verkocht. Nu reserveren is al mogelijk.

Zie verder de website van C8 MediSensor: www.c8medisensors.com

Noninvasive glucose assessment by Raman spectroscopic analysis (NiGARA)

In 2013, worldwide, approximately 382 million people suffered from diabetes, and that figure is estimated to increase to 592 million in 2035 (+55%).[1] It is estimated that approximately $548 billion euro is currently spent on managing diabetes, which is 11% of total health expense.

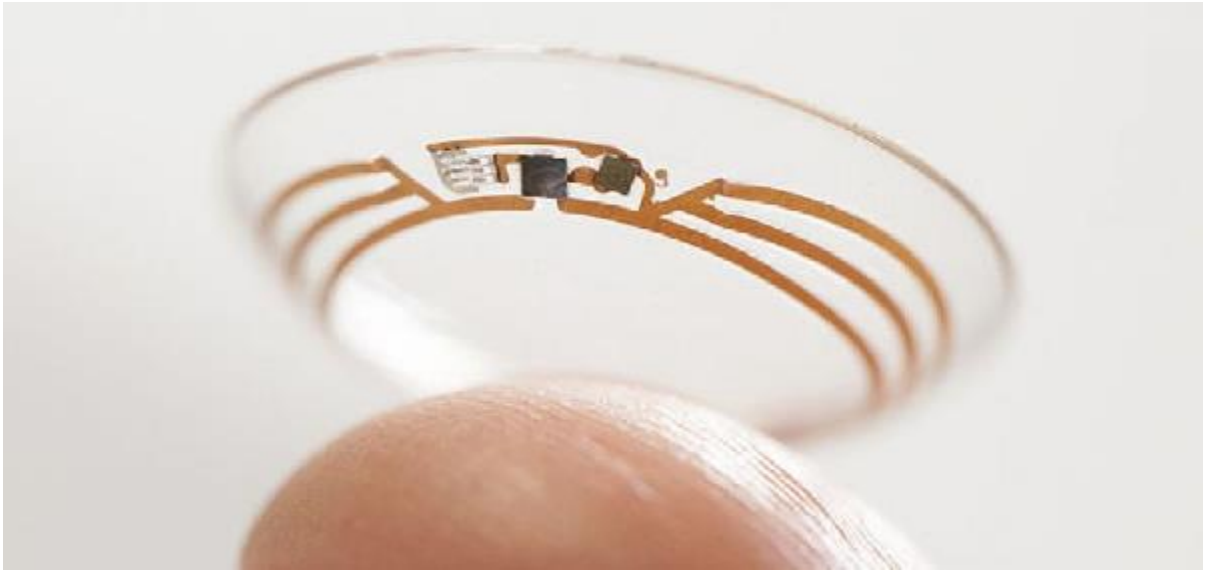




Journal of Diabetes Science and Technology 2014

Non-invasive glucometers

Non-invasive glucometers



Smart contact-lens (Google/Novartis): glucose in tear fluid

Non-invasive Bilirubin

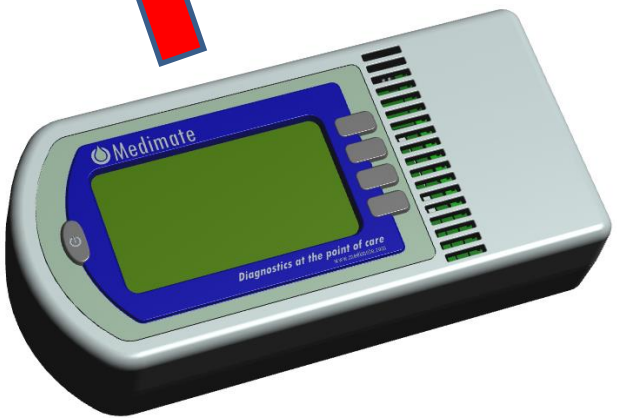
Medical testing near the patient

Daniel Kraft, 2011

Multipurpose POCT instruments

Hypertension

Kidney Failure



Bipolaire disorder

Heartfailure

Health Care asks Industry for Development

- POC Hs-Troponin

famous triage

fast **a**ssessment and **m**anagement of chest pain
with**ou**t **st**-elevation in **t**he pr**e**-hospit**a**l **g**ate**w**ay

Developments

History (anamnesis)	Highly suspicious	2	
	Moderately suspicious	1	
	Slightly suspicious	0	
ECG	Significant ST-deviation	2	
	Non specific rep disturbance / LBTB / PM	1	
	Normal	0	
Age	≥ 65 year	2	
	45 – 65 year	1	
	≤ 45 year	0	
Risk factors	≥ 3 risk factors *or* treated atherosclerosis	2	
	1 or 2 risk factors	1	
	No risk factors known	0	
Troponin	≥ 3x normal limit	2	
	1-3x normal limit	1	
	≤ normal limit	0	
		Total	

HEART	MACE/n	% pts	Risico	Beleid
0-3	3/303	34%	0.99%	Ontslag; geen vervolg
4-6	48/413	47%	11.6%	Observatie en ischemie-detectie
7-10	107/164	19%	65.2%	Observatie en CAG

Zwolle

- Pre-hospital ACS modified-HEART score, (T = hs-cTnT): safe home
- Prospectieve observational cohort study (n=1250)

Results

	Modified-HEART		
	0-3	4-6	7-10
Aantal patiënten (%)	182 (38%)	206 (42%)	92 (19%)
ACS (%)	0 (0%)	48 (23%)	55 (59%)
MACE 30 days (%)	0 (0%)	48 (23%)	64 (69%)
Hs-cTnT (≤0.014 ng/mL)	182 (100%)	123 (60%)	16 (17%)

POC Hs-Troponin

- We ask now industry
- Not industry brings a new toy
- A reversed process

Changes in Diagnostics

- Diagnostics move closer to or into patient!
- POCT, POST or In-Patient Testing (IPT)
- Non-invasive Diagnostics
- Multi-purpose POCT
- Tele-diagnostics
- Nano-scale

Authentication

More safety needed!

'you say who you are' (identification)

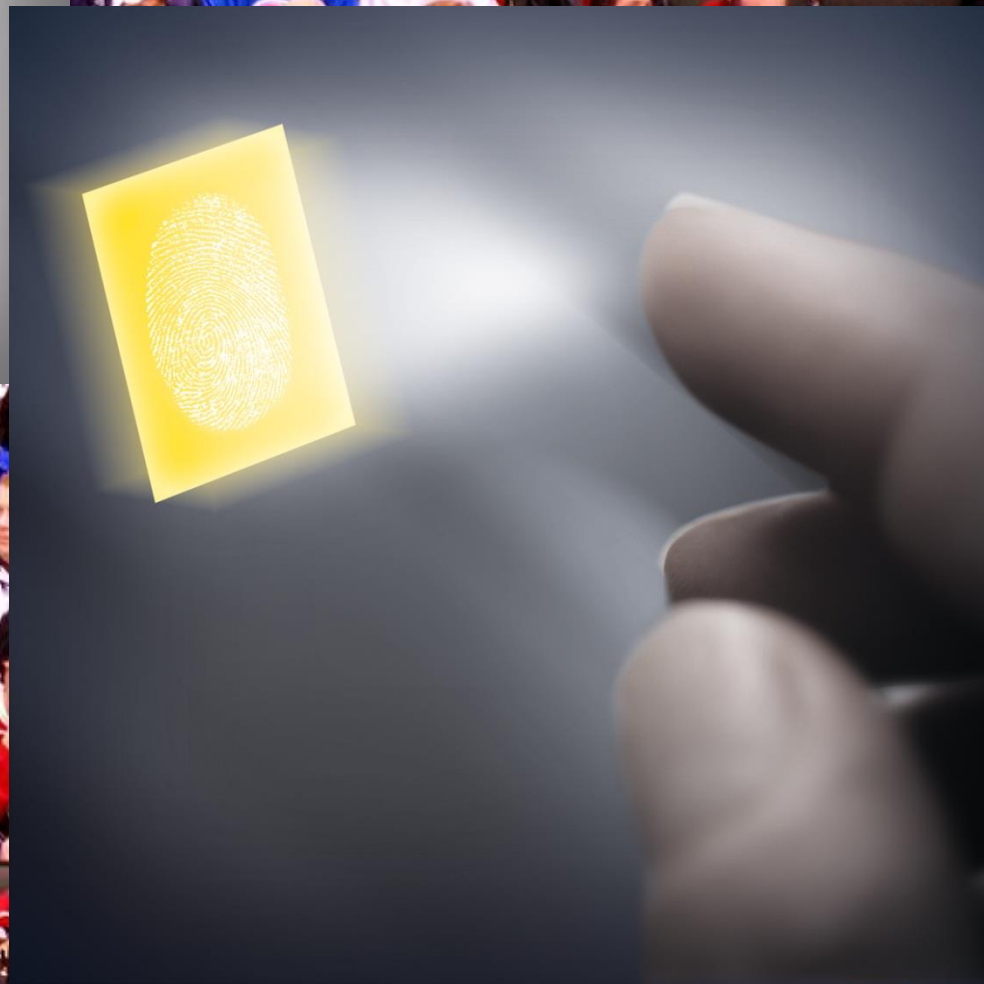
↓

'you prove who you are' (authentication)

Less credentials on digital highway!

improve the privacy, security, and convenience of online transactions!

Can’t remember passwords!



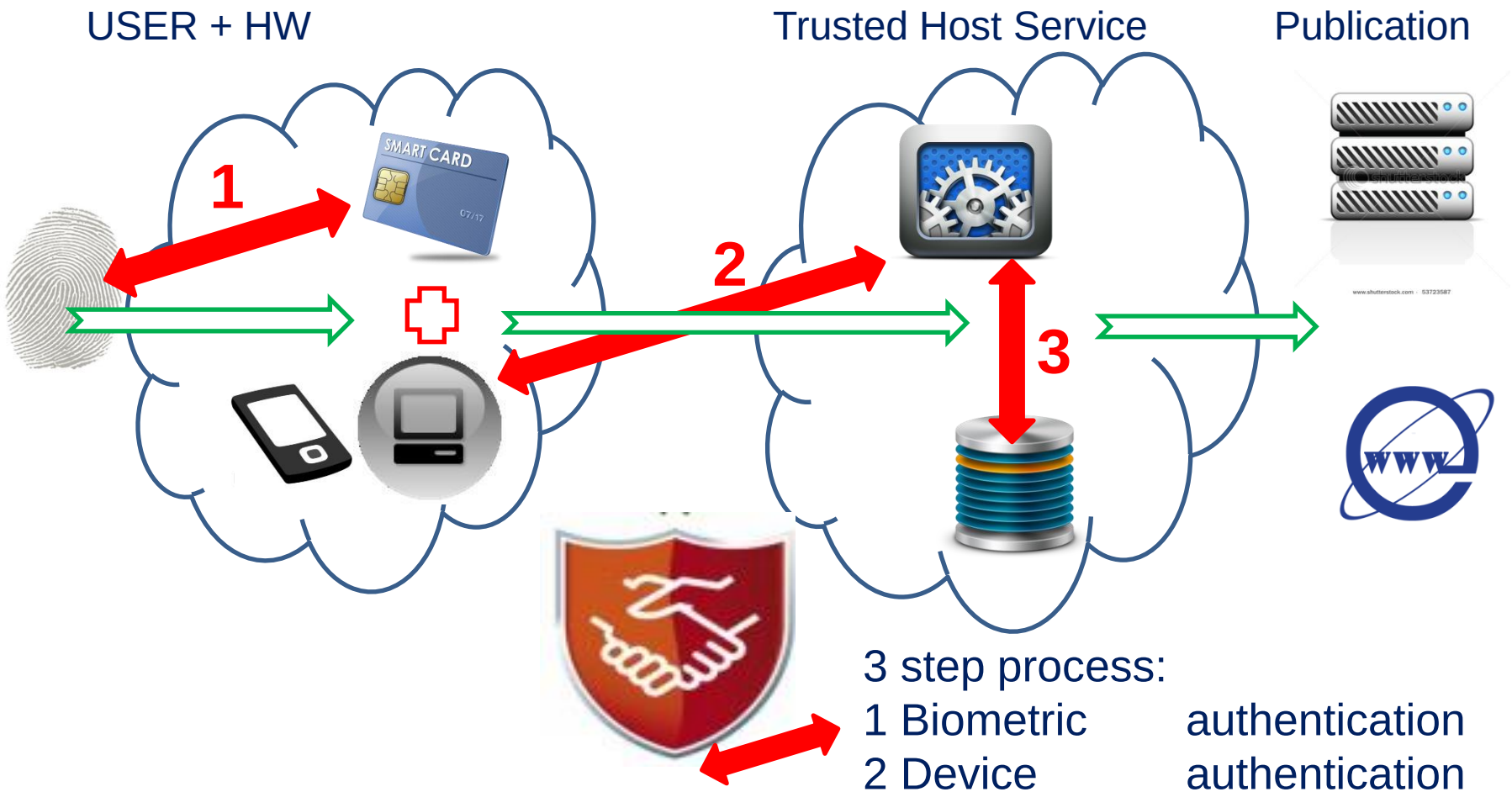
Biometrics Integrated in Devices
FP sensor + Sesam!

For desktop &
laptop/netbook/ultrabook

Reader + card

For mobile devices
(smartphone and tablet)

Anonymous Authentication Technology



Nanotech Apps in Dx in Future (1-15 yrs)!

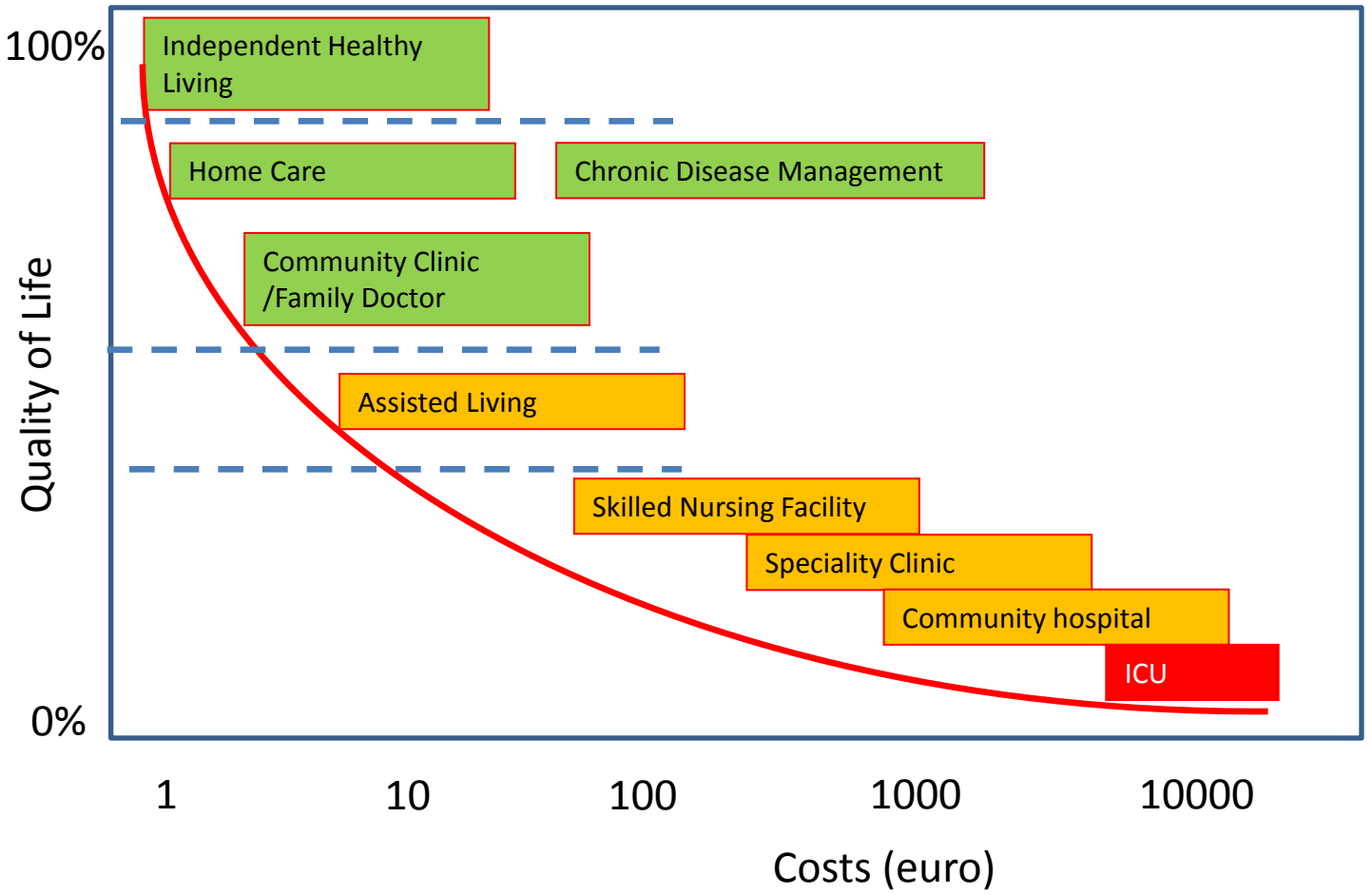
- Mass-spectrometry (already POCT) + nanolab-on-chip: 5 years
- Bio-degradable Dx chips in nano-particles spray absorbed in body: 10-50 years
- Bio-degradable Dx labchips with IT-communication: 10-50 years
- Dx nanochips with authentication: 2 year
- Dx nanochips in blood tubes: 1 year
- Non-invasive Dx POCT: 2 years

Bioinformatics problems

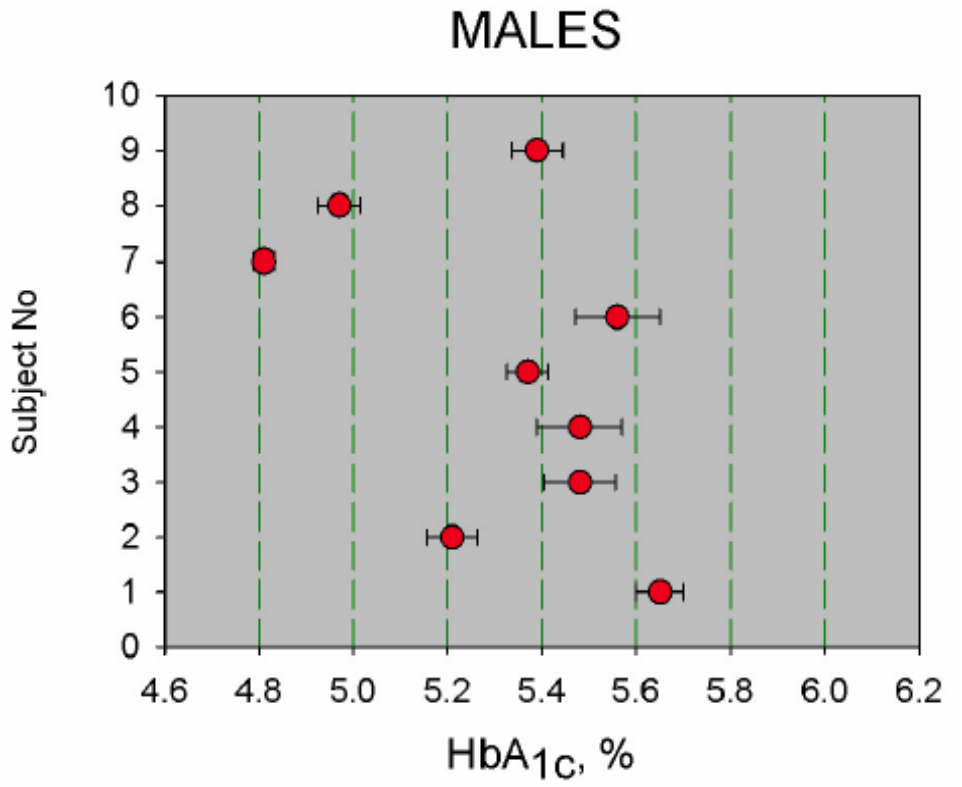
- Matrix information → expert systems for conclusions needed! Translating results for health-care providers!
- *Results must be verified with diagnosis and treatment results*
- Neural network solution?

Earlier Diagnosis

Earlier Diagnosis



Biological Variability (Mosca et al.)



Earlier Diagnosis

→Individualized Reference Values? Chance for US!

- Is it cheaper?
- Need for integrated healthcare?
- Protocols needed:
  - Reference Change values (concentration dependent)

    Biological variation

    Analytical variation

→Prevention? Steer on behaviour?

- Perverted Triggers Re-imbursement system

  (not only if you are ill, re-imburse to stay healthy!)

Behaviour

- Unawareness (detectable, but unaware): advertisement
- Consciousness (aware)
  - Financial triggers
  - Coaching
  - Life-style changes
  - Individual change management
  - Education

- Subconsciousness Subliminal Influencing Health Status?

Cognitive decline in type 2 diabetes is reversibel

Cooray et al. Psychoneuroendocrinology. 2011 Jan;36(1):77-86

NeuroSky


NeuroSky

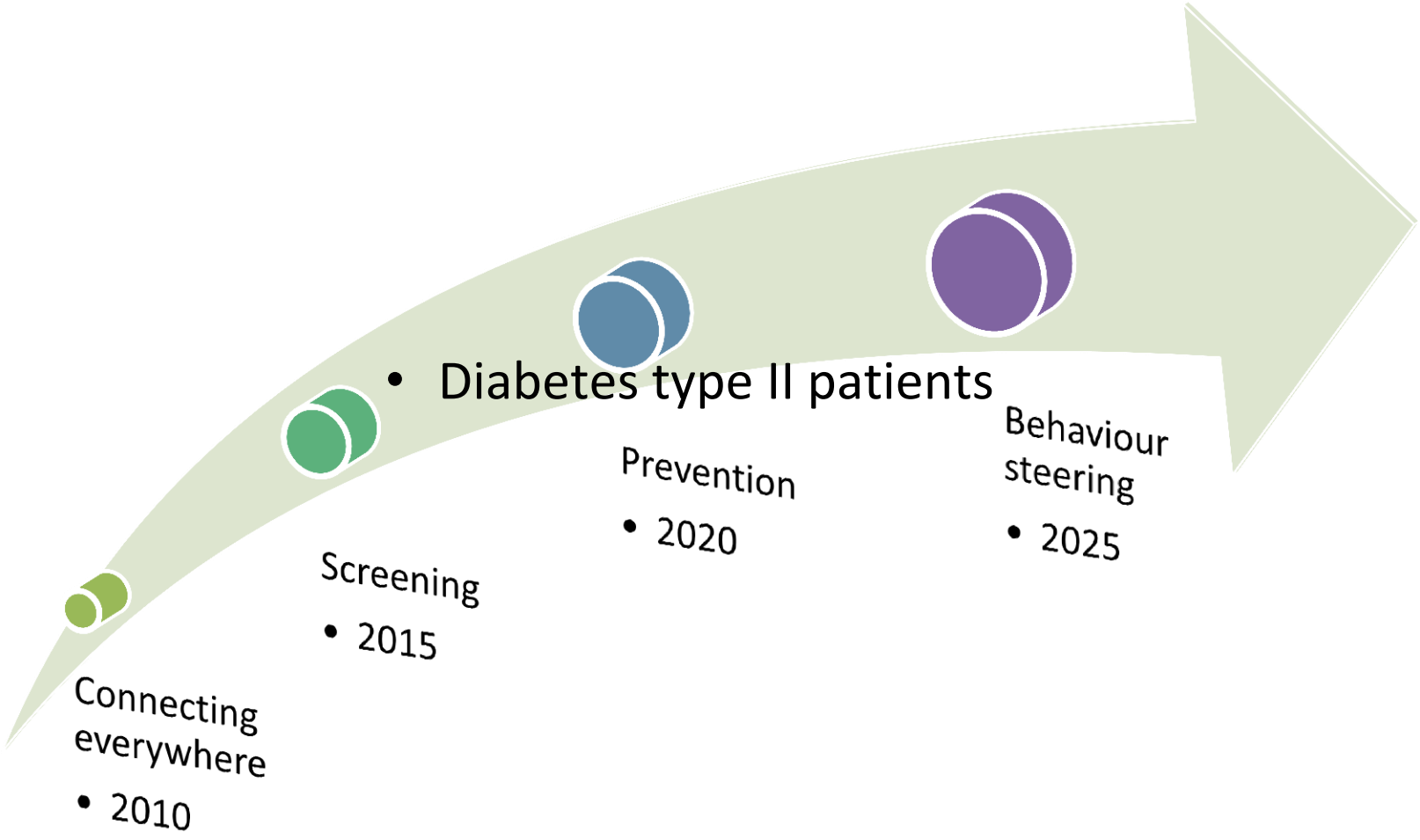
MindRdR and Google Glass

- Cheap EEG
- Open system

- Diabetes type II patients

- Is diabetes type II caused by high sugar level or a state of mind?
- If state of mind -→ can we influence?

Time-line


Connecting everywhere
• 2010
Screening
• 2015
Prevention
• 2020
Behaviour steering
• 2025
• Diabetes type II patients

Economic Models for POC?

Decisions Dx?

- Argumentation?
- Economic impact whole society?
- Economic decision model (*Boston University, Nijerode University, Isala Clinics)*

Study:

The Future of Diagnostics:

the missing link for a sustainable healthcare system?!

What is the added value of diagnostics??

For more information please contact Roald van Leeuwen (rvanleeuwen@thedecisiongroup.nl)

What are the partners of the study?

The study on 'The future value of diagnostics' is executed by The Decision Group.

Helping clients take better business decisions

The Decision Group helps clients take better decisions, with special focus on the healthcare and life sciences sector. Previous projects included advice on the strategic positioning of a major hospital and developing a new business and sales model for a pharmaceutical company.

Group of international experts for academic advice

The group of international experts supporting the study consists of prof. Bohmer (Harvard Business School), prof. Burke (George Washington University), prof. Christensen (Harvard Business School), prof. de Margerie (Grenoble Graduate School of Business), prof. dr. van Eenennaam (Erasmus University).

Isala klinieken

Isala klinieken in Zwolle are the largest top clinical hospital in the Netherlands. We have 5300 employees and 1000 hospitals bed. We represent quality, attention and personal relation with the patient.

What is the study background?

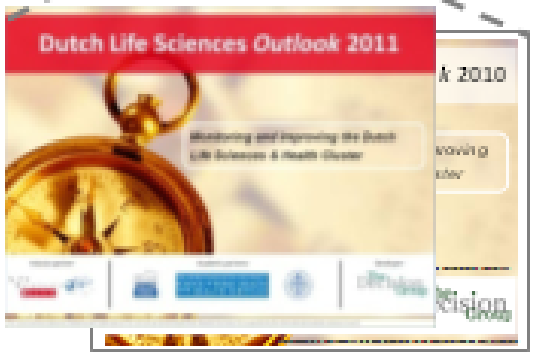
The study is part of the long term research program conducted by prof. dr. Fred van Eenennaam[1] and The Decision Group into the healthcare system.

The Future of the Dutch Healthcare System: Options and Roles of Health Insurers.

What are the strategic options for health insurers in the new healthcare system?

The Future of the Dutch Healthcare System: Changing Roles and Configurations of Hospitals

How can hospital directors and medical specialists create successful strategies?



The Life Sciences Outlook 2010 & 2011: Monitoring and improving the Dutch Life Sciences & Health cluster

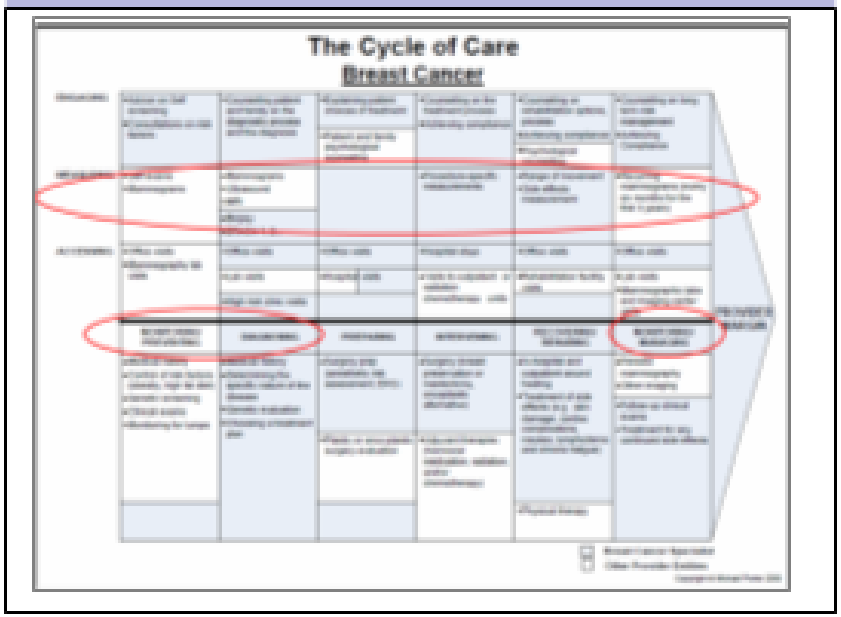
Using the perspective of entrepreneurs to improve the performance of the Dutch Life Sciences & Health cluster in the international context.

[1] Academic links of prof. dr. Fred van Eenennaam; e.g. University of st. Gallen, George Washington University, Erasmus University

What is the role of diagnostics in healthcare?

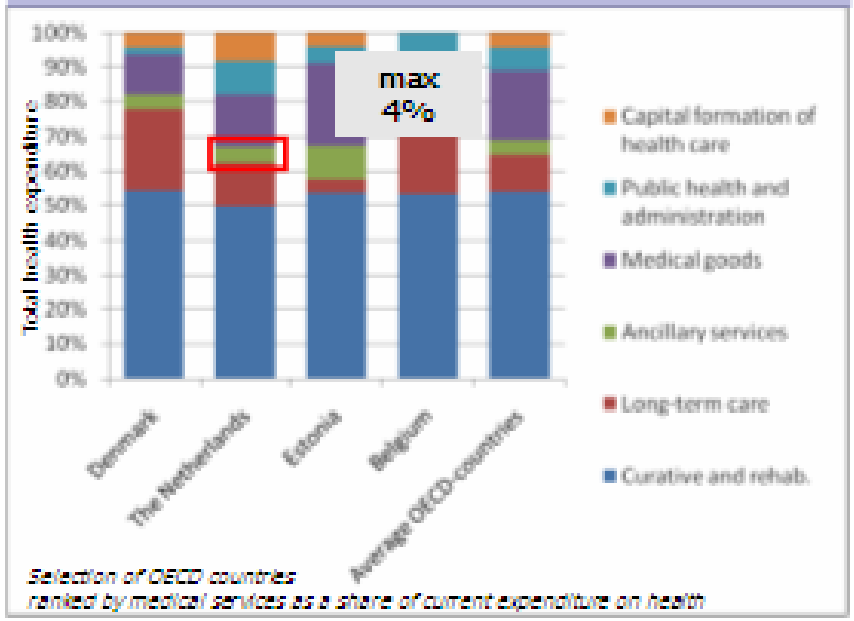
Diagnostics influence as much as 60-70% of healthcare decision making while the expenditure on diagnostics is even less than 4% of the total health expenditure.

Diagnostics influence 60-70% of decision-making in healthcare



Sources: Porter 2006, Redefining Healthcare. Lewin Group 2005, The value of diagnostics innovation, adoption and diffusion into healthcare. SMV-rapport 2010, Medische diagnostische centra zijn cruciaal voor nabije, zinnige en zuinige zorg in de eerste lijn.

Expenditure on diagnostics is less than 4% of the total health expenditure



Source: OECD, System of health accounts, 2008

Why is it difficult to assess the value of diagnostics?

Difficulties arise due to the complex definition and the unknown value of diagnostics.

Two issues on diagnostics

Issue I; Complex definition of diagnostics
Diagnostics are complex to define, traditionally diagnostic devices are defined by their technology

Issue II; Unknown value of diagnostics
As diagnostics do not have a direct impact on health outcome, the value of diagnostics is difficult to determine

Conclusion: there is no available methodology to assess the value of diagnostics

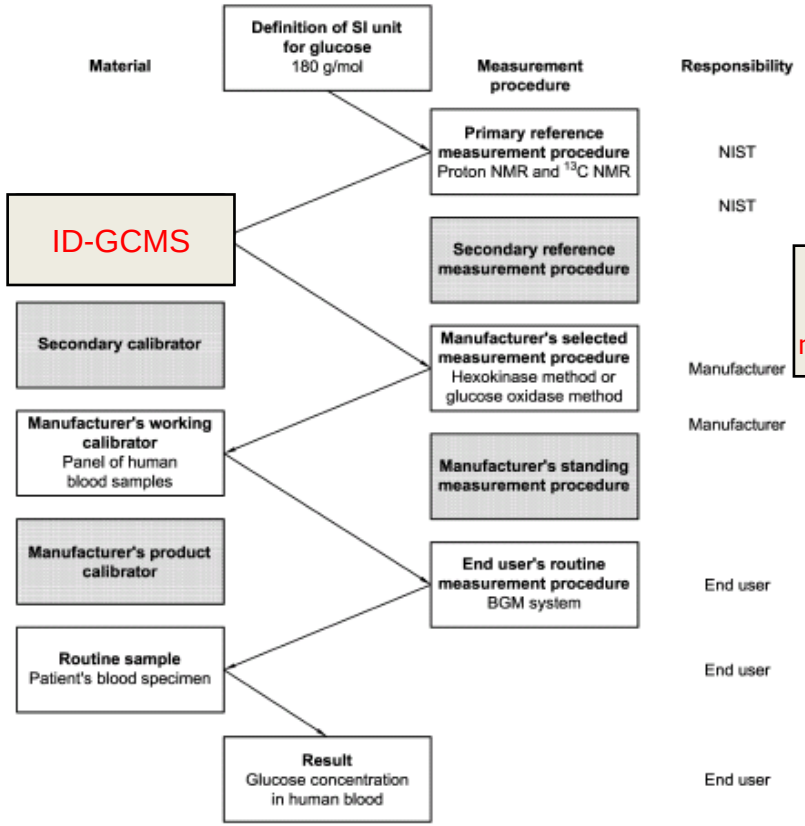
Value-Based Health Care Center Europe

Content

- Changes in Healthcare
- Consequences for POCT
- Changes in Healthcare Market
- Redefine Healthcare?
- Changes in POC-land
- *Traceability*
- Concluding remarks

Traceability!

Traceability chain



Perchloric acid whole blood
hexokinase
method with hematocrit measurement

NOTE 1 The illustration of a full traceability chain is taken from ISO 17511:—, 4.2.2 h). Steps that are not used in this particular calibration scheme are shaded in grey.

NOTE 2 This example is not intended to represent the only possible traceability chain for a blood-glucose monitoring system.

[a] NIST SRM917b refers to the Certificate of Analysis issued by the National Institute of Standards and Technology (NIST) for the standard reference material (SRM) 917b, D-glucose (dextrose), used for calibration in this example.

Traceability!

- Traceability for bloodgass
- Traceability for electrolytes
- Traceability for creatinin
- Traceability for microalbumin
- Traceability for HbA1c
- Traceability for coagulation
- Traceability for glucose

- More to do (at least 85 parameters)

Conclusion

- **E**MPOWERING THE PATIENT
- **E**NABLING THE PHYSICIAN
- **E**NHANCING WELLNESS
- **E**ARLIER DIAGNOSIS… BEFORE THEY GET PHYSICALLY ILL
- **R**OOT CAUSE ANALYSIS FOR DISEASES

- SMALLER DIAGNOSTICS
- AUTHENTICATION
- ECONOMIC DECISION MODELS
- TRACEABILITY
- FITS THE INSTRUMENT TO THE PATIENT

10 Prospects

1. Individualized reference values
2. Satellite connection diagnostix
3. Authentication/Telemedicine
4. Artificial Intelligence
5. Decision Support Software
6. Risk profiling
7. Screening
8. Preventive testing
9. Non-invasive testing
10. Mindset testing/Behaviour change

- We blijven altijd meten, want……

…meten is weten!

Vragen, opmerkingen:

l.d.dikkeschei@isala.nl

Met dank aan;

Dr. ir. R.J. Slingerland
Dr. ir. N. Greveling
Prof. dr. F. van Eenennaam