color

Risk, Prevention, and the Missing Data

Alicia Y. Zhou, Ph.D.

March 18th, 2019

Agenda

About Color

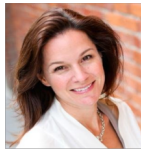
Risk Prevention and the Missing Data

Who we are: Leaders in health, software, UX, data science, and genomics

Google
Dropbox
MIT
Microsoft
Palantir
Caltech
Genentech
illumina
Stanford MEDICINE

Othman Laraki, Chief Executive Officer
- Google, Twitter, Microsoft
- Stanford, MIT
- *BRCA2* carrier

Jeremy Ginsberg, VP of Engineering
- Google, Twitter
- Stanford University



Jill Hagenkord, Chief Medical Officer
- 23andMe & Invitae
- Stanford Univ School of Medicine
- MD, FCAP

Alicia Zhou, VP of Research and Scientific Affairs
- Broad Institute, Dana-Farber Cancer Institute
- Harvard, MIT, UCSF
- Ph.D.

Gilad Mishne, Ph.D. Data Science and Machine Learning
- Twitter, LinkedIn
- Technion, IL

Wendy McKennon, VP of Product & UX
- Google, Method
- Stanford University

Scott Topper, VP of Clinical Operations
- Invitae, University of Chicago
- University of Wisconsin-Madison, Washington University in St. Louis
- Ph.D., FACMG

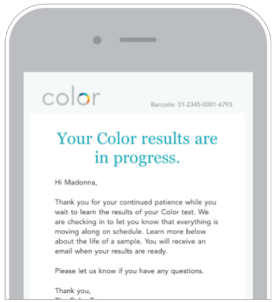
Katie Stanton, Chief Marketing Officer
- Google, White House
- Rhodes College, Columbia Univ

Caroline Savello, VP of Commercial
- Boston Consulting Group, Bloomberg
- Yale University

Elad Gil, Chairman
- Google, Twitter, McKinsey
- MIT Ph.D. Biology

Color's evolution: Expanding genetics from testing to population-level outcomes

Where we started

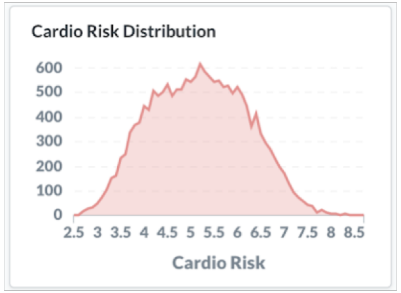


Redefined the financial & logistical costs of clinical-grade genetics

Our expansion

Accessed full populations with virtualized delivery model

Our focus



Transforming system-level outcomes through a data-driven tech stack

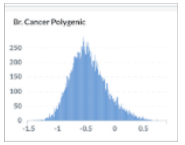
Color brings personal context back into healthcare

Hereditary cancer

Hereditary cardio

Pharmaco-genomics

Traits



Research

Dynamic return of results on multiple health areas over the course of an individual's life, based on their personalized risk level and the current medical evidence.

Genetics + **clinical risk algorithms** using 70-100+ data points collected, eg personal and family history, blood pressure, height, weight, smoking, diabetes, medications.

Engagement via the "halo effect" and inherent family virality of genetics.

Who we work with & where we're heading

Our Partners: Health Systems, Large Employers, & Research Institutions

BROAD INSTITUTE
Jefferson
All of Us The Precision Medicine Initiative
salesforce
NorthShore University HealthSystem
Wisdom
MUBADALA
LEVI STRAUSS & CO.
FH FOUNDATION Raising Awareness. Saving Lives.
GE APPLIANCES
BRCA FOUNDATION
UW Medicine

Recent Collaborations

Color Launches Initiative to Improve Polygenic Risk Scores With Low Coverage WGS, Imputation

Jan 07, 2019 | staff reporter

NIH-funded genome centers to accelerate precision medicine discoveries

Part of the All of Us Research Program, centers will sequence 1 million genomes.

Technology

Color Genomics Announces Partnership With Illinois Health System

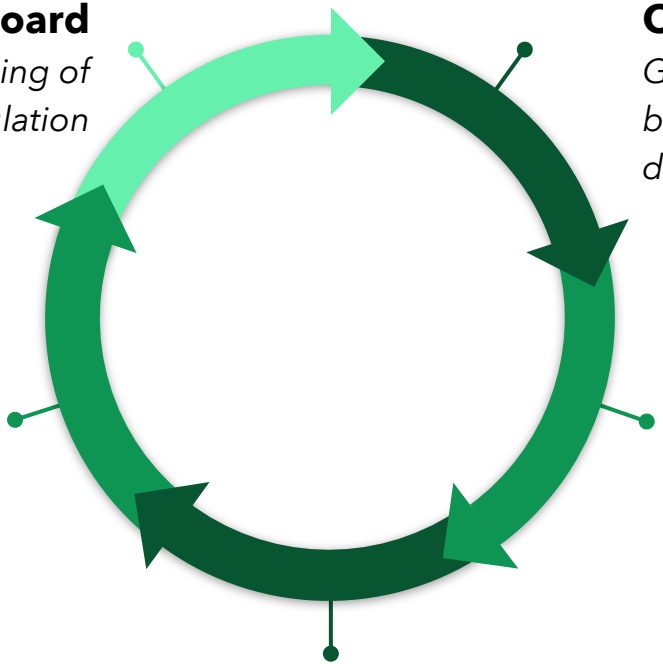
Color's model

Onboard

Simple, effective onboarding of your full population

Collect signals

Genetics, health history, daily behavioral choices, and social determinants



Engage & update

Ongoing activation moments to feed cycle of data to signal, signal to decisions, and decisions to outcomes

Translate signal to insight

Risk stratification, identification of high-value cohorts, and health risk insights

Change behavior

Intervention targeting to change behavior and choices

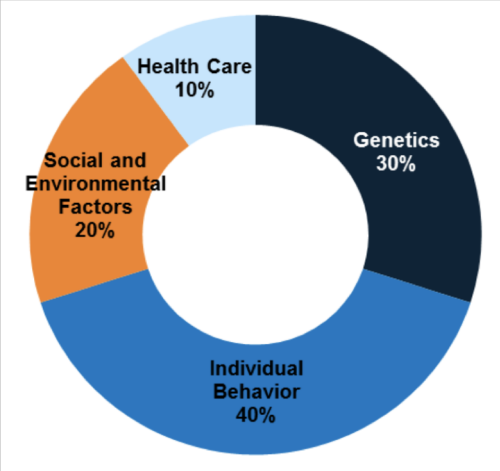
Agenda

About Color

Risk Prevention and the Missing Data

Healthcare's greatest opportunity: More contextual insights, better outcomes

Core determinants of health



Access to the data that actually drives human health

Nonadherence to depression treatment

40% - 75%

% of U.S. adults not not complying with colorectal cancer screening

35%

Technology to activate patients and change behavior

Sources: Steven A. Schroeder, "We Can Do Better – Improving the Health of the American People," *NEJM* 357 (2007); Pampallona S, " Patient adherence in the treatment of depression", Br J Psychiatry. 2002 Feb;180:104-9; CDC press release 2013.

Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Rapid recruitment & onboarding

LEVI STRAUSS & CO.

47% eligible employee utilization in 3 months

Jefferson

7,000 individuals participating in Color in the first 8 weeks after launch (**25%** utilization)

Dozens of leading employers offer Color's population health platform as an employee benefit

Financial Services	Technology	Consumer	Other
VISA	NVIDIA	Instacart	GE APPLIANCES
stripe	NETSUITE	OpenTable	oscar
loanDepot	salesforce	AngelList	Tribune Media
BLACKROCK	SAP		
	slack		

...and many more!

Overall demographics from first ~11k enterprise participants

52%	30s-40s	~44%
female	median age	non-Caucasian

Note: Demographic data as of 9/21/17
Source: Demographics of those who activated test kit

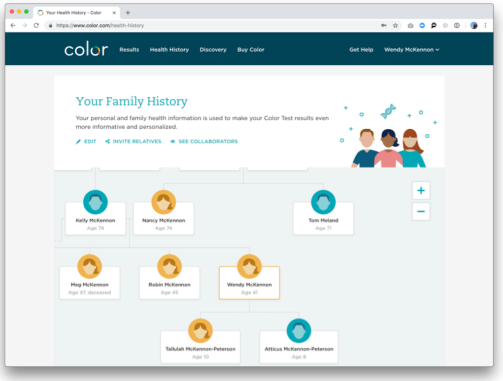
Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Rich genetic content

easy-to-use saliva collection
TAT: 2-3 weeks

Robust, frequently-updated data collection



92% personal + family health history completion rate.

Data-driven prevention

1. Onboard
2. **Collect signal**
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

NATIONAL ACADEMY OF MEDICINE

A Proposed Approach for Implementing Genomics-Based Screening Programs for Healthy Adults

By Michael F. Murray, James P. Evans, Misha Angrist, Kee Chan,Wendy R. Uhlmann, Debra Lochner Doyle, Stephanie M. Fullerton, Theodore G. Ganiats, Jill Hagenkord, Sara Imhof, Sun Hee Rim, Leonard Ortmann, Nazneen Aziz, W. David Dotson, Ellen Matloff, Kristen Young, Kimberly Kaphingst, Angela Bradbury, Joan Scott, Catharine Wang, Ann Zauber, Marissa Levine, Bruce Korf, Debra G. Leonard, Catherine Wicklund, George Isham, Muin J. Khoury

December 03, 2018 | Discussion Paper

CDC Tier 1 Genomics Conditions

HBOC: *BRCA1, BRCA2*

Lynch: *MLH1, MSH2, MSH6, PMS2, EPCAM*

FH: *LDLR, APOB, PCSK9*

PGx: CPIC level A

Gene-drug interactions as labeled by the **FDA**

Data-driven prevention

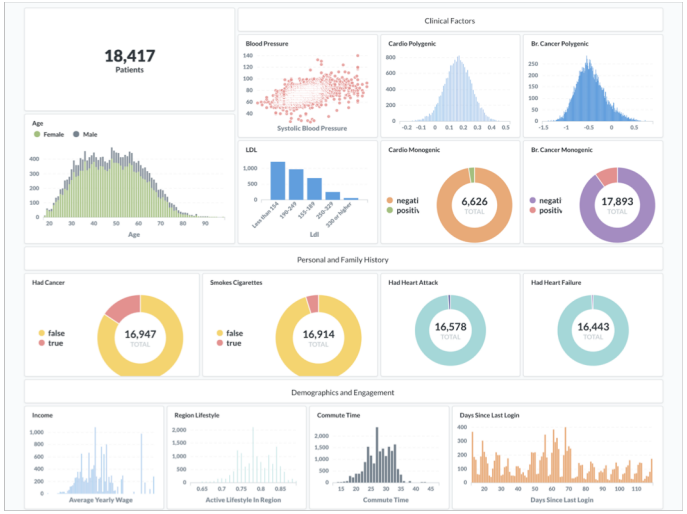
1. Onboard
2. Collect signal
3. **Translate signal to insight**
4. Change Behavior
5. Engage and Update

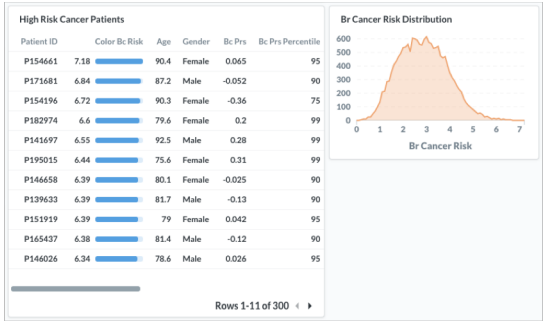
Software turns signals into insights:

- Clinical risk models, e.g. Gail, Claus, Framingham
- Genetic risk
- Collaborative family health history
- Daily behavioral choices, e.g. Smoking, BMI
- Social determinants

Focus on high-risk cohorts and change their behavior:

- Risk segmentation and targeted interventions
- Screening compliance
- Program routing

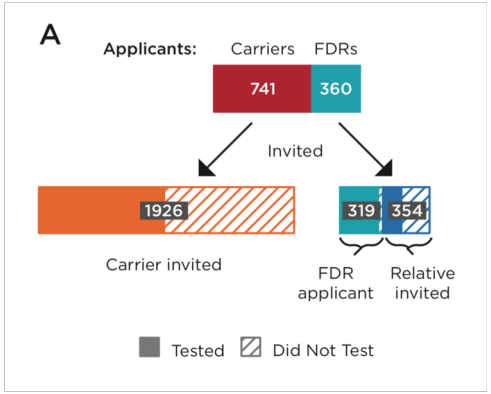


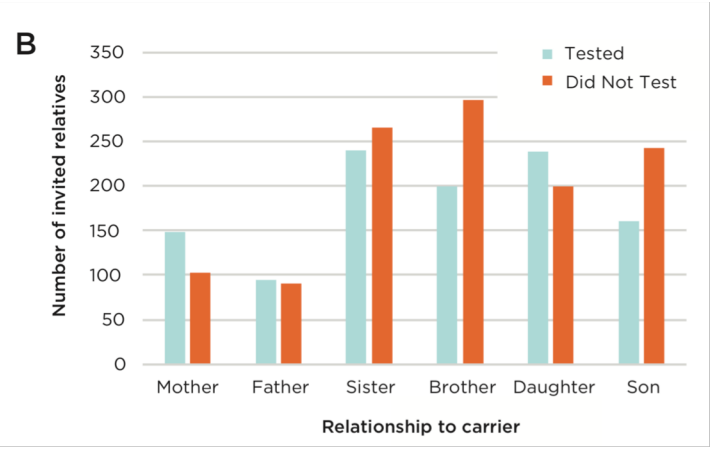


Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Color's Family Testing Program





~50% uptake on cascade testing

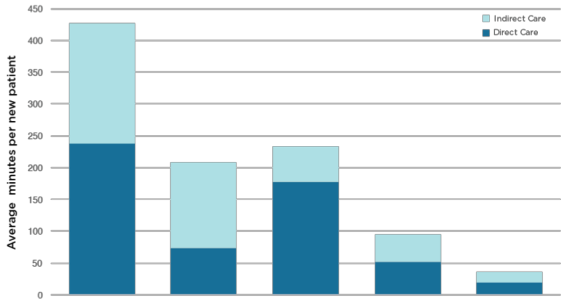
- $50 full panel testing for any first-degree relative
- Kit is shipped to patient's home
- Counseling is delivered by Color

Data-driven prevention

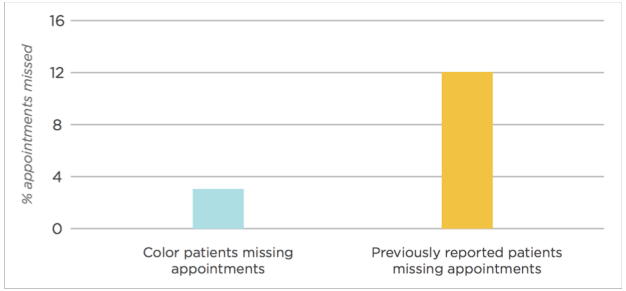
1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Digital Genetic Counseling Delivery

Overall time spent: <60 mins



Missed appointments: ~3%

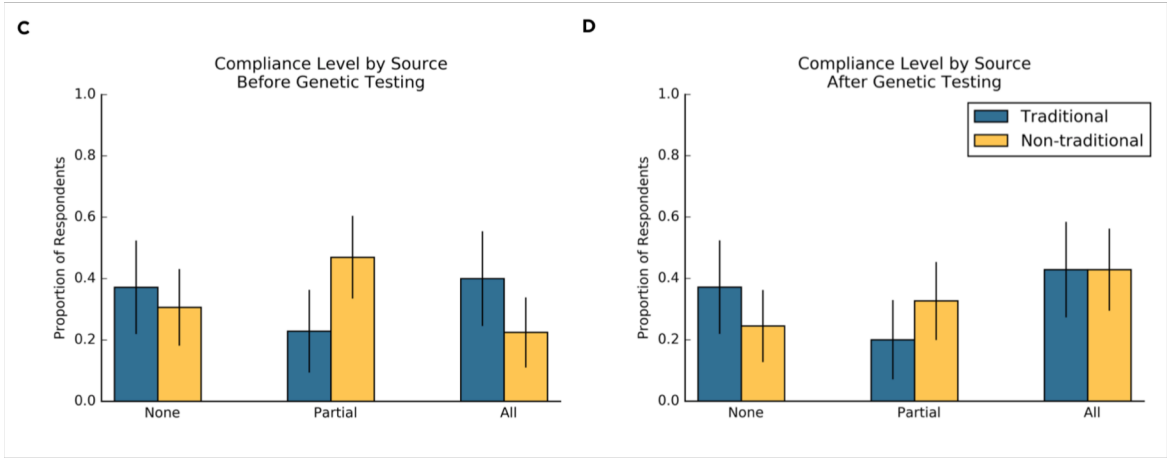


Digital delivery of genetic counseling results in more efficient and effective genetic counseling delivery

Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Screening Compliance



Genetics drives mammography screening compliance up in the average risk population

Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

Statin Adherence

Polygenic risk score results increase statin compliance by 41% (63.4% vs. 45%) [source]

Only 7% statin nonadherence following genetic diagnosis vs >50% in general population Source

Polygenic scores for population risk stratification and individual risk.

MENU nature genetics

Letter | Published: 13 August 2018

Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations

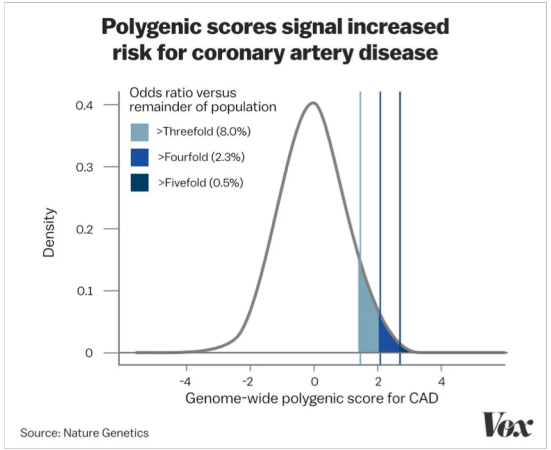
Amit V. Khera, Mark Chaffin, Krishna G. Aragam, Mary E. Haas, Carolina Roselli, Seung Hoan Choi, Pradeep Natarajan, Eric S. Lander, Steven A. Lubitz, Patrick T. Ellinor & Sekar Kathiresan

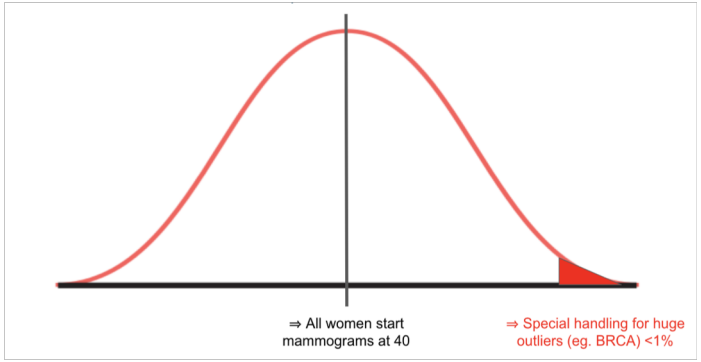
Nature Genetics **50**, 1219–1224 (2018) | Download Citation

Review Article | OPEN | Published: 13 September 2017

The WISDOM Study: breaking the deadlock in the breast cancer screening debate

Laura J. Esserman & the WISDOM Study and Athena Investigators

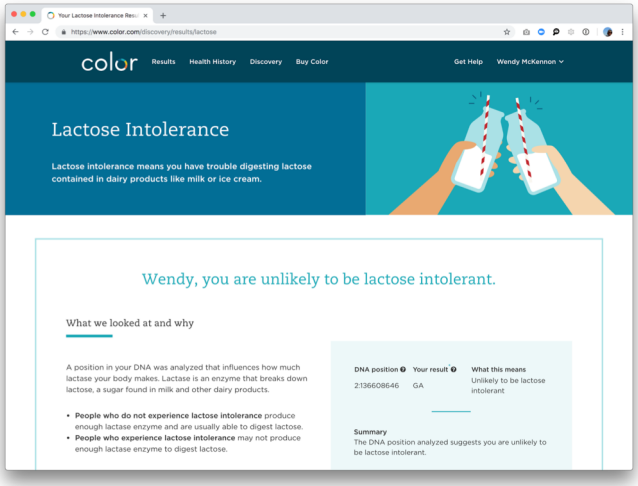




Data-driven prevention

1. Onboard
2. Collect signal
3. Translate signal to insight
4. Change Behavior
5. Engage and Update

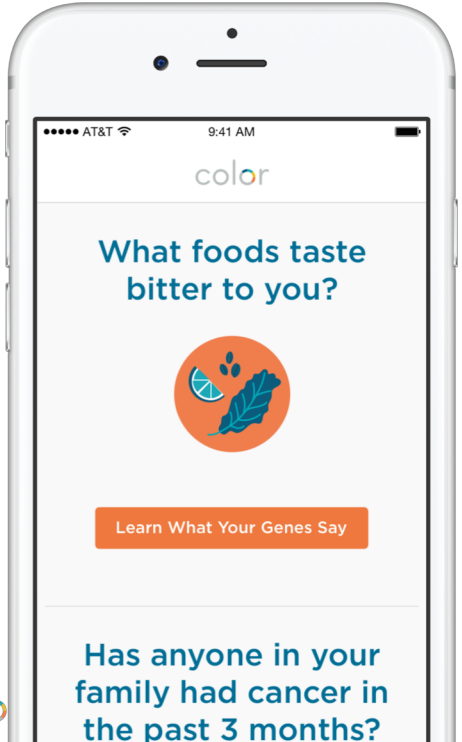
Frequent digital re-engagement



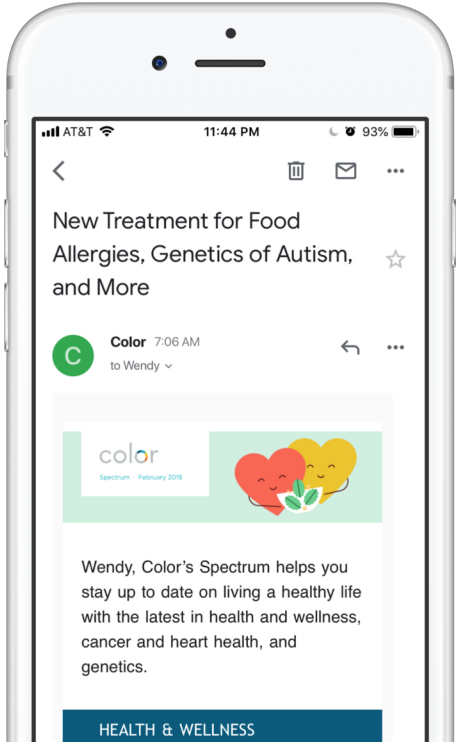
40%+ click-through on traits reports and re-engagement with clinical information

Strong ongoing engagement

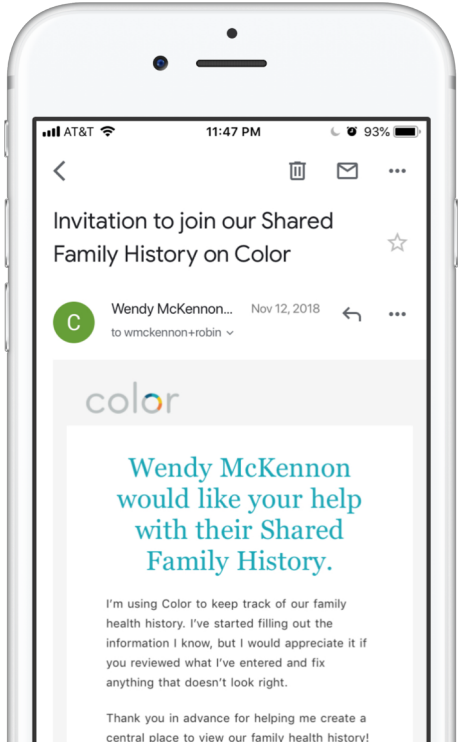
Color Discovery



Monthly newsletter



Shared Family History



Building large, engaged populations

88%

of patients complete health history

50%

of invited family accept to collaborate on health history

83%

of accepted family complete health history

85%

of patients subscribe to monthly newsletter

23%

average open rates on monthly newsletter (16% is normal)

59%

of family testing invitees follow through (10-30% is normal)

Color changes outcomes by getting the right intervention, to the right people, at the right time.

Keys to population health

Large, engaged populations

Useful, actionable insights

Enabling effective interventions

Questions?

alicia@color.com

PGx Clinical Validity

Antidepressants

- CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors.
- CPIC Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants.
- Altar CA, et al. (2013) Clinical validity of cytochrome P450 metabolism and serotonin gene variants in psychiatric pharmacotherapy. Int Rev Psychiatry 25(5):509-33.

Cardiovascular PGx

- CPIC Guidelines for CYP2C19 Genotype and Clopidogrel Therapy
- CPIC Guideline for SLCO1B1 and Simvastatin-induced Myopathy
- CPIC Guidelines for Pharmacogenetics-guided Warfarin Dosing

Pain PGx:

- CPIC Guidelines for Cytochrome P450 2D6 (CYP2D6) Genotype and Codeine Therapy
- CPIC Guidelines for CYP2C9 and HLA-B Genotype and Phenytoin Dosing
- CPIC Guideline for HLA Genotype and Use of Carbamazepine and Oxcarbazepine

How it Works

Sample

Online physician-ordered test shipped home with pre-paid return shipping

Results

Detailed risk profile with evidence-based screening guidelines

Counseling

Discuss results and next steps with a board-certified, licensed Color genetic counselor

Share

Results are easily shared with healthcare providers and family members

Genetics: Where to Start?

CDC Tier 1 Conditions	Genes	Clinical Risk	Disease-altering intervention	Prevalence
Hereditary Breast and Ovarian Cancer Syndrome	*BRCA1, BRCA2*	Early onset breast, ovarian, prostate, and other cancers	Targeted screening with optional prophylactic medical or surgical intervention	1:202
Lynch Syndrome	*MLH1, MSH2, MSH6, PMS2, EPCAM*	Early onset colon, endometrial, and other cancers	Targeted screening and management of precancerous lesions	1:293
Familial Hypercholesterolemia	*LDLR, APOB, PCSK9*	Early onset coronary artery disease	Targeted screening and medical management	1:222
Based on Geisinger MyCode study*			TOTAL	1:78

*RoR from Research Exomes, Mike Murray, MD.
Manickam K, et al. JAMA Network Open. 2018;1(5)
Genet Med. 2018 Apr;20(5):554-558, PMID: 29261187

The **CDC's Office of Public Health Genomics** defines Tier 1 genomic applications as those having significant potential for positive impact on public health

- Significantly underdiagnosed
- Disease risk is well understood in an unselected population
- Well-established, effective preventive guidelines exist

The **National Academy of Medicine's Genomics and Population Health Action Collaborative** recommended the Tier 1 conditions as an appropriate population genomic screen in healthy adults

Source: CDC website for Genomics Implementation
See also: National Academy of Medicine, Genomics and Population Health Action Collaborative
Murray, MF, et al. A Proposed Approach for Implementing Genomics-Based Screening Programs for Healthy Adults, Dec 2018

Pharmacogenomics Reportable Range and Selection Criteria

Clearest clinical evidence for commonly prescribed medications

- CPIC level A and B genes + some VIP genes not yet reflected on CPIC
- Technically challenging genes will be covered in future assay releases (e.g. HLA-A, HLA-B)

Least controversial, most useful

- Antidepressants
- Cardiovascular medications
- Pain management

Gene	Star alleles analyzed
CYP2D6	*2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *19, *29, *35, *41, *xN
CYP2C19	*2, *3, *4A, *4B, *10, *17

Gene	Star alleles and variants analyzed
CYP1A2	*1F, *1J, *1K
CYP2C9	*2, *3, *4, *5, *6, *8, *11
CYP3A4	*1B, *22
CYP3A5	*3, *6, *7
CYP4F2	*3
DPYD	*2A, *13
F5	rs6025 (Leiden)
IFNL3	rs12979860
NUDT15	rs116855232
SLCO1B1	rs4149056
TPMT	*2, *3A, *3C, *4
VKORC1	rs9923231