TRANSFoRm

The Learning Health System in Europe

Using health data for innovative trial designs

Stuart Dollow

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www.vermilion-lifesciences.co.uk

Why is this important?

- Medicines development is risky, time and cost intensive
- Pipeline failures increase cost of development and cost of medicines
- High medicine costs reduce patient access and benefit
- The $2.6bn problem

- Curative Hepatitis C therapy
- 12 week course
- $84,000 / €51,000 - €41,000

- Alternate week lipid lowering MAb
- Lifetime treatment
- $14,100 pa / €7,000 – €8,000

- Malignant melanoma IgG4 PD-1 Checkpoint inhibitor
- Every 3 weeks
- $150,000 pa / ~£69,000 pa

- Squaring the circle of affordability, cost effectiveness and uptake vs risk, investment prioritisation and need for return

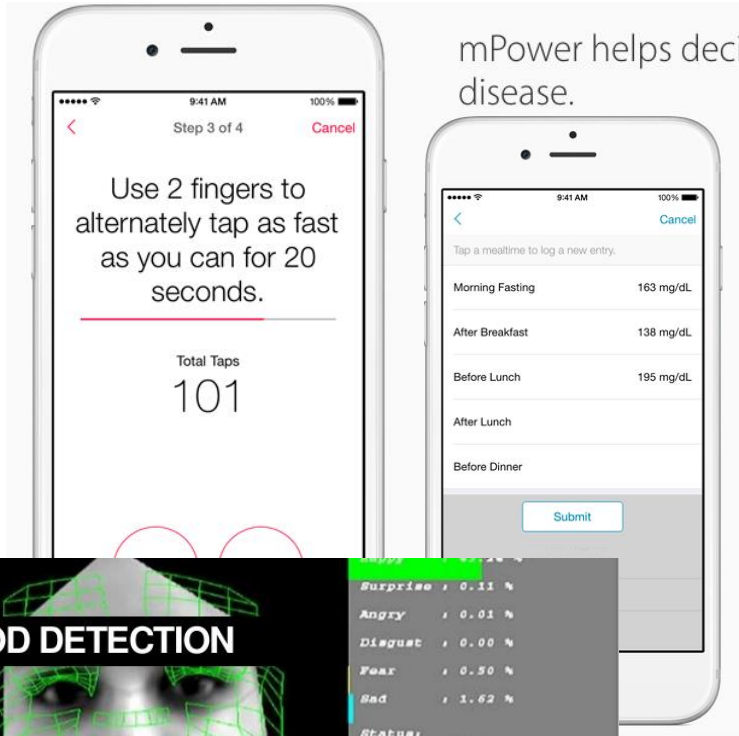
Regulatory Requirements

- Regulatory hurdles to protect public
  - Safety scares increase desire for certainty, study duration and exposure
  - RCT seen as the gold standard
  - Poorly relevant to reimbursement needs or real life clinical practice
- New models provides opportunity to capitalise on new data
  - MAPPs / 21st Century Cures / Conditional approval
  - Change the paradigm of *'RCT Studies – Approval - Widespread use'*
- Improve on RCTs with a new methodology?
  - Faster, less costly, more relevant while protecting public health
  - Develop real world utility assessment
  - Build on observational studies: the 'poor relation' of RCTs

Health Data - measures of patient value

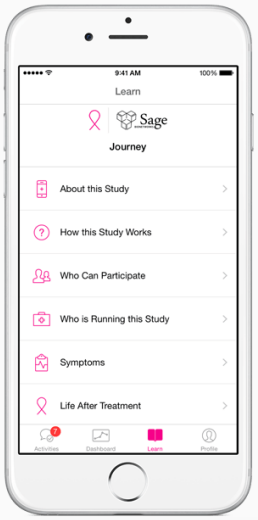
- mHealth devices capture relevant patient data in clinical trials
- Involving patients in design and data parameters

Collection: Active input with passive measures



mPower helps decipher Parkinson's disease.

Keeping tabs to keep diabetes in check.



Integration: Correlate labs with other inputs

Following the post-treatment journey of breast cancer patients.

The Dana-Farber School of Public Bionetworks dev learn more abou chemotherapy u enables particip information abo mood. The study a better post-tre

Share the Journey
Dana-Farber Cancer Institute, UCLA Fielding School of Public Health, Penn Medicine and Sage Bionetworks
View in the US App Store ›

To see how your activity levels correlate to symptoms, you need to input data on a regular and frequent basis. Your iPhone enables this while you're on the go — daily or even hourly.

Endurance: Reducing loss to follow up. Active reminders and passive collection

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Health Data – Design benefits

- Identify patient populations in databases
  - Traditional approach for RCTs
    - Prevalence and incidence
    - Geographic distribution
    - Feasibility and selection criteria
  - Disruptive approach
    - Wider cohort for more representative population
    - Improve patient measures to improve participation (RWD)
    - Broaden comparator evaluation
    - Improved IMP management

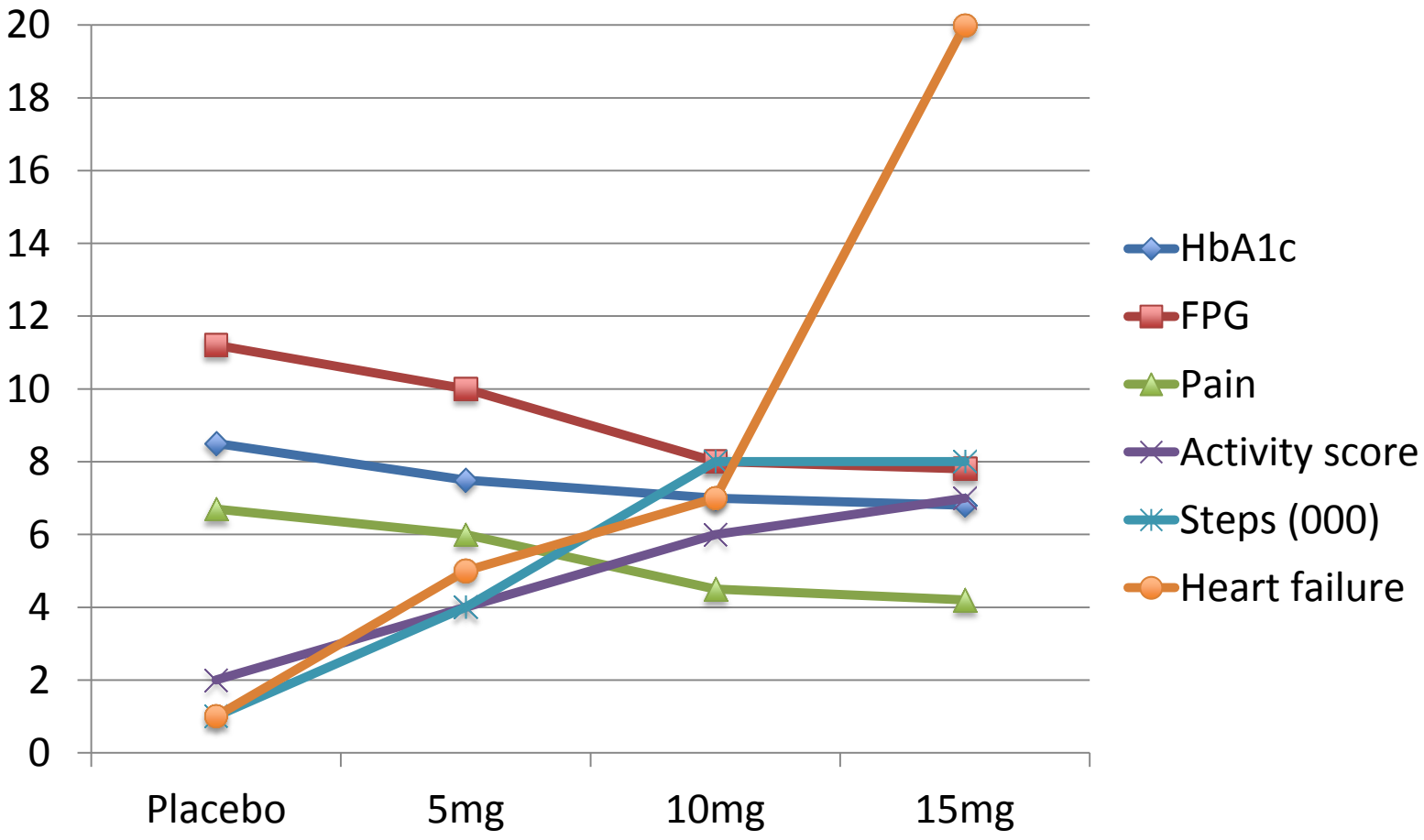
Health Data – Comparator and IMP benefits

- Cluster randomisation to investigational product
  - Open label or single blind geographic cohorts
- Matched case control
  - Standard of care = placebo
  - Standard of care plus competitor = comparative effectiveness
  - New comparator flexibility
- Disruptive Benefits (Front / Middle / Back)
  - Substantial time & cost savings (IMP / patient accrual)
  - Simultaneously generate data for regulatory approval and reimbursement
- Real time data feeds for ongoing viability assessment
  - In existing or sponsor constructed databases depending on parameters

Health Data – Ongoing indicative value assessment

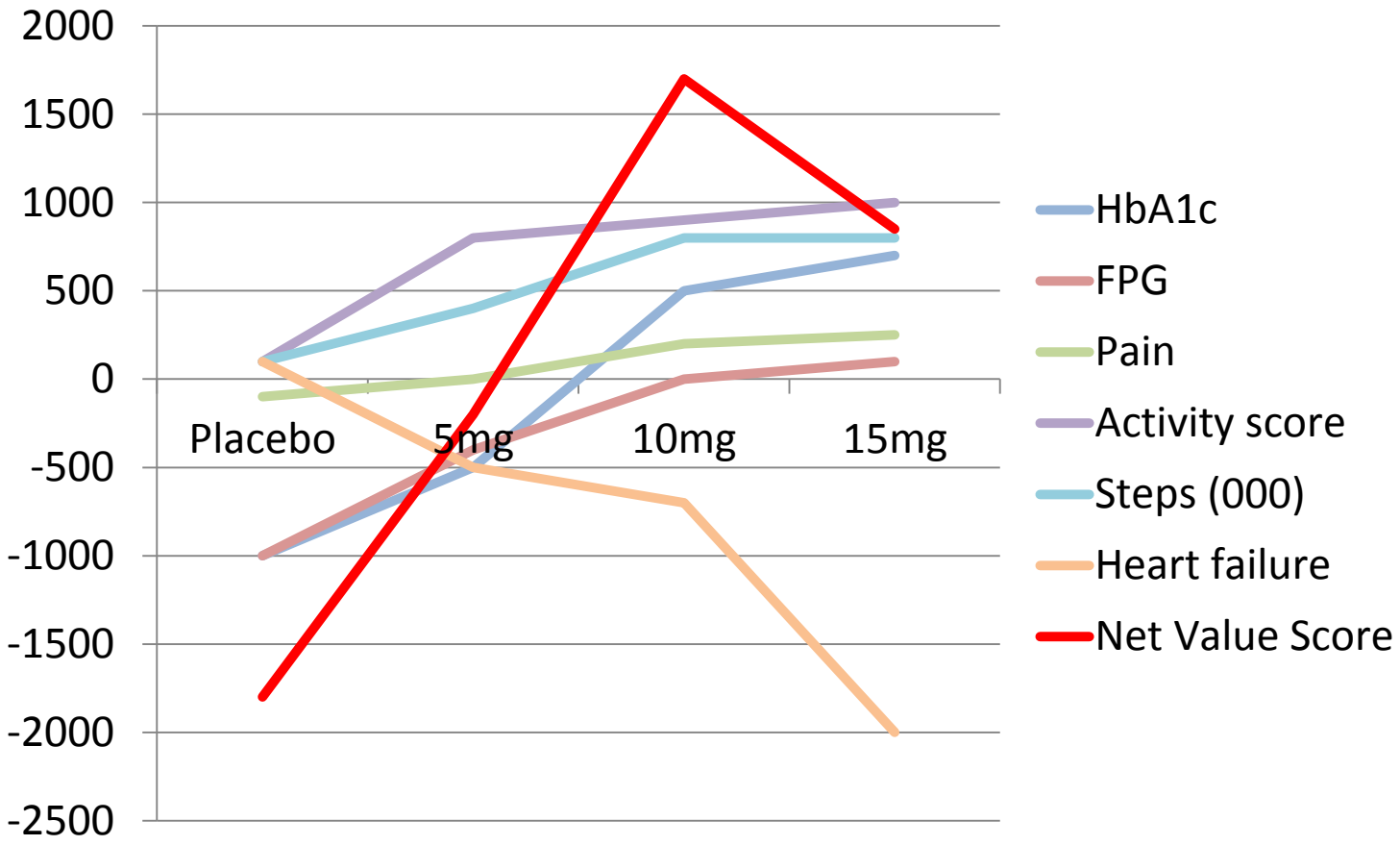
- Target Product Profile
  - Regulatory efficacy and safety parameters
  - Patient QoL and benefit measures
- Indicative prediction to assess net value
  - Efficacy benefits vs safety / tolerability penalties
  - Weighted patient relevant measures
  - Construct value : response curves for each parameter
  - Fit value curve to price models to estimate cost effectiveness
  - Set individual and net thresholds for progression or termination in TPP
- Value indicators become development decision factor
  - Knowledge of likely acceptable price for sponsor / payer
  - Ability to analyse in real time and investigate stratification if needed

Hypothetical Data Series



Hypothetical Value Indicator Scale

Impact value apportioned to each data scale

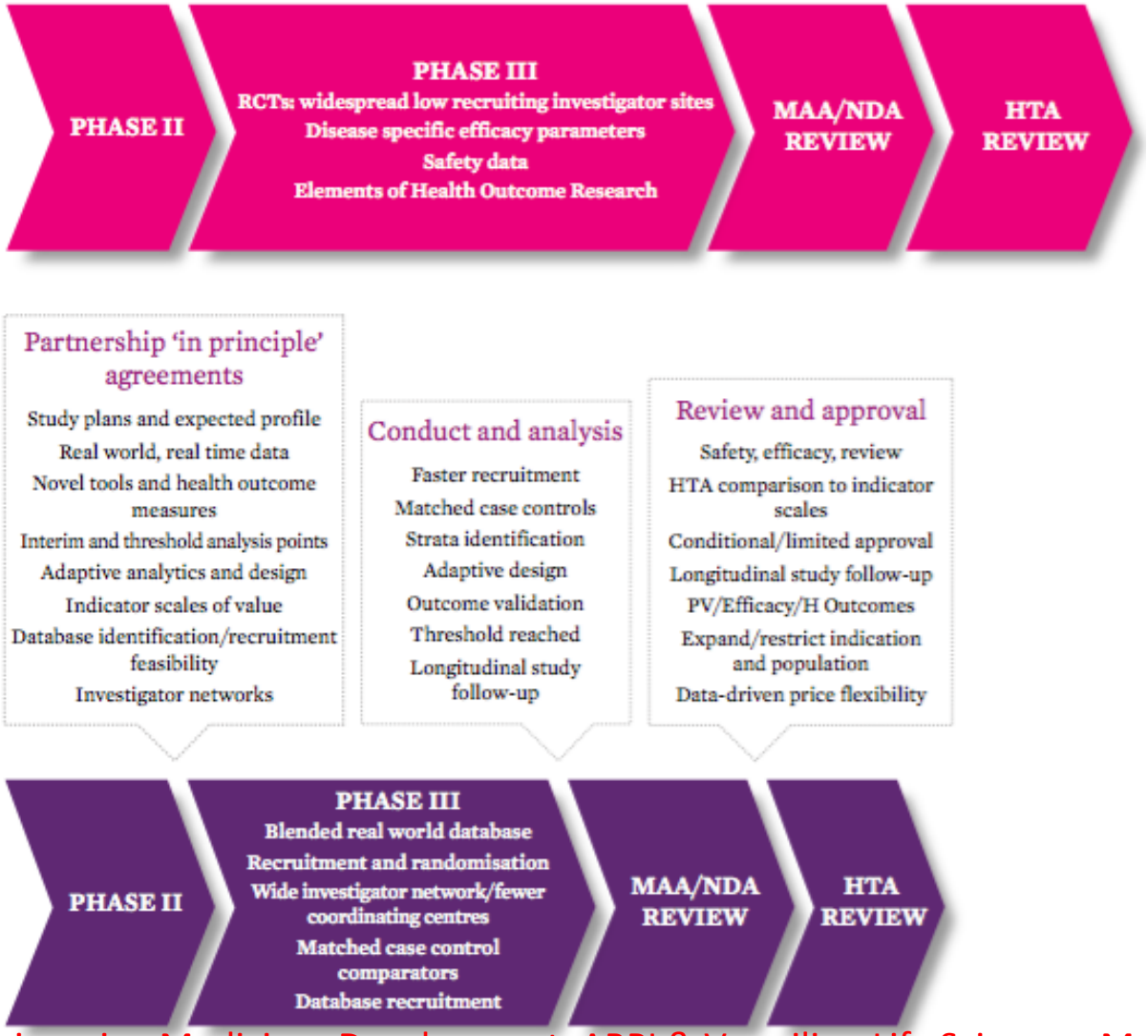


Health Data - Adaptive design, analysis, stratification

- Real time analyses against TPP thresholds
  - Review safety, efficacy and value
    - Extend benefit:risk to concept of benefit:risk:value
  - Earlier identification of thresholds for approval & value
    - Earlier go / no-go decisions increases portfolio efficiency to file fast
    - Earlier identification of futility to fail fast
  - Adaptive designs with stratification opportunities
    - Improve benefit:risk and benefit:risk:value
  - Streamlined regulatory review with a more parallel reimbursement process
    - Phased, or adaptive approval with ongoing study conduct and data updates
    - Control of clinical use and ongoing database monitoring
- Lower investment to approval and earlier return on investment

Data is an enabler. People make it work

- Need scientific validity to establish PoC and dose range in Phase II
- Establish ‘end of Phase II' dialogue and stakeholder partnership
  - Agree value parameters, thresholds, development and analysis plans
- Earlier, threshold-based, decision points
  - File fast or fail fast
- Phased approvals
  - Improved robustness of cost effectiveness data
- Earlier uptake
  - Study continuation and ongoing monitoring to outcomes
- Incremental indications / expanded populations
  - Sequential filing and uptake as part of ongoing lifecycle plan
- Lower initial price?
  - Adaptive pricing reflecting strength of data?
- Partnership and predictability



From: Reengineering Medicines Development. ABPI & Vermilion Life Sciences. March 2015

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People will make it work

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