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Single Day Event

Next Gen Statistical Programming and Digital Health

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Agenda

- Evolution of digital health
- Industry landscape
- Regulatory Perspective
- Process of DHT employed in clinical trials from Biometrics perspective
- AZ case study
- Potential challenges – Biometrics
- Lessons learnt / Conclusion

Evolution of Digital Health Technology(DHT) in Clinical Trials

Source - https://dimesociety.org/communication-education/library-of-digital-endpoints/

What is Digital Health?

Digital health is the convergence of **digital technologies** with health, healthcare, living, and society **to enhance** the efficiency of healthcare delivery and make medicines more **personalized and precise.**

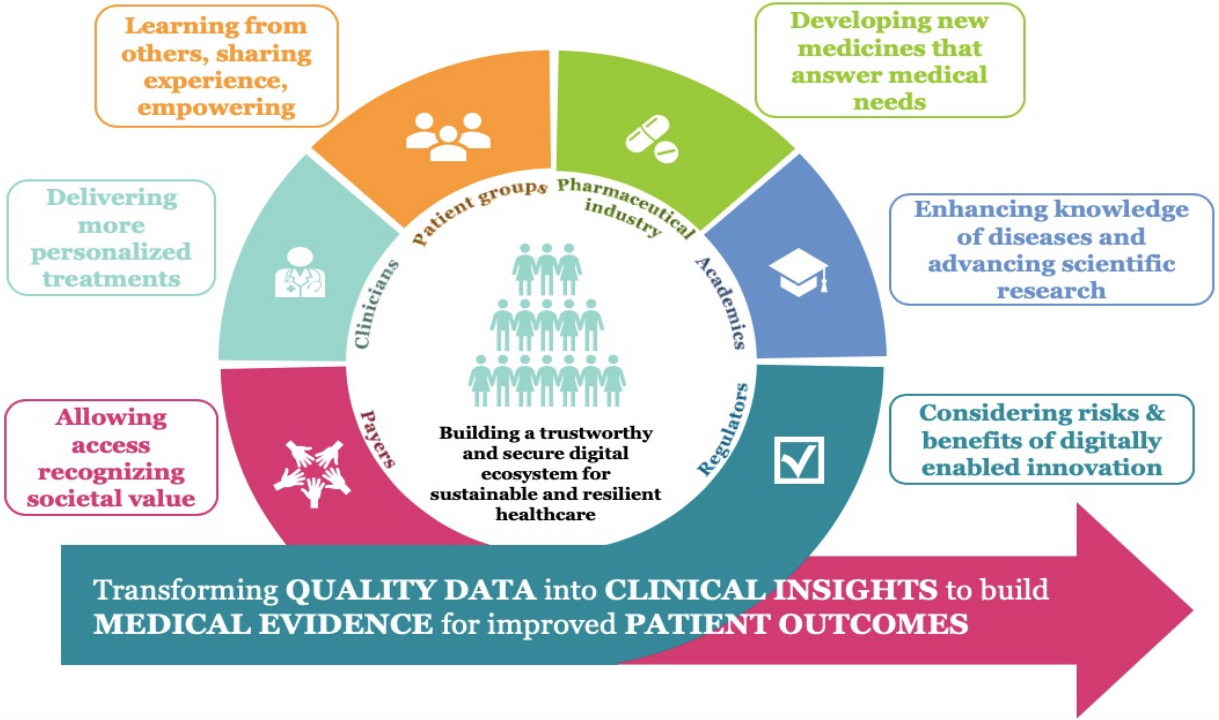
It means embracing **information technology, big data, AI and machine learning** to collect, share, analyze and use data on patient outcomes to help healthcare professionals make **informed decisions** and to **improve care**.

Source- Wikipedia

Use of Digital Technology in Healthcare Industry

Source - https://www.efpia.eu/about-medicines/development-of-medicines/digital-health/

Digital Ecosystem



Source - https://www.efpia.eu/about-medicines/development-of-medicines/digital-health/

Regulatory Perspective

- The FDA has created the Digital Health Center of Excellence within the Center for Devices and Radiological Health (CDRH) .
- FDA has authorized more than 500 AI/ML – enabled devices
- EMA has recently released guidance on use of digital technology to capture electronic trial data
- Japan's Pharmaceuticals and Medical Devices Agency (PMDA) has translated a document about the use of "electromagnetic means" to get informed consent from participants in clinical trials and post market studies.

GUIDANCE DOCUMENT

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Draft Guidance for Industry, Investigators, and Other Stakeholders

JANUARY 2022

Download the Draft Guidance Document | Read the Federal Register Notice

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

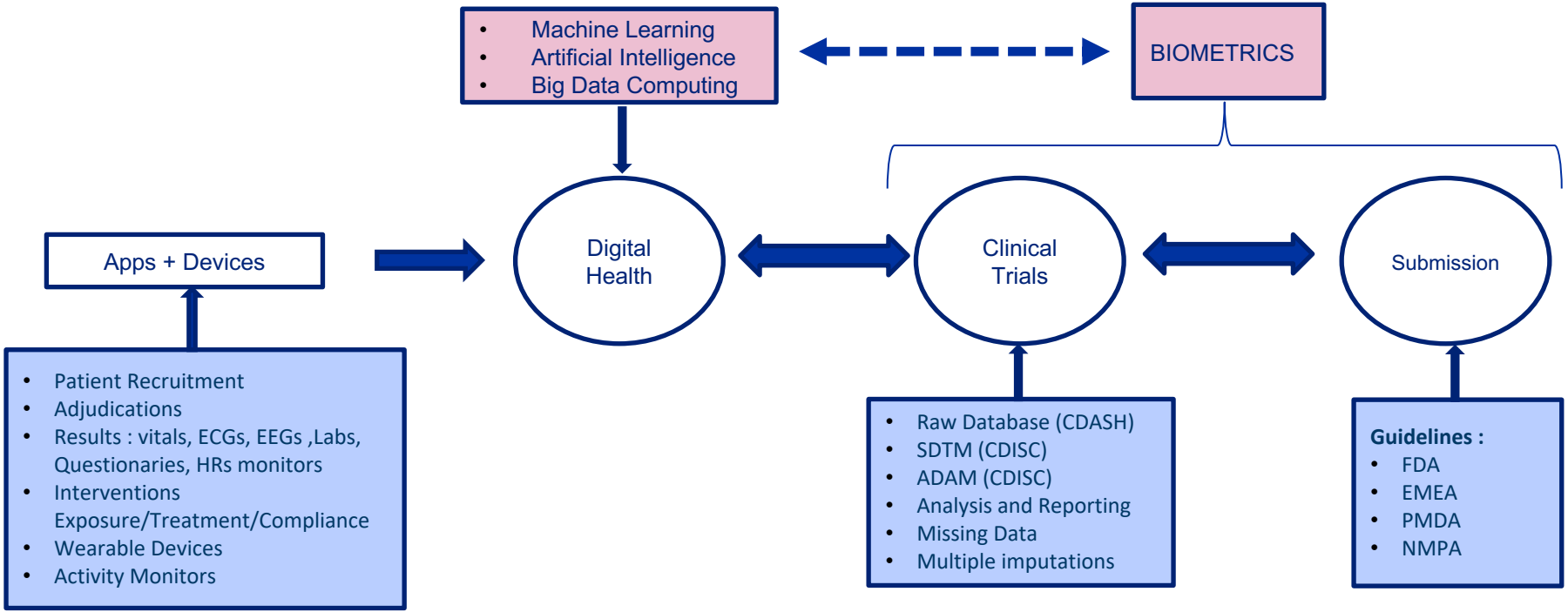
9 March 2023
EMA/INS/GCP/112288/2023
Good Clinical Practice Inspectors Working Group (GCP IWG)

Guideline on computerised systems and electronic data in clinical trials

www.fda.gov/digitalhealth

https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-electronic-data-clinical-trials_en.pdf

Process of DHT employed in Clinical Trials from Biometrics Perspective



CASE Study - Determine-Preserved and Determine-Reduced

International, multi-centre, parallel-group, randomized, double-blind, placebo controlled , Phase III studies with HFpEF and HFrEF respectively evaluating the effect of Dapagliflozin 10 mg vs Placebo on changes in HF system

Primary Objective

To determine whether dapagliflozin is superior to placebo in patients with chronic HFrEF and reduced ejection fraction (LVEF ≤ 40%) [HFrEF] in:

- reducing patient-reported HF symptoms
- reducing patient-reported physical limitation
- improving exercise capacity

Outcome Measures

Family of primary endpoints:

- Change from baseline in the KCCQ-TSS at week 16.
- Change from baseline in the KCCQ-PLS at week 16.
- Change from baseline in 6MWD at week 16.

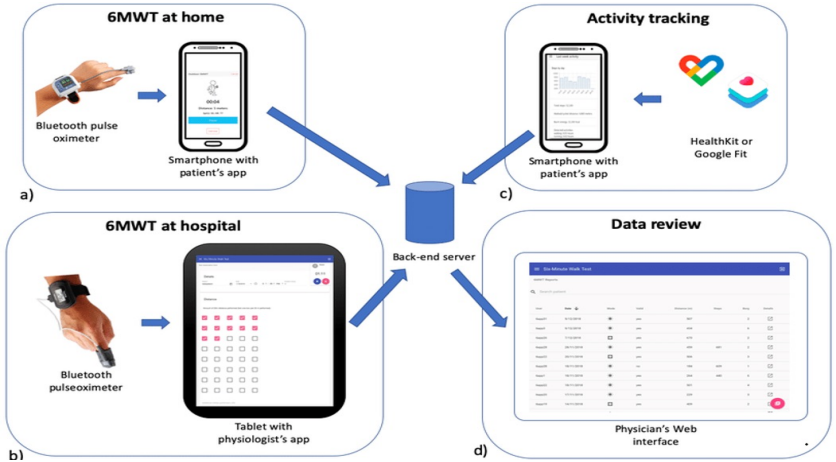
HFrEF – Heart failure with reduced ejection fraction , HFpEF - Heart failure with preserved EF
KCCQ - Kansas City Cardiomyopathy Questionnaire (KCCQ)

CASE Study - Determine-Preserved and Determine-Reduced

- Electronic Patient Reported Outcomes (ePROs) were used to assess health status of subjects by EQ-5D-DL, Quality of Life, Social Limitations, symptom burden and system stability.
- Patients performed assessments by using site-based tablets during clinical visits.

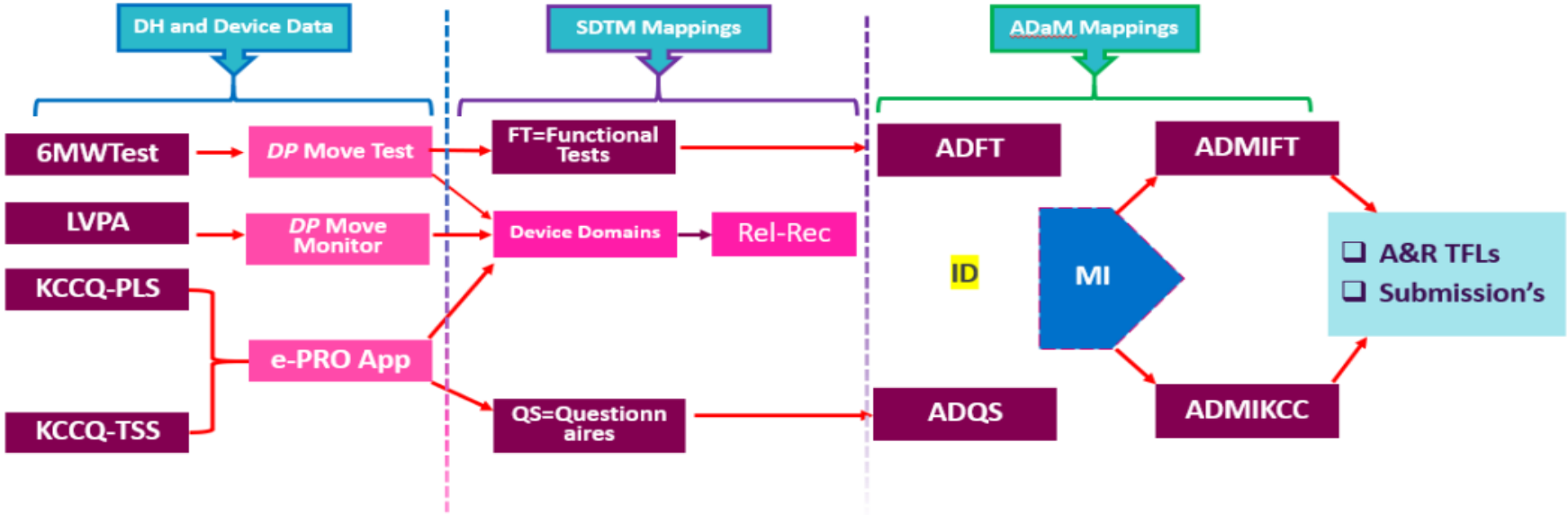
Two different Accelerometers were used

- Move Test Accelerometer was used at clinic and was used to evaluate primary endpoint of 6MWD
- Move Monitor accelerometer was used by patients at home as wearable device to assess physical ability during day-to-day activities.



Source – Google image

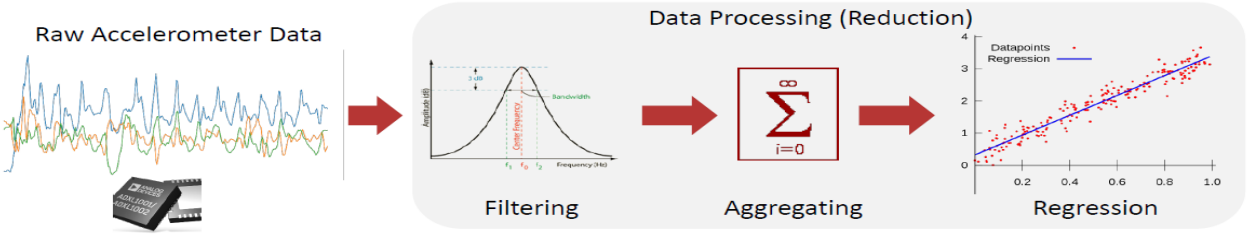
Case Study – Data Mapping Process



Figures 2: Implicating the Mapping process for the Device and DHT Data from Raw Data Collection to Submission, 6MWTest= Six Min Walk Test, LVPA= Light to Vigorous Physical Activity, PLS= Physical Limitation Score, TSS=Total Symptom Score, ID=Intermediate Datasets, MI=Multiple Imputation, AD=ADaM, A&R=Analysis and Reporting.

Programming Challenges

- Complexity of analyses combined with huge volume of data were additional challenge for digital endpoint data.



- Metadata and data generated from accelerometers did not conform to AZ raw data standards.
- Additional efforts required in mapping to CDISC compliant data.
- There were differences in proportion of missing data from devices used at home versus at clinic.
  - Data generated by accelerometer at clinic was more complete than data generated by move monitor used by patients at home.
  - There was very small proportion of missing data generated by e-PRO instruments

https://healthpolicy.duke.edu/events/digitalhealthtechnologies

Case Study-Lessons Learnt

- Risk Management plan
- High volume of data
- Standardization
- Statistical procedures
- Data privacy and integrity

Conclusion

- Increased Integration of Digital Health in Clinical Trials
- Decentralized Trials are increasingly Popular
- Biometrics groups need to build and expand capabilities to seize opportunities
- Rapid Technology Evaluation and Adoption
- Patient Centricity

The Global Healthcare Data Science Community

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