EULAR World Arthritis Day Conference 2018
Bringing chronic diseases to the forefront of health innovation: From the lab to individualised health care
Thon EU Hotel (Brussels), 9 October 2018 (9:00 — 17:00)

Agenda

Chairs:
Prof. Johannes W. J. Bijlsma, EULAR President
Neil Betteridge, EULAR Liaison Officer for Public Affairs

8:00 – 09:00 Registration

9:00 – 9:30 Opening session
   o Prof. Johannes W. J. Bijlsma (EULAR President)
   o Lieve Wierinck (Member of the European Parliament)
   o Pierre Meulien (Executive Director, Innovative Medicines Initiative)

9:30 – 10:30 Keynote speeches
   ♦ Analysing the impact of research and innovation in reducing the burden of chronic diseases in Europe
     o Prof. Stephen Hanney, Health Economics Research Group (Brunel University)
   ♦ Innovation in basic science
     o Prof. Timothy R.D.J. Radstake (Utrecht University)
   ♦ Barriers, challenges and opportunities for biomedical research & innovation in Europe – A policy view
     o Barbara Kerstiëns (Head of Unit, Non-communicable diseases and the challenge of healthy ageing, DG Research and Innovation, European Commission)

10:30 – 10:45 Coffee break

#EULARBrussels2018
10:45 – 11:50 Panel debate

- How to foster European innovation to tackle chronic diseases?
  Panellists: Barbara Kerstiëns (DG Research and Innovation, European Commission); Prof. Rik Lories (EULAR / KU Leuven); Carolina Rubio Miner (Savana Médica); Gerlinde Bendzuck (Deutsche Rheuma-Liga Bundesverband e.V.); Moderator: Kathy Smith

11:50 – 12:00 Wrap-up morning session

- Prof. George Griffin (President, Federation of European Academies of Medicine, FEAM)

12:00 – 13:00 Lunch

13:00 – 14:00 Promoting innovation in health care

- Innovative solutions in the diagnosis and treatment of chronic diseases: Trends and challenges
  o Valentina Laurenzia Ancona (Senior Manager Government Affairs, MedTech Europe)
- Innovation in RMDs: digital population health, present and future
  o Prof. William Dixon (Manchester University)
- Challenges and opportunities of implementing innovative solutions in health care services
  o Pascal Garel (CEO European Hospital and Healthcare Federation — HOPE)
- Fostering innovation in health care – The role of the EU
  o Andrzej Rys (Director for Health systems, medical products and innovation, DG SANTE, European Commission)
- Q&A

14:00 – 14:30 Innovative solutions in RMDs

- Moderator: Prof. Tanja Stamm (EULAR Vice-President Health Professionals in Rheumatology)
  o Inertial Movement Sensors (IMUs), Philip V. Gardiner (Western Health and Social Care Trust)
  o MedXcell Science SAS, Prof. Christian Jorgensen (Institut national de la santé et de la recherche médicale, INSERM)
  o REMORA, Prof. William Dixon (Manchester University)
14:30 – 14:40 Coffee to take on the way to the workshops

14:40 – 15:55 Workshops

- Can citizens have a leading role in health care innovation?
  - Chairs: Dieter Wiek (EULAR Vice-President representing PARE) & Elsa Mateus (Portuguese League Against Rheumatic Diseases & EULAR)

- Organisational and human challenges in the introduction of digital solutions in health care services
  - Chairs: Prof. Laure Gossec (EULAR & Université Pierre et Marie Curie) & Pascal Garel (European Hospital and Healthcare Federation — HOPE)

- Policy issues in the use of big data in health care and research
  - Chairs: Prof. Loreto Carmona (EULAR) & Carolina Rubio Miner (Savana Médica)

- How to foster innovation through Horizon Europe (FP9)?
  - Chairs: Prof. Xenofon Baraliakos (EULAR) & Prof. George Griffin (FEAM)

15:55 – 16:05 Coffee break

16:05 – 16:35 Report of workshops

- Report of workshops
- Q&A

16:35 – 17:00 Closing session

- Dieter Wiek (EULAR Vice-President representing PARE)
- Prof. Johannes W. J. Bijlsma (EULAR President)

17:00 – 18:30 Networking
Innovative solutions in the diagnosis and treatment of chronic diseases. Trends and challenges

Valentina Laurenzia Ancona
Senior Manager Government Affairs, MedTech Europe

#EULARBrussels2018
Innovative Solutions in the Diagnosis and Treatment of Chronic Diseases. Trends & Challenges

Valentina Ancona
Senior Manager Government Affairs & Public Policy
MEDICAL TECHNOLOGY

are products, services or solutions which are used to save and improve lives of people in need of acute care or living with a chronic condition at all stages of life.
THE VALUE OF MEDICAL TECHNOLOGY

For Patients

1. Accurate & timely diagnosis
2. Less invasive and personalised treatment
3. Support for self-management
4. Shorter hospital stay/home care solutions

For HCPs

1. Supports decision-making
2. Connects disciplines across pathway
3. More efficient treatment
4. Optimises time for care

For Medical Systems

1. Connects disciplines & settings
2. Optimizes resource allocation
3. Reduces hospitalisation / re-admission
4. Achieves budget and system efficiencies
Collaboration

Digitalisation

What’s happening today?
INNOVATIVE SOLUTIONS ACROSS PATIENT PATHWAY 1/2

Medical Technologies – An Enabler of the Digital Transformation of Health and Care

Healthcare reality today:
• Ageing population
• Varying patient outcomes
• Shortage of medical staff
• Limited access to healthcare in remote areas

Accelerating new ways of healthcare delivery:
• Preventive care
• Personalized care
• Integrated care
• Remote care

- Prevention
- Diagnosis
- Therapy
- Monitoring
- After Care

- App prevention & coaching tools
- Early detection of disease outbreaks
- Automated and molecular testing
- Implantable recorders
- Chronic disease treatment
- Robotic surgeries
- Remote follow-up for implantable devices
- Advanced analysis of monitoring data
- Digital ecosystems for post-operation care
- Remote rehabilitation
INNOVATIVE SOLUTIONS ACROSS PATIENT PATHWAY 2/2

Medical Technologies – An Enabler of the Digital Transformation of Health and Care

Prevention
- App prevention & coaching tools
- Early detection of disease outbreaks

Diagnosis
- Automated and molecular testing
- Implantable recorders

Therapy
- Chronic disease treatment
- Robotic surgeries

Monitoring
- Remote follow-up for implantable devices
- Advanced analysis of monitoring data

After Care
- Digital ecosystems for post-operation care
- Remote rehabilitation

Digital Health full ecosystem solutions

Patient management
- Chronic disease management
- Continuous remote patient monitoring

Productivity
- Data integration and AI solutions
- Robotic surgery decision-making systems

Digital Future
- Overcoming space and time
- Augmented decision-making
- Empowering patients
- Increased accessibility
REALITY OF RHEUMATIC CONDITIONS TODAY

- Most common cause of disability
- Affects all ages
- Major impact on people’s quality of life
- Cost more than 200B Euros/year in Europe
- Poorly diagnosed

* Source: EULAR Fact Sheet
Diagnostic Information Brings Multidimensional Value - from healthcare pathway to health path

Clinical benefit
- Patient empowerment
  - ‘Value of knowing and deciding’
  - ‘Planning value’
  - Value of a ‘rule out’ test
  - ‘Option value’

Economic Efficiencies
- Patient triage
- Waiting time
- (Re)-Hospitalization
- Avoided cost of disease progression
- Avoided adverse events
- Shift to community care

Public Health Benefit
- Identification of notifiable disease allowing to take measures to contain the spread of infection

Operational Efficiencies
- Turn around time
- Operational costs
- Quality (reliability, reproducibility)

Patient Management
- Facilitate rapid, appropriate clinical management
- Reduce unnecessary or ineffective testing
- Manage patient expectations regarding prognosis and treatment course
- Monitor condition and provide intervention
THE ROAD AHEAD

Challenges

• Fragmented healthcare IT infrastructure
• Lack of trust and acceptance
• Reimbursement policies sometimes deliver wrong incentives

Opportunities

• Efforts at harmonization and interoperability
• GDPR provides assurances and legal/ethical framework
• Fit-for-purpose methodologies to measure the Value of Diagnostic Information
THANK YOU!

v.ancona@medtecheurope.org
Prof. Johannes W. J. Bijlsma
EULAR President
About the Conference

• World Arthritis Day (WAD)
• WAD Brussels Annual Conference
  – Since 2010
  – Bring together Rheumatic and Musculoskeletal Disease (RMDs) community, EU and national policy makers, and stakeholders
  – Focus on relevant policy developments

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About the Conference

Conference goals:

- To identify key **challenges in innovation in biomedical research and health care**
- To discuss the **future of EU health research and innovation policies**
- To develop **recommendations on**:
  - Citizens’ roles in the development of innovative solutions in health care
  - Policies on big data
  - Implementation of innovative solutions in health care settings
  - Health innovation in Horizon Europe

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Structure of the Conference

Morning
• 9:00: Opening session
• 9:30: Keynote speeches
• 10:45: Panel debate
• [12:00: Lunch]

Afternoon
• 13:00: Plenary session
• 14:00: Innovative solutions in RMDs
• 14:40: Workshops
• 16:35: Closing session

• 17:00: Networking

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Workshops

1. Can citizens have a leading role in health care innovation?
2. Organisational and human challenges in the introduction of digital solutions in health care services
3. Policy issues in the use of big data in health care and research
4. How to foster innovation through Horizon Europe (FP9)?

#EULARBrussels2018
Streaming and pictures

• Live streaming (only plenary sessions)
• Videos and pictures to be uploaded to the EULAR Website
• Should you not want appear in videos/pictures:
  ➢ Space on the back of the room
  ➢ Let us know, so we will remove pictures of you
Social media

- Livestream: over EULAR Facebook and on EULAR website
- EULAR Facebook: @eular.org
- Discussion: over EULAR Twitter using #EULARBrussels2018
- EULAR Twitter: @eular_org
- Hashtag: #EULARBrussels2018
Innovation in RMDs: digital population health, present and future

Prof. William Dixon
Manchester University

#EULARBrussels2018
Digital Population Health: Present and Future

Will Dixon
Professor of Digital Epidemiology
Director, Arthritis Research UK Centre for Epidemiology &
Honorary Consultant Rheumatologist, Salford Royal Foundation Trust

Brussels, October 9 2018
Rheumatologist & Epidemiologist
Rheumatologist & Epidemiologist
Rheumatologist & Epidemiologist

Questions important to patients and carers

Population health research
What matters to patients?

• What caused me to get this disease?
  – *Diagnoses, environmental risk factors, genetics*

• What can I do to help ease my symptoms?
  – *Disease severity, lifestyle factors, medication*

• Which of these treatments is best for me?

Need Data...
Uptake of technology
Digital Epidemiology

Salathe et al. PLoS Computational Biology, 2012
Digital Epidemiology

- Number of users of digital devices in billions

- What we say and do is stored digitally
  - Occurrence of disease
  - Experiences and consequences of disease
  - Behavioural risk factors: Exercise, smoking, diet

- Huge opportunities for health research

Salathe et al. PLoS Computational Biology, 2012
Data Sources

1. Electronic Health Records
2. Smartphones
3. Wearables
4. Social Media
5. Digital Traces
1. Electronic Health Records

David JONES

GP

Hospital
The opiate epidemic

• 7-fold rise in UK prescriptions 2000-2010

• Account for >7 in 10 U.S. overdoses

• Multiple different drugs... but which is safer?
Comparative safety of opiates

- Opiates taken, change in respiratory rate
1. Electronic Health Records

2. Smartphones
Opportunities

• Self-management
• Clinical care
• Research

• Benefits
  – Wide coverage
  – Frequent data collection in daily life
  – Novel data types
  – Feedback on device
Smartphones for research

• Mass participation ✓
  – 13,256 participants

• Ongoing engagement ✓
  – 1 in 7 entered daily data for 6+ months
Smartphones for clinical care

Remote Monitoring in Rheumatoid Arthritis
Innovative solutions in RMDs: today at 1400-1430
3. Wearables

2. Smartphones

1. Electronic Health Records
Wearables for population health research

- Self-reported data (on a small screen) and
- Sensor data
  - Physical activity, heart rate

**Bad day:** high pain > low activity > high pain
**Good day:** low pain > high activity > high pain
Knee Osteoarthritis: Linking Activity and Pain

Combining self-reported data with sensor data
1. Electronic Health Records
2. Smartphones
3. Wearables
4. Social Media
@MelissaDee_ Humira never really workd for me. Orecnia was good. Xeljanz was the best but ate a hole in my stomach. #RABlows
Text-mining
Twitter analysis of steroid safety

2012-2015

Prednisolone or prednisone

- Steroid-related insomnia: almost no research
- Steroid-related weight gain: research very limited

Patel et al., npg Digital Medicine 2018
1 in 20 searches are health-related

6 in 10 search for health information per year

1 in 3 admit to seeking an online diagnosis

1 in 4 have read or watched other patients’ experiences
Small data, where n=me

What happens when each patient becomes their own “universe” of unique medical data?

https://www.youtube.com/watch?time_continue=10&v=IAEhSGYEHWU
Population health insights from
• search history?
• physical activity?
• location?
• Technology will revolutionise healthcare

• Data from technology has the potential to support vital research and improve healthcare

• Need to collect the right high-quality data, aligning self-management, clinical care and research whilst maintaining public trust
REMORA

Prof. William Dixon
Manchester University

#EULARBrussels2018
Remote Monitoring in Rheumatoid Arthritis

Will Dixon
Professor of Digital Epidemiology
Director, Arthritis Research UK Centre for Epidemiology &
Honorary Consultant Rheumatologist, Salford Royal

Brussels, October 9 2018
Rheumatology clinic

“How have you been in the last six months?”

“Oh... alright, I suppose.”
“I can’t talk about what’s going on because I forget. Yeah I’ve been in pain, yeah this has been sore, yeah that’s been sore, I can’t remember for how many days because I just try and get on with it as much as I can.”

*Patient with rheumatoid arthritis*
Remote Monitoring In Rheumatoid Arthritis

• Smartphone app to collect daily symptoms in patients with RA
  1. Self-management
  2.
  3.
• Smartphone app to collect daily symptoms in patients with RA
  1. Self-management
  2. Clinical care
  3.
• Smartphone app to collect daily symptoms in patients with RA
  1. Self-management
  2. Clinical care
  3. Research
Self-management

RA as an invisible disease

“I’m not one that moans about being ill. But because it was every night, [my partner]’d be like ‘How are you scoring today? Why didn’t you say?’ It did make more communication between us”
Clinical care

Patient 1

• “Last time I gave you the steroid injection. How have you got on since then?”
• “The injection was great. By the time I was going home from work later on that day I was feeling so much better”
• “Okay, and how have your symptoms been over the last month since then?”
• “I’ve been fantastic. I feel a bit of a fraud for your research because it has just been steadily good”
Clinical care

Patient 1

• “Any symptoms at all over the last month?”

• “No, other than the fact I just have a few limitations as to what I can do - but no actual pain.”

• “So let’s have a look at your graph...”
Clinical care

Patient 1

• “So that’s the day of the last clinic visit, isn't it, the 23rd, when your pain was nine out of ten?”
• “Yeah”
• “The pain’s then between zero and one for the next seven to ten days ... and then you did have a couple of days when the pain was worse?”
• “Yeah”
Clinical care

Patient 1

• “So it's actually interesting that, having discussed with you before this, you didn’t mention that.”

• “No, I'd forgotten that”
Clinical care
Patient 2

• “There is quite a significant day to day fluctuation ... but it looks, as you say, that the extent of the fluctuation is going down...”

• “It’s funny on this, you can see the trend can't you?”
• Patients were positive about the app
  – “a great idea”
  – “a brilliant thing, I can’t wait until it’s out there properly.”
  – >90% possible entries completed

• Data collection
  – “captured the moment”
  – made “fleeting symptoms visible”
  – picked up “changes that would otherwise be missed”

• Symptom graphs in the EHR
  – made it easier for a “shared conversation”
  – the data “says it for you”, “provides evidence” and “personalises care”
• Smartphone app to collect daily symptoms in patients with RA

1. Self-management
2. Clinical care
3. Research

Can we identify pre-flares?
What are the triggers?
Can we intervene?
Next steps

• Ability to ‘prescribe’ remote monitoring in real-time
• User authentication with health system ID
• Patient-generated health data repository with interoperability with any EHR
• Proof of clinical benefits for early and late adopters
• Route to sustainability
  – commissioning digital services
Summary

• Proof of concept of transformative value from integrating patient-generated health data into clinical consultation

• Huge opportunities for self-management, clinical care and research
Measuring Movement in Rheumatic Diseases: Moving into the 21st Century

Philip Gardiner, Altnagelvin hospital, Derry, N. Ireland

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Innovation Begins with Frustration!

HAQ, BASFI

PAIN

Patients

Dr, Physio

Ownership

Empowerment

Engagement
The Vision

• Research:
  – Validate an ‘Outcome Tool’ to measure spinal mobility ‘IMU-ASMI’
  – New information on the Biomechanics of axSpA ‘Dyn-ASMI’
  – Performance based functional assessment tool ‘PB-ASFI’

• Health Professionals:
  – Personalised exercise prescriptions e.g. for flares
  – Visualising flares/trends in PROs/mobility

• Patients
  – Data ownership/tracking (sensors/PROs) => engagement
  – Motivate regular exercise – use gamification/graduated
  – Social networks Patients share information anonymously
  – Patients contribute to research

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Which Sensor Should we Use?

• How did we pick which sensor to use? The chosen product had to:
  – be CE approved to be ‘ready for action’
  – have robust published validation as a spinal measurement tool
  – Have a clear protocol to assist positioning/reliability
  – Access to raw data and agreement around app development
    • We wanted our ‘app’ to be generic – to be able to read IMU data from any device that makes the raw data available
axSpA Sensor Project Outline

• Validate sensor **accuracy** against optical motion tracking system (UCOTrack)
• Validate **reliability** of repeated sensor tests & develop composite measurement score ‘IMU-ASMI’
• Investigate **ambulatory** use of sensors to monitor movement and standardised functional tests
• Investigate **responsiveness** to change before and after biologics therapy
Methods: 40 patients with axSpA (12F, 28M) mean age of 48 (27-71yr)
Repeated BASMI and IMU movement tests twice over two weeks

Results:

<table>
<thead>
<tr>
<th>Measure</th>
<th>Day One</th>
<th>Day Two</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rater A</td>
<td>Rater B</td>
</tr>
<tr>
<td>BASDAI</td>
<td>4.5 (0.3-9.7)</td>
<td></td>
</tr>
<tr>
<td>BASFI</td>
<td>4.97 (1.1-9.7)</td>
<td></td>
</tr>
<tr>
<td>BASMI</td>
<td>4.85 (1.0 - 8.2, SD 1.85)</td>
<td></td>
</tr>
<tr>
<td>IMU-ASMI</td>
<td>4.88 (1.5 - 8.7, SD 1.85)</td>
<td></td>
</tr>
</tbody>
</table>

- The IMU-ASMI score can be further split into movement or regional components – each part of the test is reliable (unlike BASMI)
- The responsiveness/sensitivity to change of this score will be tested in Phase II studies.

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# Trunk Flexion

<table>
<thead>
<tr>
<th></th>
<th>IMU vs UCOTrack</th>
<th>ViMove</th>
<th>VC</th>
<th>RMSE</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar Anterior flexion</td>
<td>103.6(17.3)</td>
<td>99.0(17.4)</td>
<td>4.4%</td>
<td>6.57</td>
<td>0.93</td>
</tr>
<tr>
<td>Lumbar Extension</td>
<td>24.6(9.3)</td>
<td>22.3(9.6)</td>
<td>9.4%</td>
<td>4.22</td>
<td>0.90</td>
</tr>
<tr>
<td>Lumbar L rotation</td>
<td>27.7(10.4)</td>
<td>27.4(11.0)</td>
<td>1.1%</td>
<td>1.83</td>
<td>0.99</td>
</tr>
<tr>
<td>Lumbar R rotation</td>
<td>26.8(10.4)</td>
<td>25.3(10.1)</td>
<td>5.6%</td>
<td>3.14</td>
<td>0.95</td>
</tr>
<tr>
<td>Lumbar L lateral flexion</td>
<td>70.7(13.9)</td>
<td>72.6(16.6)</td>
<td>2.7%</td>
<td>8.71</td>
<td>0.84</td>
</tr>
<tr>
<td>Lumbar R lateral flexion</td>
<td>68.4(15.4)</td>
<td>67.6(16.7)</td>
<td>1.2%</td>
<td>7.87</td>
<td>0.88</td>
</tr>
</tbody>
</table>

# Occiput Cervical Flexion

<table>
<thead>
<tr>
<th></th>
<th>IMU vs UCOTrack</th>
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<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical Flexion</td>
<td>50.9(12.5)</td>
<td>52.3(12.8)</td>
<td>2.8%</td>
<td>2.73</td>
<td>0.98</td>
</tr>
<tr>
<td>Cervical Extension</td>
<td>43.1(16.0)</td>
<td>39.3(14.4)</td>
<td>8.8%</td>
<td>5.44</td>
<td>0.94</td>
</tr>
<tr>
<td>Cervical Left rotation</td>
<td>66.1(20.2)</td>
<td>63.8(20.5)</td>
<td>3.5%</td>
<td>9.13</td>
<td>0.90</td>
</tr>
<tr>
<td>Cervical R rotation</td>
<td>62.1(19.2)</td>
<td>64.7(21.7)</td>
<td>4.2%</td>
<td>9.72</td>
<td>0.89</td>
</tr>
<tr>
<td>Cervical L lateral flexion</td>
<td>34.3(15.8)</td>
<td>32.9(15.5)</td>
<td>4.1%</td>
<td>7.77</td>
<td>0.88</td>
</tr>
<tr>
<td>Cervical R lateral flexion</td>
<td>34.7(15.9)</td>
<td>34.0(16.3)</td>
<td>2.0%</td>
<td>7.10</td>
<td>0.90</td>
</tr>
</tbody>
</table>
What We’ve Learnt so Far

• Sensors are accurate and reliable measurement tools for measuring movement in axSpA
• We have much to learn about dynamics of movement in axSpA
  – Regional spinal movement
  – Lumbo-pelvic movement
• Extracting data is complex – we need cross-disciplinary co-operation with care of the elderly/rehab/sports medicine specialists

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The FOREUM ‘app’ for AS
A gamification application design for remote monitoring of Ankylosing Spondylitis using IMU sensor technology

- Co-design with patients & users
- IMU-ASMI Summary scores
- Real-time sensor data analysis
Gerlinde’s Challenge: Maximise Participation

- The Patient in Crisis: Flare up in neck pain
  - App measures 50% reduction in lateral rotation and flexion on baseline
  - App records 40% worsening of PRO
  - Alerts patient and suggests a message to Dr and Physio 75 miles away
  - The patient can share this with their axSpA social network
Gerlinde’s Challenge: Maximise Participation

• What can be done?
  – The Dr increases the dose of medication for a short period until the flare settles
  – The Physio directs the exercise programme for the specific problem: these exercises videos appear on the app
  – The patient is engaged in their own management
  – The social network gives support and encouragement
Challenges and opportunities of implementing innovative solutions in health care services

Pascal Garel
CEO European Hospital and Healthcare Federation, HOPE
European Hospital and Healthcare Federation
Challenges and opportunities of implementing innovative solutions in healthcare services
Disruptive Forces
The Basic Change in Health Care Conditions

Aging Population, Fewer Caregivers

An Increase in Chronic Diseases

New Health Technology

Information Revolution

Conscious Health Consumer
Organisational innovation

- Integrating care in health and social
- Design challenges and leadership
- Outcome challenges: variations and unnecessary differences
Other challenges

- Financial sustainability
- Climate change
- Socio-economic factors: inequalities, literacy
Complexity of hospitals and hc services

- Hospitals and healthcare services as providers
- Hospital and healthcare services as employers
- Hospital and healthcare services as purchasers
- Hospitals and healthcare services as buildings
Human resources

Demography and migration

Adaptation to innovation

Carers
Diversity of health systems

History

Resources

Fragmentation
Opportunities

Strategies and Tactics Universal For Best Population Health Managers

Managing Three Types of Patient Demand

- **High-Risk Patients**: 5% of patients; usually with complex disease(s), comorbidities
  - Intense, comprehensive personalized care

- **Rising-Risk Patients**: 15-35% of patients; may have conditions not under control
  - Balance of self-service supported by critical care access

- **Low-Risk Patients**: 60-80% of patients; any minor conditions are easily managed
  - Convenient, transactional access to system

Source: Advisory Board interviews and analysis.
New Technologies

Artificial intelligence and Big Data
Robot Technology
Internet of things, apps, wearables & sensors
Precision Medicine
The patient is offered individualized optimal treatment from All Health Data (raw) available through Regional Data Support Centers, which is accessed by Clinicians, Researchers, Quality Developers, Industry, Lab. dataindex, Image dataindex, National Registries, Clinical Databases and Electronic Care Records, Biobanks, National hole Genome Dataindex, General Practice Records and Municipal data, Pharmac y Records, and PRO Data. One Point of Entry to Health Data is facilitated by these data sources.
Patient empowerment

- Patients are more than a health condition
- Sharing the decision process
- Health literacy
Balancing Security, Trust and Transparency

Precision medicine for better patient outcomes - EAHM 2018
The example of ICT4LIFE

Parkinson and Dementia care actors

Social Professionals
- Social carers

Health Professionals
- Family doctor
- Specialist doctor
- Nurse...

Formal & Informal Caregivers

Patients
Pilot Scenarios

Home scenario

Patient & Caregiver support
- Information – Training – Communication
- Calendar – Medication – Social Support

Sensor deployment
- Security / Abnormal behaviour / Symptoms
- 3D Cams / binary sensors / wearables

Shared Information
- Health & Social Professionals
- Knowledge acquired from sensors

Rehabilitation scenario

Patient & Caregiver support
- Information – Training – Communication
- Calendar – Medication – Social Support

Sensor deployment
- Rehabilitation exercise evolution
- 3D Cameras / Wearables

Shared Information
- Health & Social Professionals
- Patient therapy evolution

Day-care centre scenario

Care Professionals
- Patient specific data and reminders
- Patient symptom information

Sensor deployment
- Security / Symptom data / Socialization
- 3D Cameras / wearables

Shared Information
- Health & Social Professionals
The example of MedEye

The medication process is complex

- Doctors
- Pharmacy
- Wards
- Nurses
- Medication
- Patients

- ePrescribing
- EPMA
- Clinical Decision Support

- Pharmacy review
- Stock management
- Repackaging
- Automation

- ADC’s
MedEye - versatile, efficient and safe

MedEye scanner – Barcode scanner
MedEye camera – MedEye software
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Analysing the impact of research and innovation in reducing the burden of chronic diseases in Europe

Prof. Stephen Hanney
Health Economics Research Group, Brunel University
Analysing the impact of research and innovation in reducing the burden of chronic diseases in Europe

Steve Hanney
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Brunel University London
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‘Economically the return on investment in biomedical research cannot be better illustrated than by a recent UK report, “Medical research: what’s it worth?”’

Overview of presentation

- Brief introduction to assessing full range of impacts from health research programmes by using Payback Framework

- Are research active clinicians & organisations more likely to innovate & provide improved healthcare?
  - Was widely assumed, but no synthesis of evidence or possible reasons

- How valuable are health gains from MSD-related research?
  - “Medical Research: What’s it Worth” shows public & charitable health research investment leads to returns on the:
    - 1) GDP or ‘spillover’ gain from direct & indirect impact on economy - GDP gains disease-independent: original figure 30% (HERG, 2008), revised 15-18% (Sussex, et al, 2016)
    - 2) Net health gain (monetised health gains minus care delivery cost) – disease-specific: CVD 9% (HERG et al, 2008); Cancer 10% (Glover et al, 2014); MSD?
HERG Payback Framework: categories and model

- Payback Framework: 2 elements: multidimensional categorisation of benefits (2 traditional academic benefits; 3 wider societal impacts); & model for assessing them (Buxton & Hanney, 1996, 2008 – in Spanish)

- Multidimensional categorisation of impacts or payback:
  - knowledge production: traditional benefits measured by articles etc;
  - targeting future research, research capacity building, & absorption/innovation;
  - informing policies (messy & diverse: clinical, public) & product development
  - health & health sector benefits, eg health gain, health equity [Key impacts?]
  - broader economic benefits eg to GDP, value of any health gain

- Model of where to look when assessing impacts
  - 2 elements combined to inform range of methods used in impact assessments
  - reviews show Payback Framework widely used in many countries
  - our applications identified diverse impacts from chronic disease research programmes, eg Arthritis Research Campaign (Wooding et al, 2005), Asthma UK (Hanney et al, 2013a)
Are research active clinicians and organisations more likely to innovate and provide improved healthcare?
Evidence synthesis of papers & reasons (Hanney et al, 2013b)
NIHR Dissemination Centre infographic of full review report
How valuable are the health gains from MSD research?

Estimating the returns to United Kingdom publicly funded musculoskeletal disease research in terms of net value of improved health outcomes

Matthew Glover¹, Erin Montague², Alexandra Pollitt³, Susan Guthrie³, Stephen Hanney¹, Martin Buxton¹ and Jonathan Grant²*  

Funded by: Academy of Medical Sciences, Arthritis Research UK, Medical Research Council, National Institute for Health Research, Wellcome Trust
Why assess the returns from public & charitable-funded MSD-related research?

Team’s previous “Medical Research: What’s it Worth” studies on the returns on research in CVD and cancer focused on diseases where:

- most of the health gains from research came from reduced mortality
- research leading to reduced smoking formed a major (but contestable) element in the net health gains

So assessing returns on public & charitable-funded MSD-related research presented new challenges (health gains from reduced morbidity much more important, benefits from smoking cessation not included)

MSD conditions form about 9% of UK burden of disease, but only 3% of research spend (UK Clinical Research Collaboration, 2015)
Identified & prioritised main conditions where research-based developments in patient interventions delivered in the period 1994-2013 have accounted for the largest health gain (measured in quality-adjusted life years - QALYs)

Working with MSD experts we prioritised 9 conditions (eg rheumatoid arthritis, osteoarthritis) & about 20 interventions (but some overlaps, eg early & aggressive combination therapy for several types of arthritis)

Next Table shows a slightly simplified version of the full list we used
## Conditions and related interventions

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Interventions by condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>Early and aggressive combination therapy</td>
</tr>
<tr>
<td></td>
<td>Biologic DMARDs</td>
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<tr>
<td>Juvenile Idiopathic Arthritis</td>
<td>Early and aggressive combination therapy</td>
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<tr>
<td></td>
<td>Biologic DMARDs</td>
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<tr>
<td>Psoriatic Arthritis</td>
<td>Early and aggressive combination therapy</td>
</tr>
<tr>
<td></td>
<td>Biologic DMARDs</td>
</tr>
<tr>
<td>Ankylosing Spondylitis</td>
<td>Biologic DMARDs</td>
</tr>
<tr>
<td>Gout</td>
<td>Allopurinol</td>
</tr>
<tr>
<td></td>
<td>Febuxostat</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>Total hip replacement (inc. cement less prostheses &amp; hybrid prostheses)</td>
</tr>
<tr>
<td></td>
<td>Hip and knee replacement surgical technique (inc knee mini-incision &amp; hip mini-incision)</td>
</tr>
<tr>
<td></td>
<td>Cox-II inhibitors (inc Etodolac, Meloxicam, Celecoxib, Etoricoxib)</td>
</tr>
<tr>
<td></td>
<td>Proton pump inhibitors (inc Etodolac, Meloxicam, Celecoxib, Etoricoxib)</td>
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<tr>
<td></td>
<td>Reduced length of stay for hip and knee replacement</td>
</tr>
<tr>
<td>Low Back Pain</td>
<td>Structured exercise programmes</td>
</tr>
<tr>
<td></td>
<td>Manual therapy</td>
</tr>
<tr>
<td></td>
<td>Combined physical and psychological therapy</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Mycophenolate mofetil</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>Primary and secondary fracture prevention (Biphosphonates &amp; other bone density acting)</td>
</tr>
</tbody>
</table>
Estimating health gain from each intervention, valuing the health gain

For each included intervention, we have to identify relevant studies that have estimated:

a) the life time QALY gains &/or b) the health service costs

Estimate numbers of new patients with any of the conditions receiving each intervention in each year

Calculate total QALY gains derived from patients starting treatment with each intervention by year: total = 871,693 QALYs (largest number came from the various interventions for RA – 349,523)

Place a monetary value on the QALYs gained (using a base case of £25k per QALY) = £21,791,000,000
QALYs gained in each condition from all the key MSD interventions applied, 1994 – 2013

<table>
<thead>
<tr>
<th>Year</th>
<th>Rheumatoid Arthritis (M00-06)</th>
<th>Psoriatic Arthritis (M07)</th>
<th>Juvenile Idiopathic Arthritis (M08-09)</th>
<th>Gout (M10-12)</th>
<th>Osteoarthritis (M15-19)</th>
<th>Connective tissue disorders (M30-35)</th>
<th>Ankylosing spondylitis (M45)</th>
<th>Low Back Pain (M54.5)</th>
<th>Osteoporosis (M80-82)</th>
<th>Total QALYs</th>
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<td>698</td>
<td>67</td>
<td>205</td>
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<td>1,944</td>
<td>6</td>
<td>0</td>
<td>534</td>
<td>0</td>
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<td>113</td>
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<td>7</td>
<td>0</td>
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<td>1,786</td>
<td>171</td>
<td>523</td>
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<td>2,825</td>
<td>8</td>
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<td>10</td>
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<td>4,007</td>
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<td>13,422</td>
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<tr>
<td>2013</td>
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<td>4,813</td>
<td>13,248</td>
<td>2,143</td>
<td>15,153</td>
<td>128</td>
<td>853</td>
<td>2,812</td>
<td>12,875</td>
<td>107,834</td>
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<tr>
<td>Total</td>
<td>349,523</td>
<td>32,507</td>
<td>92,753</td>
<td>26,032</td>
<td>189,136</td>
<td>1,801</td>
<td>4,983</td>
<td>68,245</td>
<td>106,660</td>
<td>871,693</td>
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<tr>
<td>Value</td>
<td>£8,738m</td>
<td>£813m</td>
<td>£2,319m</td>
<td>£651m</td>
<td>£4,728m</td>
<td>£45m</td>
<td>£125m</td>
<td>£1,706m</td>
<td>£2,667m</td>
<td>£21,791m</td>
</tr>
</tbody>
</table>
Estimating cost of delivering the interventions and calculating the net health gain

Calculate the health service costs of providing the new interventions = £5,767,200,000

And net off the health service costs to give the net health gain = £16,023,800,000

Largest: interventions for osteoarthritis - £6,996,800,000 – the biologic DMARDs are generally expensive, but research has helped reduce lengths of stay (and hence costs) for joint replacement

We’ve now got the net health gain but need 3 more steps in order to work out the rate of return on the net health gain...
To calculate the return on investment from the health gain, we had to make four key estimates.

\[ \text{Net Health Gain} = \text{health gain (monetised)} - \text{costs of care delivery} \]

The proportion of UK health gain that can be attributed to UK research.

Time lag between research investment and health gain.
Total economic returns from health research: GDP gains + net health gain

15% to 18%  
+ 7% to 10%  
= 22% to 28% ie c25% per year

SO THERE IS EVIDENCE TO SHOW IT IS WORTH SPENDING MONEY ON MSD-RELATED RESEARCH
Additional References

• Buxton M, Hanney S (1996) How can payback from health services research be assessed? J Health Serv Res Policy, 1:35-43.


• Hanney SR, Watt A, Jones TH, Metcalf L. (2013a). Conducting retrospective impact analysis to inform a medical research charity’s funding strategies: the case of Asthma UK. Allergy, Asthma & Clinical Immunology, 9:17


Prof. Christian Jorgensen
Institut national de la santé et de la recherche médicale, INSERM
MedXcell science
SPIN OFF Montpelliéraine
Unmet need OA & DDD

- 853,900 patients diagnosed and treated in 2023e
- 2nd cause of GP consultations after cardiovascular diseases (2016, 14 millions / year)
- 121 / 100,000 citizens of member countries had total knee replacement surgery in 2013

Total OA related costs

1 to 2.5% of GDP(*)

High unmet medical need for OA

To date... no therapeutic solution exists besides heavy surgical procedures, only symptomatic treatments are available...
Stem cells in OA

- **Osteoarthritis unmet medical needs**:
  - More effective symptomatic treatment: NSAIDs improve less than 50% WOMAC scores.
  - Safer treatment. Traditional NSAIDs carry significant GI risk & COX-2 inhibitors CV risk.

- **Biologics**: anti-IL1b, anti-NGFR

- **Cell Therapy**:
  - Clinicaltrials.gov lists 62 registered trials of knee OA in 2018 including bone marrow-derived mesenchymal stem cells (BMSCs), umbilical cord-derived (UCMSCs), adipose-derived (ADSCs), synovium-derived (SMSCs).
  - Cupistem (Anterogen) was approved by the Korean Food and Drug Administration (FDA).
  - Invossa (TissueGene), allogenic chondrocytes irradiated expressing TGFB1.
The market

- Figures in thousands of treatments:
  - 2013: 10,591
  - 2014: 11,431
  - 2015: 12,285
  - 2016: 13,136
  - 2017: 13,971
  - 2018: 14,775
  - 2019: 15,544
  - 2020: 16,271
  - 2021: 16,955
  - 2022: 17,592
  - 2023: 18,182

Annual Growth: 5.6%

Demographic factors:
- Aging world population
- Increased incidence of obesity
- Increased active population

Expanded patients pool:
- Increasingly relevant demographic phenomena will increase the share of world population affected by Osteoarthritis.
- An augmented pool of diagnosed patients will lead to a steady increase in market size for OA-related products.
- Diagnosed patients will become increasingly aware of available options to counter OA's action, although currently treatment options remain scarce and extremely expensive.
- At present, the Hyaluronic Acid viscosupplementation market remains the best proxy for OA-related markets.
- Research shows an increased interest towards premium-priced products.
Mesenchymal stem cell therapy

- Self renewal
- Differentiation
- Migration

Secreted factors:
- Anti inflammatory
- Growth factors
- Metabolism: glycolysis
- Prevent apoptosis
- Prevent fibrosis

Tissue regeneration

Cartilage, muscle, osseux, adipex, cardiomyocytes
ADIPOA2: phase 2a

- Lipoaspiration
- ADSC isolation/expansion
  - GMP conditions
  - Cell viability
  - Release criteria/toxicology
- Intraarticular injections

Phase 2 trial
Randomization 3 arms
n=150 OA patients
Clinical evaluation (VAS, WOMAC, KOOS)
MRI and Genric month 12
3 Metaanalysis confirm reproducible clinical impact. Imaging impact still pending

<table>
<thead>
<tr>
<th>Studies</th>
<th>Intervention</th>
<th>time</th>
<th>Nb patients</th>
<th>WOMAC initial</th>
<th>WOMAC after injection</th>
<th>Δ score WOMAC</th>
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<tbody>
<tr>
<td>Orozco et al, 2013</td>
<td>Auto_BM</td>
<td>1 an</td>
<td>12</td>
<td>24 ± 14</td>
<td>6 ± 6</td>
<td>18 ± 13</td>
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<tr>
<td>Jo et al, 2014</td>
<td>Auto_ASC</td>
<td>6 m</td>
<td>12</td>
<td>56 ± 19</td>
<td>34 ± 23</td>
<td>22</td>
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<tr>
<td>Vega et al, 2016</td>
<td>Allo_BM</td>
<td>1 an</td>
<td>15</td>
<td>46 ± 15</td>
<td>30 ± 16</td>
<td>16 ± 23</td>
</tr>
<tr>
<td>Pers et al, 2016</td>
<td>Auto_ASC</td>
<td>6 m</td>
<td>12</td>
<td>44 ± 4</td>
<td>22 ± 1</td>
<td>21 ± 13</td>
</tr>
</tbody>
</table>

![Graph showing mean differences in WOMAC scores over 12 months follow-up]

The MedXcell biotech project

- SME created August 2018
- Founders:
  - CHU de Montpellier
  - Prof. John De Vos (UM/CHU)
  - Prof. Christian Jorgensen (UM/CHU)
  - Dr. Danièle Noël (DR2, Inserm)
  - MedXCell SA (World Trade Center, Av de Gratta-Paille 2, CH - 1018 Lausanne, Suisse)
- Implantation in « cyborg » incubator
- Capital 20 000€
- Benefit from science & clinical trials with support of FP7 ADIPOA, H2020 ADIPOA2, H2020 RESPINE
1. Adult mesenchymal stem cell tissue homeostasis and regeneration
2. Genome and stem cell plasticity in development and ageing
3. Genetic and immunopathology of inflammatory osteoarticular diseases
4. Lymphocytes differentiation, tolerance and metabolism: basis for immunotherapy
MedXcell objectives

• Develop Adipose derived Stem (ASC) based cell therapy in osteoarthritis & DDD
• Based on data obtained ADIPOA and RESPINE
• Inserm patent on ASC specific signature
• Develop, produce GMP grade innovative MedXcell cell product on the EU market
• Propose complete therapeutic package
Etapes de la thérapie cellulaire

1. Test d'éligibilité du donneur
2. Lipo-aspiration du donneur
3. Production cellulaire automatisée
   Bonnes pratiques de fabrication
   Contrôle qualité
4. Cryoconservation des doses thérapeutiques
5. Injection des doses décongelées par du personnel formé dans des centres agréés
6. Procédure d'envoi de doses thérapeutiques
7. Commandes traitées
strategy

- 2018: implement R&D ASC production centre
- 2019-2020: initiate phase 2/3 clinical trials of confirmation in DDD in partnership with Danish GMP facility
- 2021: open GMP cell facility Montpellier based on bioreactors
- 2022: MedXcell product on the EU market
MedXcell strategy

- **2018**: Production Process optimization UTC
- **2020**: GMP Production Process - Scale-up
- **Sept 2018**: GMP Production Process with DK
- **2021**: MedSpine trial (Europe) - Phase 2/3
- **MedSpine (US)** - Phase 3
- **2022**: Commercialisation
Barriers, challenges and opportunities for biomedical research & innovation in Europe – A policy view

Barbara Kerstiens
Head of Unit, Non-communicable diseases and the challenge of healthy ageing, DG for Research and Innovation, European Commission
Challenges and opportunities for biomedical research & innovation in Europe

Barbara Kerstiëns, MD, MPH
Head of unit
Health Directorate
DG Research & Innovation
European Commission

EULAR WAD Conference 2018,
Brussels, October 9 2018
Overview

• Horizon 2020
• Innovations stemming from research
• Horizon Europe
Horizon 2020 Health, demographic change and well-being challenge

**OBJECTIVE**

- Better health for all
- A more competitive European health industry and care sector
- Maximising the digital potential
- Addressing health as a global challenge
- Evidence for informed healthcare policies
Addressing musculoskeletal disorders – fostering innovations
€ 468 million on research on rheumatic and musculoskeletal diseases (2007-2017)

- Rheumatoid arthritis: 22%
- Osteoporosis: 2%
- Osteoarthritis: 9%
- Medical devices, prostheses and implants: 16%
- Cell therapy and tissue engineering:...
- Other musculoskeletal diseases: 13%
The ELECTOR project developed a web-based ICT platform for home-based monitoring of self-reliant patients with rheumatoid arthritis. This provides clinicians with a tool that can completely substitute a large proportion of the conventional visits at a rheumatologic outpatient clinic. An eHealth solution provides an integrated and direct collection of data into patient notes in the setup of an e-Health clinic.
an innovative set of biomarkers that is able to predict response to treatment with TNF-α inhibitors in Rheumatoid Arthritis (RA) to the market and clinical practice.
Aims for a radically new treatment for patients suffering from osteoarthritis (OA) of the knee – using a patient’s own stem cells. A large-scale clinical trial
Through a public private partnership

Develop new diagnostic methods to discover the early forms of Rheumatoid Arthritis and RA-like diseases - http://btcure.eu/

data on over 10 000 patients and healthy people used to identify groups of patients with similar profiles for a more personalised treatment https://www.approachproject.eu/
Commission proposal for
Horizon Europe

THE NEXT EU RESEARCH & INNOVATION PROGRAMME (2021 – 2027)

#HorizonEU
Horizon Europe: investing in R&I to shape our future

- The vision:
  "a Europe that protects, a Europe that empowers, a Europe that defends"
  *Jean-Claude Juncker*

- Tackling **climate change** (35 % budgetary target)

- Helping to achieve **Sustainable Development Goals**

- Boosting the Union's **competitiveness and growth**
While benefiting from world–class research and strong industries…

→ 7%
→ 20%
→ 1/3

…Europe fails to transform leadership in science into leadership in innovation and entrepreneurship
Lessons Learned
Novelties
from Horizon 2020 Interim Evaluation

- Support breakthrough innovation
- Create more impact through mission-orientation and citizens' involvement
- Strengthen international cooperation
- Reinforce openness
- Rationalise the funding landscape

Key
in Horizon Europe

- European Innovation Council
- R&I Missions
- Extended association possibilities
- Open science policy
- New approach to Partnerships
Horizon Europe: evolution not revolution

Specific objectives of the Programme

- Support the creation and diffusion of high-quality knowledge
- Strengthen the impact of R&I in supporting EU policies
- Foster all forms of innovation and strengthen market deployment

Optimise the Programme’s delivery for impact in a strengthened ERA

Pillar 1
Open Science
- European Research Council
- Marie Skłodowska-Curie Actions
- Research Infrastructures

Pillar 2
Global Challenges and Industrial Competitiveness
- Health
- Inclusive and Secure Society
- Digital and Industry
- Climate, Energy and Mobility
- Food and natural resources
- Joint Research Centre

Pillar 3
Open Innovation
- European Innovation Council
- European innovation ecosystems
- European Institute of Innovation and Technology

Strengthening the European Research Area
- Sharing excellence
- Reforming and Enhancing the European R&I system
Global Challenges & Industrial Competitiveness:

<table>
<thead>
<tr>
<th>Area</th>
<th>Funding (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clusters</td>
<td>52.7 billion</td>
</tr>
<tr>
<td>implemented through usual calls, missions &amp; partnerships</td>
<td>2021-24</td>
</tr>
<tr>
<td>Health</td>
<td>€ 7.7</td>
</tr>
<tr>
<td>Inclusive and Secure Societies</td>
<td>€ 2.8</td>
</tr>
<tr>
<td>Digital and Industry</td>
<td>€ 15</td>
</tr>
<tr>
<td>Climate, Energy and Mobility</td>
<td>€ 15</td>
</tr>
<tr>
<td>Food and Natural Resources</td>
<td>€ 10</td>
</tr>
<tr>
<td><strong>Joint Research Centre</strong></td>
<td><strong>€ 2.2</strong></td>
</tr>
<tr>
<td>supports European policies with independent scientific evidence &amp; technical support throughout the policy cycle</td>
<td><strong>2021-27</strong></td>
</tr>
</tbody>
</table>
Pillar 2: Cluster 1
“Health”
Rationale for EU funded health R&I

*Everyone has the right to timely access to affordable healthcare of good quality*

Newly emerging or persisting health challenges:
- Threats to citizens and public health
- Sustainability of social and health care systems
- Competitiveness of EU's health and care industry

→These challenges are complex, interlinked and global

The Health Cluster builds linkages between:
- Discovery, clinical, epidemiological, environmental and socio-economic research
- Academia – industry – healthcare providers – patients
- Expertise within the EU and beyond

* EU Pillar of Social Rights, UN SDGs
Aligned with major European policy goals…

- EU Pillar of Social Rights
- EU Digital Single Market
- EU Directive on cross-border healthcare
- European One Health Action Plan against antimicrobial resistance (AMR)

...and with global strategies
- United Nation's 2030 Agenda for Sustainable Development
- World Health Organization (WHO)
Six main areas of intervention

- Health throughout the Life Course
- Environmental and Social Health Determinants
- Non-communicable and Rare Diseases
- Infectious diseases
- Tools, Technologies and Digital Solutions for Health and Care
- Health Care Systems
Cross-cutting issues

- **Digitalisation and personalisation** of health and care cut across all intervention areas

- **Health economics** and **health systems** are key for uptake of results and achieving impact

- **Patient-centered solutions and technologies** for health and care call for integrated approaches from medicines to medical devices (supported in Horizon 2020 under the pillar ‘Leadership in Enabling and Industrial Technologies’)

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https://www.facebook.com/cmoedas/

http://ec.europa.eu/horizon-europe
http://ec.europa.eu/research/eic
http://ec.europa.eu/budget/mff/index_en.cfm

Thank you!
Pierre Meulien
Executive Director, Innovative Medicines Initiative
Health Innovation: Tackling Chronic diseases

Pierre Meulien- Executive Director- Innovative Medicines Initiative
EULAR Conference 2018- Bringing Chronic Diseases to the Forefront of Health Innovation
What is driving the profound changes in the world of healthcare

- Science and technology (including digital technology)
- The epidemiology of disease (global trends - outbreaks etc)
- The role (and behaviour) of the consumer of healthcare - the patient
- Unsustainable financial burden of chronic disease on our health systems

All actors involved in the system from public or private spheres have to adapt to the impacts of these four drivers
What determines health of an individual

- Their Genome (+)
  - Epigenome
  - Microbiome

- Their Environment
  - Demographic
  - Nutrition
  - Air and water quality
  - Exposure to infectious diseases
  - Lifestyle
Molecular Medicine Continuum

Health Maintenance and Disease Prevention

Early Detection

Treatment of Disease

Increasing Knowledge of Underlying Disease Mechanisms

Environment

Behaviour

Lifestyle
“Big” Health Data

Genomic data
Population registries, Clinical trials databases
Bio-sensors
Care pathways, decision support, trends and alerts
Environmental data
Mobile devices
Social networks
Clinical applications
Investment Priorities  (a personal view)

- Prevention

- Bring more innovative health economics into mainstream thinking

- Integrate social sciences and humanities into health R&I

- Investing in the application of digital solutions when they make sense

- Creating more productive interfaces between health systems and innovation providers – in an integrated manner

- Educating the public so that they can adjust lifestyles and behaviours
IIMI 10th Anniversary Scientific Symposium
October 22-23, Brussels

IMI Stakeholder Forum
October 24, Brussels

Thank you!
Innovation in Science

“From population to the lab and back to individualized health care”

Prof. Dr. T.R.D.J. Radstake
Department of Rheumatology and Clinical Immunology
Laboratory of Translational Immunology
Director UMC Utrecht Infection & Immunity FOCIS Center of Excellence
University Medical Center Utrecht
The Netherlands.

EULAR WAD conference— Oct 9th 2018
History of medical practice = symptom / location driven

We use proxy markers to measure disease activity and determine therapy strategy.
RMDs in Medicine in the (near) future....

Thinking the unthinkable

Rheumatology 4.0: big data, wearables and diagnosis by computer

Nothing is unthinkable, nothing impossible to the balanced person, provided it comes out of the needs of life and is dedicated to life’s further Development.

Lewis Mumford, US historian, sociologist, philosopher and literary critic. 19 October 1895–26 January 1990
Etiology of RMDs – a molecular multihit model

- **Health**: No autoimmunity without additional hits
- **Preclinical disease**: Incremental ‘hits’
- **Clinical disease**: Clinical symptoms that occur after the initial hits in the hit model
- **Severe disease**: Incremental ‘hits’

**Severity of clinical symptoms**

**Incremental ‘hits’**

- **Past clinical practice**: Hit 1
- **Current clinical practice**: Hit 2
- **Future clinical practice**: Hit n

*van der Vlist et al. NRR 2016*
Times are changing......data driven medicine
Principles of Personalised Medicine
Molecular classification of disease
Primary Sjogren's syndrome (pSS) as an example

- **Low risk**
  - No GC or LFS 1
  - No lymphoma, less EG manifestations

- **High risk**
  - GC or LFS >3
  - High chance of lymphoma and increased EG manifestations

- **Non-Sjogren sicca**
  - LFS <1

Which factors contribute to increased LFS and lymphoma development?

- No predictive biomarkers / molecular fingerprints
- No treatment available
Molecular profiling: nSS = pSS!

Healthy donors vs. non-Sjogren sicca vs. Sjogrens syndrome

- **Discovery**
  - nSS vs. HC: 1823
  - pSS vs. HC: 2238
  - pSS vs nSS: 103

- **Replication**
  - nSS vs. HC: 1054
  - pSS vs. HC: 368
  - pSS vs nSS: 1147
  - pSS vs nSS: 84
  - pSS vs nSS: 2317
  - pSS vs nSS: 1164

- **Coordinate 1 vs. Coordinate 2**
  - Healthy donors (HC)
  - nSS
  - pSS
Outliers in big data – incorrect clinical decisions?

Biopsy analysis (local activity)

3.5 yrs after diagnosis nSS re-invited

nSS2 now LFS of 1.7

= progression to Sjogrens disease

Manuscript in preparation
Can we predict progression from nSS → pSS

<table>
<thead>
<tr>
<th>Donor</th>
<th>Meets new Criteria</th>
<th>LFS (/4mm²)</th>
<th>Anti-Ro/ SSA Schirmer (/5min)</th>
<th>UWS (/5min)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>nSS1</td>
<td>yes</td>
<td>1.0</td>
<td>neg</td>
<td>3.5</td>
<td>0.0</td>
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<tr>
<td>nSS8</td>
<td>no</td>
<td>0.0</td>
<td>pos</td>
<td>18</td>
<td>4.5</td>
</tr>
<tr>
<td>nSS1</td>
<td>yes</td>
<td>0.6</td>
<td>pos</td>
<td>0.0</td>
<td>0.3</td>
</tr>
<tr>
<td>nSS7</td>
<td>yes</td>
<td>0.5</td>
<td>pos</td>
<td>3.0</td>
<td>0.1</td>
</tr>
<tr>
<td>nSS9</td>
<td>no</td>
<td>0.9</td>
<td>neg</td>
<td>12</td>
<td>0.1</td>
</tr>
<tr>
<td>nSS11</td>
<td>no</td>
<td>0.0</td>
<td>neg</td>
<td>16</td>
<td>0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor</th>
<th>Meets new Criteria</th>
<th>LFS (/4mm²)</th>
<th>Anti-Ro/ SSA Schirmer (/5min)</th>
<th>UWS (/5min)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>nSS3</td>
<td>no</td>
<td>0.0</td>
<td>neg</td>
<td>2.5</td>
<td>0.6</td>
</tr>
<tr>
<td>nSS4</td>
<td>no</td>
<td>0.7</td>
<td>neg</td>
<td>40</td>
<td>0.6</td>
</tr>
<tr>
<td>nSS6</td>
<td>no</td>
<td>0.2</td>
<td>neg</td>
<td>3.5</td>
<td>1.0</td>
</tr>
<tr>
<td>nSS7</td>
<td>yes</td>
<td>1.3</td>
<td>neg</td>
<td>4.0</td>
<td>4.5</td>
</tr>
<tr>
<td>nSS2</td>
<td>no</td>
<td>0.0</td>
<td>pos</td>
<td>24</td>
<td>1.7</td>
</tr>
<tr>
<td>nSS5</td>
<td>no</td>
<td>0.6</td>
<td>neg</td>
<td>18</td>
<td>0.8</td>
</tr>
<tr>
<td>nSS10</td>
<td>no</td>
<td>0.0</td>
<td>pos</td>
<td>8.0</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*Manuscript in preparation*
Big Data → Social networks of genes → target prediction → trial design

Molecular profiling of immune cells

Healthy donors vs. non-Sjogren sicca vs. Sjogrens syndrome

Discovery

Repetition
Big Data → **Social networks of genes** → **target prediction** → **trial design**

**TLR mediated DC activation**
**Hydroxychloroquine**

**PBMCs**
**Antigen mediated activation**
**Leflunomide**

Fold change (log2) 1.0 0.6 0.2
Additive effects of combination leflunomide + hydroxychloroquine

Big Data → Social networks of genes → target prediction → trial design
Molecular profiling

Big Data → Social networks of genes → target prediction → trial design
RepurpSS-I – clinical efficacy on primary and secondary endpoints

**ESSDAI (clinical disease activity)**

**SWS (Oral dryness)**
RepurpSS-I – An ideal opportunity for stratification of response?

**ESSDAI** (clinical disease activity)

![Graph showing ESSDAI over weeks for responders and non-responders](image-url)
RepurpSS-I – Response prediction by a complex model

89% correctly predicted

ESSDAI (clinical disease activity)
Innovation in RMDs – the use of big data in Clinical decision support
Conclusions – innovation in healthcare in RMDs

- Molecular fingerprints enable early diagnosis and prediction of disease progression in RMDs and find their way to clinics – clinical decision support in RMDs

- Computational analysis of deep molecular data from patients with RMD lead to novel trial design – data driven – paving the way for effective therapies

- Drug repurposing on the basis of analysis of big data is a huge opportunity to treat EU citizens with relatively cheap therapeutic options. Drug repurposing is an attractive tool to significantly lower healthcare costs without compromising efficacy.

- Personalised medicine using molecular fingerprints - Bringing the right drug to the right patients and the right moment is becoming feasible fast.

- EULAR fosters projects to innovate in RMD research
  - EULAR projects: EULAR recommendations for the use of Big Data in RMDs.
  - Virtual EULAR Centre of Research and Innovation.
Workshop 1

Can citizens have a leading role in health care innovation?

Chairs:
Dieter Wiek
EULAR

Elsa Mateus
EULAR & Portuguese League Against Rheumatic Diseases

#EULARBrussels2018
2 Tasks

- Challenges/barriers for citizens-centred innovation

- What should policy makers and stakeholders do to ensure health innovation meets citizens needs and priorities?
Hurdles preventing citizens to have a leading role in health innovation

• Lack of education of researchers to include patients
• Lack of basic/common understanding, lack of communication skills
• Lack of incentive for research
• Hindrances for patients: time; accessibility, competences
What should policy makers and stakeholders do to ensure health innovation meets citizens needs and priorities?

<table>
<thead>
<tr>
<th>EU</th>
<th>Member States / Regions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mandatory involvement of patients from de beginning (design of projects) till the end</td>
<td>• Training of patients / patient academy</td>
</tr>
<tr>
<td>• Overcome languages barriers</td>
<td>• Training of professionals</td>
</tr>
<tr>
<td>• Marketing of research results</td>
<td>• Recognition of the role of expert patients</td>
</tr>
</tbody>
</table>

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What should policy makers and stakeholders do to ensure health innovation meets citizens needs and priorities?

<table>
<thead>
<tr>
<th>Patient’s/Consumer’s organisations</th>
<th>Other stakeholders</th>
</tr>
</thead>
<tbody>
<tr>
<td>• European Citizen/patient umbrella organisations defining own projects and priorities</td>
<td>• Scientific support</td>
</tr>
<tr>
<td>• European umbrella organisations providing support to national organisations, capacity building</td>
<td>• Role of expert patient</td>
</tr>
<tr>
<td>• Empowering national organisations</td>
<td></td>
</tr>
</tbody>
</table>

#EULARBrussels2018
Workshop 2
Organisational and human challenges in the introduction of digital solutions in health care services

Chairs:
Prof. Laure Gossec
EULAR & Université Pierre et Marie Curie

Pascal Garel
European Hospital and Healthcare Federation - HOPE

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What are the main challenges in the implementation of digital solutions in health care services?

1. Interoperability/integration (lack of standardisation)
2. Costs and cost-benefit evidence
3. Variability (practical application)
4. Patient and health care provider behaviour
5. Data privacy
6. Accessibility barriers (e.g. language, digital infrastructure, digital literacy)
What should policy makers and stakeholders do to facilitate an adequate implementation of digital solutions?

<table>
<thead>
<tr>
<th>Other stakeholders</th>
<th>Health care providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Researchers: understanding of best digital solutions (evidence-based, incl. economic benefits)</td>
<td>• Defining core sets of outcomes/data</td>
</tr>
<tr>
<td>• Codes of conduct/quality standards developed by all stakeholders (incl. patient organisations)</td>
<td>• Increased collaboration</td>
</tr>
<tr>
<td>• Sustainable business models</td>
<td></td>
</tr>
<tr>
<td>• Patient engagement in product development</td>
<td></td>
</tr>
<tr>
<td>• EULAR recognition of good projects</td>
<td></td>
</tr>
</tbody>
</table>

#EULARBrussels2018
What should policy makers and stakeholders do to facilitate an adequate implementation of digital solutions?

<table>
<thead>
<tr>
<th>EU</th>
<th>Member States / Regions/payers</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Targeted and increased investment (common priority-setting)</td>
<td>• Targeted investment</td>
</tr>
<tr>
<td>• Recognition of best practices at EU level (targeted awards)</td>
<td>• Incentives (financial or other)</td>
</tr>
<tr>
<td>• Understanding of best digital solutions in Europe (evidence-based), incl. stamp of approval at EU level also considering data privacy</td>
<td>• Taking on board European guidelines and best solutions</td>
</tr>
<tr>
<td>• Bottom-up development of standards for interoperability</td>
<td>• Developing standards for electronic health records</td>
</tr>
<tr>
<td>• Data sharing agreements (templates)</td>
<td>• Interoperability</td>
</tr>
<tr>
<td>• Patient engagement projects and inclusion in panels</td>
<td>• Awareness and education</td>
</tr>
</tbody>
</table>
Workshop 3

Policy issues in the use of big data in health care and research

Chairs:
Prof. Loreto Carmona
EULAR

Carolina Rubio Miner
Savana Médica

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What are the main challenges/barriers in the use of big data in health care and medical research?

<table>
<thead>
<tr>
<th>1. <strong>FEAR OF RISK</strong> due to lack of regulation and knowledge on possible uses of personal health data</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. <strong>FRAGMENTATION</strong> in terms of missing interoperability of national and local health care systems (IT, teams...) and in terms of unstructured collection of data</td>
</tr>
<tr>
<td>3. <strong>LACK OF TRUST</strong> when it comes to ethical issues, ownership and privacy of personal health care data</td>
</tr>
</tbody>
</table>
What should policy makers and stakeholders do to facilitate address these challenges and barriers?

<table>
<thead>
<tr>
<th>EU</th>
<th>Member States / Regions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• REGULATIONS to guarantee safe health data collection and use (easy and clear)</td>
<td>• IMPLEMENTATION AND INFORMATION on rules and regulations that safeguard data ownership and privacy</td>
</tr>
<tr>
<td>• INFORMATION and RISING AWARENESS on the benefits of big data and new technologies</td>
<td>• IMPROVE interoperability of national and local health systems</td>
</tr>
<tr>
<td>• RECONCILIATION between GDPR and research</td>
<td></td>
</tr>
</tbody>
</table>
Workshop 4

How to foster innovation through Horizon Europe (FP9)?

Chairs:
Prof. Xenofon Baraliakos
EULAR

Prof. George Griffin
FEAM

#EULARBrussels2018
1. Increasing budget of Horizon Europe and prioritise allocation of EU funds for health cluster
2. Implementation of ‘moon-shot’ missions in the health sector
3. Balance between basic & clinical research and innovation
4. Relevance of the UN Sustainable Development Goals
5. Identification of the most relevant areas of intervention for health research & innovation
6. Participation of scientific societies, health professionals and patients in strategic programming process
7. Connections between different pillars and funding instruments of Horizon Europe
8. Others?
What are the solutions to the Top-3 challenges?

| Challenge: (6) Participation of scientific societies, health professionals and patients in strategic programming process |
| Recommendation(s): Intersocietal education and communication, involved from the very start. To define and enhance endpoints/aims. PRP involvement. |
### What are the solutions to the Top-3 challenges?

| Challenge: (6) Participation of scientific societies, health professionals and patients in strategic programming process |
| Recommendation(s): Intersocietal education and communication, involved from the very start. To define and enhance endpoints/aims. PRP involvement. |

| Challenge: (3) Balance between basic & clinical research and innovation |
| Recommendation(s): 1) maintain appropriate good balance between areas, 2) Support moon shot projects with potential breakthrough, 3) encourage training and education |
What are the solutions to the Top-3 challenges?

<table>
<thead>
<tr>
<th>Challenge: (6) Participation of scientific societies, health professionals and patients in strategic programming process</th>
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</thead>
<tbody>
<tr>
<td>Recommendation(s): Intersocietal education and communication, involved from the very start. To define and enhance endpoints/aims. PRP involvement.</td>
</tr>
<tr>
<td>Challenge: (3) Balance between basic &amp; clinical research and innovation</td>
</tr>
<tr>
<td>Recommendation(s): 1) maintain appropriate good balance between areas, 2) Support moon shot projects with potential breakthrough, 3) encourage training and education</td>
</tr>
<tr>
<td>Challenge: (8) Reduce the gap of entrepreneurship between Europe and the rest of the world</td>
</tr>
<tr>
<td>Recommendation(s): 1) Identify reasons for the gap and 2) use the information to be included in dedicated future calls</td>
</tr>
</tbody>
</table>