

Mitochondrial Disease Roadmap to a Cure Mitochondrial Disease Community Registry Update

Southeast Regional Mitochondrial Medicine Symposium

April 2017



HOPE. ENERGY. LIFE.

Guiding Principles of a Roadmap Project

➤ **Global in scope**

- Opportunity to identify partners around the world, each with unique capabilities

➤ **Community-Driven**

- UMDF would like to steward and manage the project, but broad stakeholder involvement/buy-in is mission critical

➤ **Leverage knowledge/experience of UMDF SMAB to jump-start the process**

- Allowed framework to be quickly created

➤ **An iterative process**

- Versions will be renewed on a regular basis, reflective of changes in landscape

Why does our community need a Roadmap?

“If you don’t know where you are going, any road will get you there.”

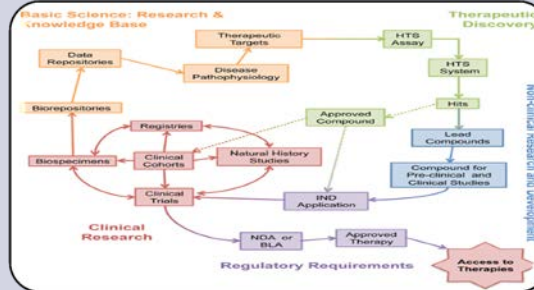
Lewis Carroll (George Harrison, *Any Road*)

- UMDF’s Mission: “...is to find treatments and cures for Mitochondrial Disease...”
- Desire of the UMDF Board of Trustees
- Timing: Significant progress towards therapeutics, understanding mitochondrial biology, increased interest of pharma, increased government awareness.
- UMDF could be the steward for aligning resources in the most efficient and effective manner

The Roadmap is simply a mechanism for identifying, aligning and mobilizing all the various activities and resources necessary to accelerate the discovery of treatments and potential cures.

Mitochondrial Disease Roadmap

A 3-Pillar Approach



Diagnosis

- Increase Awareness
- Improving Diagnoses
- Developing Tools to Measure Mitochondrial Health/Disease

Therapeutic Development

- Facilitating Drug Development
- Identifying & Funding Gaps, from Basic Science to Clinical Trials

Patient Care

- Personalized Medicine
- Patient/Clinician Education
- Developing Coordinated Care Models
- Establishing Centers of Excellence

Summary Findings – Diagnosis Pillar

Current Landscape

- Challenging due to extreme complexity of disease
- **Broad need to better identify and characterize patients**

Key Existing Assets

- Patient Registries: NAMDC/RDCRN/MDCR/MSeqDR/Global DBs
- Patient Biobanks: NAMDC/Mayo (limited)

Key Needs

- Improved diagnostic methods
- Consensus indices to measure mitochondrial health
- **Increased patient access to genetic testing**

Near-Term UMDP Focus

- **MDCR Growth: create infrastructure to support research data**
- Improved Patient Biobanking: utilize MDCR to steward biosamples in collaboration with Mayo



Diagnosis

- Increase Awareness
- Improving Diagnoses
- Developing Tools to Measure Mitochondrial Health/Disease

Summary Findings – Therapeutic Development Pillar

Current Landscape

- Rapidly advancing activity in both academia and industry
- Committed pool of clinician researchers in place, but shallow and stretched thin, making clinical trial expansion challenging

Key Existing Assets

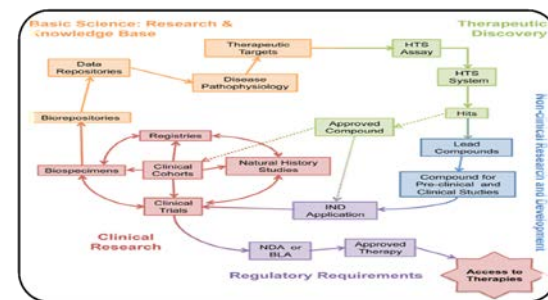
- Patient registries and biobanks
- **UMDF Grants: advance basic, translational and clinical projects**
- Availability of translational tools (limited)

Key Needs

- **Broad stakeholder consensus on priority research topics**
- Development of additional translational tools and validated outcome measures
- Increased collection of natural history data

Near-Term UMDF Focus

- Evolve to increased focus on directed funding of priority topics
- **Financially support industry-sponsored pilot clinical investigations**



Therapeutic Development

- Facilitating Drug Development
- Identifying & Funding Gaps, from Basic Science to Clinical Trials

Summary Findings – Patient Care Pillar

Current Landscape

- Small group of highly expert clinicians
- **Complexity of disease demands involvement of many specialties- a difficult reimbursement scenario**

Key Existing Assets

- Handful of Centers of Excellence (CoE) established
- UMDF Grand Rounds

Key Needs

- **Validation, standardization, support and oversight of CoE models + additional locations**
- Expanded educational tools for patients and clinicians
- Increased advocacy around insurance reimbursement in coordinated care models

UMDF Focus

- **Development of oversight process for Centers of Excellence**
- Collection of patient care experience to support advocacy efforts



Patient Care

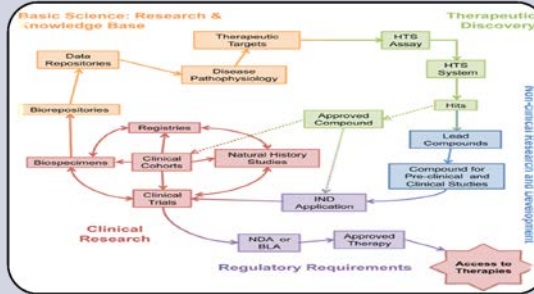
- Personalized Medicine
- Patient/Clinician Education
- Developing Coordinated Care Models
- Establishing Centers of Excellence

Key Assets Aligned to Roadmap



Diagnosis

- Increase Awareness



Therapeutic Development



Patient Care

- Personalized Medicine

Mitochondrial Disease Community Registry

- Multi-stakeholder governance
- Increased data collection
- International deployment

MSeqDR – Genomic Data

- Patient eConsent via MDCR

Education

- Online materials
- Symp/Grand Rounds

Scientific Investment Portfolio

- Academic research grants
- Support of MDCR/MSeqDR/NAMDC
- Funding pilot clinical trials

Patient Care Project

- MMS Project
- Coordinated care

Mitochondrial Disease Community Registry

- Goals for a Patient-Populated Registry
 - Keywords: Sustainable, Compatible, Valuable
 - UMDF as steward, not owner
 - Registrants should have full control of who may see their data, analyze their data and who may contact them
 - Patient-populated in order to cast a wider net
 - Complementary, NOT competitive to NAMDC
 - Collect contact and health information
 - Collection of health information over time (longitudinal)
 - Ability to accept study/trial proposals from researchers, query the database and supply de-identified data

Mitochondrial Disease Community Registry

www.umdf.org/registry

Who?

Patients, caregivers & family members
Confirmed diagnosis **NOT** required

Why?

Need patient data collected over time in order to improve diagnoses and develop treatments

Key

Registrants have full control of privacy settings

- Allow, deny or “ask me”
- Who can see anonymous data
- Who can analyze anonymous data
- Who can contact you about research studies and clinical trials

Mitochondrial Disease Community Patient Registry
Our Disease. Your Information. The Community's Best Hope for Treatments and Cures!

Every 15 minutes, a child is born who will develop a mitochondrial disease by the age of 10. The mitochondrial disease community's new Privacy Assured patient registry is the best chance we have to collect information that will facilitate the diagnosis and treatment of mitochondrial disease, as well as to discover ways to manage the symptoms and improve the quality of life of those individuals who are already affected by it. We need you to participate by providing and sharing the information that will enable the development of treatments and cures for mitochondrial disease. Simply click on **Start Now!** to begin, or **Sign In** if you are a returning user.

It's quick and simple!
Start Now! **Start Now!**
Answer Health Questions
Let Researchers Find YOU!
Share with others

With your help, we can accelerate research into effective therapies and possibly even a cure for different types of mitochondrial disease. 53

Mari J. Fall, MD
Geneticist and Pediatrician
Children's Hospital of Philadelphia
Chair of the Scientific and Medical Advisory Board (SMAB)

Respecting Your Wishes is Our Priority
To help us protect your individual privacy in accordance with rules that your research institution, we harness the power of Privacy Assured with the specific goal of helping you make your health information available to top mitochondrial disease researchers, under your own terms.

MY DOCTOR OR DISEASE ADVOCACY GROUP RECOMMENDED THIS SOURCE AND PROVIDED ME WITH A REFERENCE CODE.
Enter referral code here **Submit**

Privacy Policy Terms of Service [Data Protection](#)

Answer Health Survey **For Thomas**

YOU ARE CURRENTLY ANSWERING QUESTIONS BY Thomas

Questions My Answers My Progress
Your answers: 82

In these future updates, the sorts of topic(s) it would be most important to explore is (are)...

- Quality of life issues
- Usage of dietary supplements
- Challenges of diagnosis
- Symptoms experienced
- Clinical trial participation
- Natural history of specific types of mitochondrial disease
- Other

Feedback on question (2)

He would prefer (or if you would be handing this on for him, then you would prefer) that the total number of questions asked in each update be limited to...

- 1 question
- 2 questions
- 3 questions

What types of information can be shared?

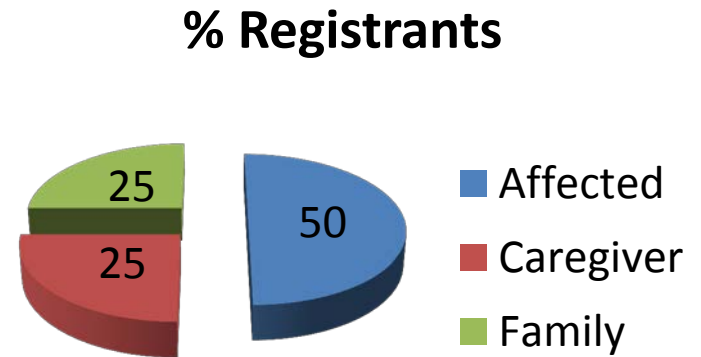
Who can access it?	VISIBLE Anyone with the link to the survey can see this information.	ANONYMIZED Only people with the survey ID can see this information.	PRIVATE Only you and the survey administrator can see this information.
Ability to Support/Engage			
Other Mitochondrial Disease Foundation (UMDF)	Visible	Visible	Private
Current UMDF survey team (you and survey administrator)	Visible	Visible	Private
Survey administrator (you)	Visible	Visible	Private
Research			
UMDF UMDF survey team	Visible	Visible	Private
Researcher recommended by UMDF	Visible	Visible	Private
Researcher recommended by a researcher (with my link)	Visible	Visible	Private
Researcher recommended by a researcher (with my link)	Visible	Visible	Private
Researcher recommended by a researcher (with my link)	Visible	Visible	Private
Researcher recommended by a researcher (with my link)	Visible	Visible	Private
All researchers	Visible	Visible	Private
Data Access Platform			
Complex (with other users)	NA	Visible	NA
Simple (with other users)	NA	Visible	NA
Simple (with other users)	NA	Visible	NA
Simple (with other users)	NA	Visible	NA
Simple (with other users)	NA	Visible	NA
Simple (with other users)	NA	Visible	NA

1 Select a different page | **Cancel** | **Save and continue**

PLEASE REGISTER & SHARE!

MDCR Current Status

- Launched August 2014
- March 2017: ~2,050 registrants
- Baseline survey
 - ~100 Q's/~150K Responses
 - Baseline demographics
 - Diagnostic State
 - Opinions on patient-centered drug development
- International: 46 countries represented!
 - ~90% from the US



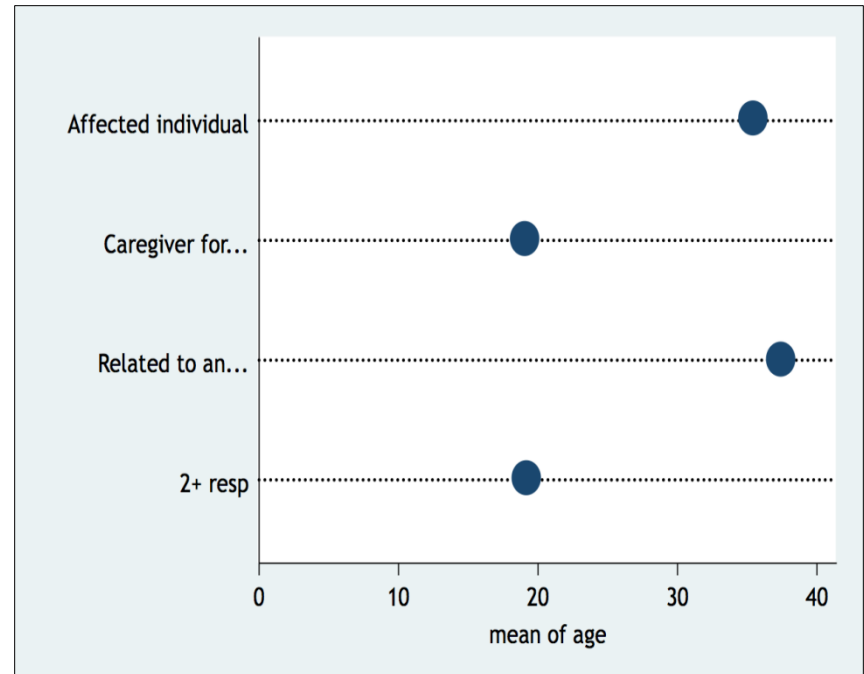
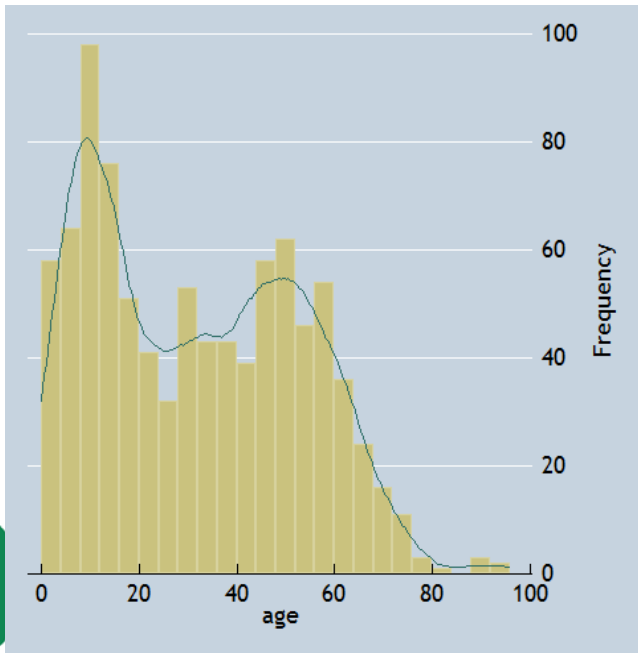
MDCR Data Mining Project

Analysis of Data Collected
2014-2016

Demographics

- Gender
 - Greater female participation
- Age
 - Majority between 20-40
 - Caregivers responding for younger probands
 - 99.7% living

My gender (self-identified) is...	No.	Column %	Cumulative %
Female	523	62.3	62.3
Male	308	36.7	99
Other (specify on next question)	3	0.4	99.4
skipped	5	0.6	100
Total	839	100	



Mito Disease Diversity

- Broad syndrome representation
- Disorder vs. Age/Race relationships too thin for substantive conclusions

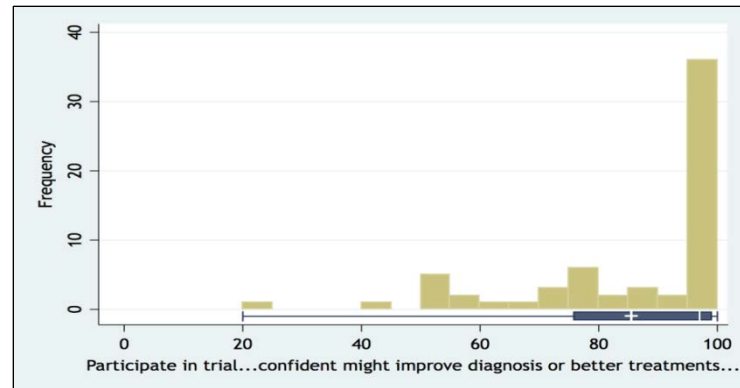
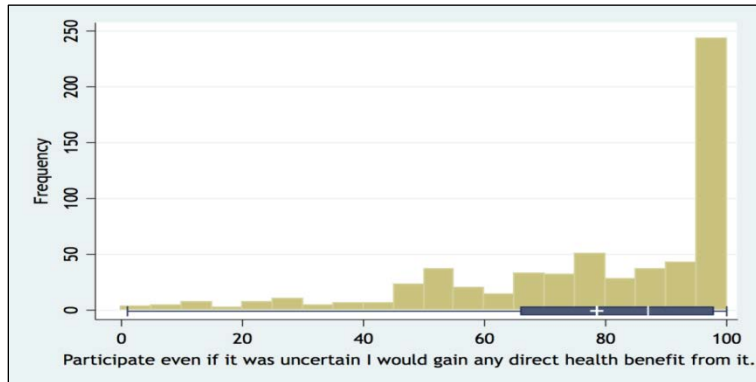
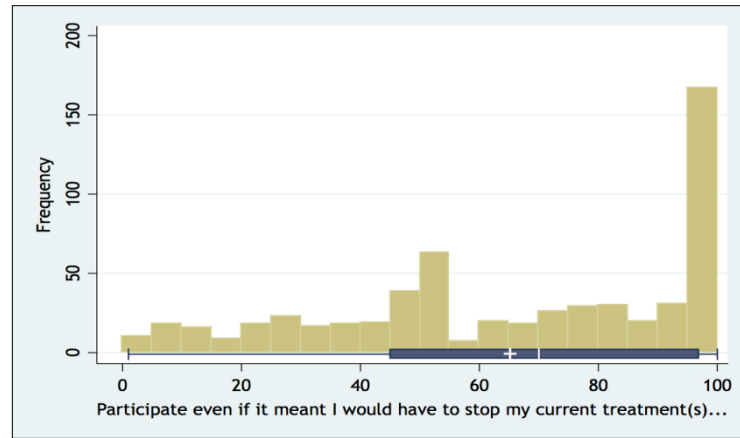
mitochondrial dis dx	racecat				Total
	asian	white	other rac	2 + races	
Complex I Deficiency	1	1	0	0	2
Complex III Deficienc	0	0	0	1	1
Complex IV Deficiency	0	0	0	2	2
CPEO	0	0	1	0	1
Encephalomyopathy	0	0	0	1	1
Encephalopathy	0	0	0	1	1
MELAS	0	0	0	2	2
MNGIE	0	1	0	0	1
Multiple Respiratory	0	0	0	1	1
NARP	0	0	0	1	1
Total	1	2	1	9	13

I was diagnosed with (or may have) one of the following	No.	Col %	Cum %
Alpers syndrome	1	0.9	0.9
Encephalopathy	11	9.6	10.5
KSS (Kearns-Sayre Syndrome)	20	17.5	28.1
Leukoencephalopathy	1	0.9	28.9
LHON (Leber Hereditary Optic Neuropathy)	1	0.9	29.8
MELAS	12	10.5	40.4
Myoclonus Epilepsy Ragged-red Fibers	3	2.6	43
Mitochondrial DNA Depletion Syndrome	11	9.6	52.6
MNGIE	8	7	59.6
Multiple Respiratory Chain Enzyme Deficiencies	25	21.9	81.6
NARP	6	5.3	86.8
Pearson syndrome	2	1.8	88.6
SANDO	1	0.9	89.5
Sensory Ataxia Neuropathy	12	10.5	100
Total	114	100	

I was diagnosed with (or may have) the following	My gender (self-identified) is...					
	Female		Male		Total	
	No.	Col %	No.	Col %	No.	Col %
Alpers syndrome	0	0	1	2.6	1	1
Encephalopathy	4	6.8	5	13.2	9	9.3
KSS (Kearns-Sayre Syndrome)	11	18.6	7	18.4	18	18.6
Leukoencephalopathy	0	0	1	2.6	1	1
LHON (Leber Hereditary Optic Neuropathy)	1	1.7	0	0	1	1
MELAS	7	11.9	2	5.3	9	9.3
Myoclonus Epilepsy Ragged-red Fibers	1	1.7	0	0	1	1
Mitochondrial DNA Depletion Syndrome	5	8.5	5	13.2	10	10.3
MNGIE	5	8.5	2	5.3	7	7.2
Multiple Respiratory Chain Enzyme Deficiencies	14	23.7	9	23.7	23	23.7
NARP	5	8.5	0	0	5	5.2
Pearson syndrome	0	0	2	5.3	2	2.1
SANDO	0	0	1	2.6	1	1
Sensory Ataxia Neuropathy	6	10.2	3	7.9	9	9.3
Total	59	100	38	100	97	100

Willingness to Participate in Research

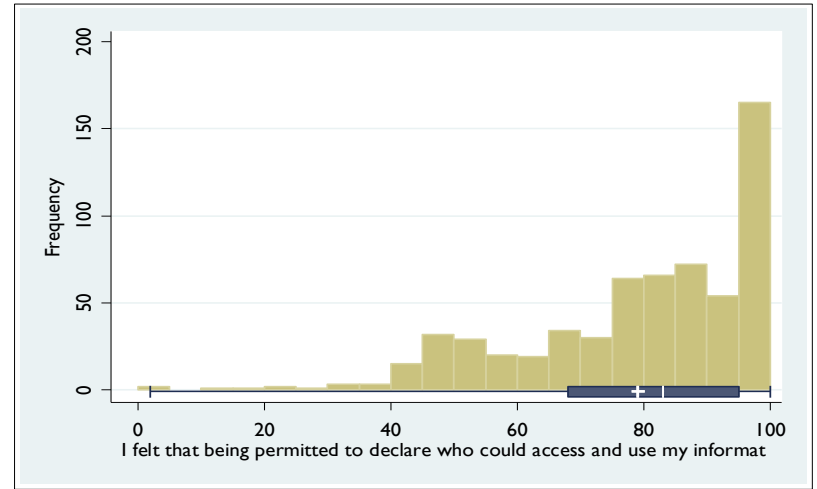
- Generally high willingness/interest in community to HELP with clinical studies



Response to "I am not interested in participating in research because..."				
Item	Yes	%	No	%
"Do not want to be a guinea pig"	3	0.20%	5	0.33%
"The project was not recommended by a doctor"	1	0.07%	7	0.46%
"Results may not be kept private or confidential"	0	0.00%	8	0.53%
"The project will take a lot of time"	0	0.00%	8	0.53%
"Not paid for taking part"	0	0.00%	8	0.53%
"The project involves medical tests, like drawing blood or having x-rays"	1	0.07%	7	0.46%
"The research might reveal something bad"	0	0.00%	8	0.53%
"No obvious benefit to self or family"	1	0.07%	7	0.46%
"Worried about privacy"	0	0.00%	8	0.53%
"Don't know"	3	0.20%	5	0.33%
"Would rather not say"	1	0.07%	7	0.46%
"Would rather not say"	1	0.07%	7	0.46%
Total	1509			

Miscellaneous

- High marks for PEER platform experience
- High interest in sharing of genetic testing results



If I could control who saw my information, I would be willing to ask my health providers to update my profile and/or link all or some of my health records to it...	I have access to the results of genetic testing...						Total
	Although I/he/she recall(s) that genetic testing was performed, I/he/she do/does not have a copy of the report and would not be inclined to request a copy for this purpose.	Genetic testing was never done.	Genetic testing was performed and I/he/she have/has a copy of a report from the doctor or testing lab that lists the genetic variations that are a possible cause of the medical condition.	Other (please specify)	While I/he/she do/does not have a copy of the report, I/he/she recall(s) that genetic testing was performed. I/he/she would be willing to request a copy of the report if this would be useful to gathering information concerning the mitochondrial disorder.	skipped	
Definitely not	0	0	1	0	0	0	1
Definitely would want	1	11	12	3	5	0	32
Somewhat likely	0	5	5	0	1	0	11
Somewhat unlikely	0	0	2	0	0	0	2
Uncertain	0	1	10	2	3	1	17
Very likely	0	6	9	2	5	0	22
Very unlikely	2	1	0	0	0	0	3
Skipped	0	0	0	0	1	0	1
Total	3	24	39	7	15	1	89

Near-Term Growth Initiatives

- Increased MDCR Activity
 - Advisory Board in place and recommended:
 - Philip Yeske, UMDF; Amy Goldstein, CHOP; Michio Hirano, Columbia; Jodie Vento, UPMC; Jodi Wolff, Santhera Pharma
 - Regular communication with registrants- plan developed & data mining project complete
 - More frequent, simple surveys- One launched, one in dev, many conceptualized
 - Broaden type of data collected- expand to include genomic & biosamples
- Increased Partnering/Internationalization
 - MDCR is now ready to be broadly deployed
 - IMP and AMDF also very interested in utilizing PEER
 - Establishes a central global repository of patient-derived data on a single platform
 - Flexible platform ideal for driving large global priorities while also allowing or local customization