DataSpeaks

# Precision Clinical Drug Development:
## Four Main Steps to Higher Productivity

**Curtis A. Bagne, Ph.D.**
President and Founder,
DataSpeaks, Inc.

Cutting Edge / Drug Discovery & Development in Michigan
October 10th, 2017 @Wayne State University

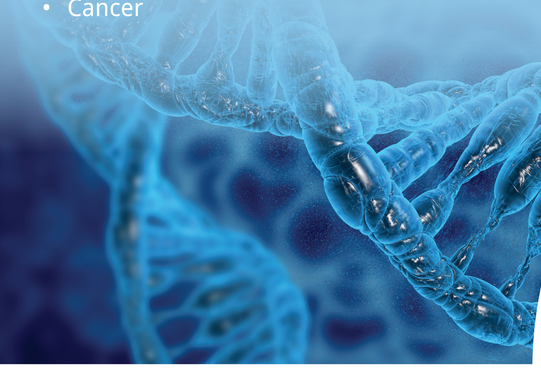
**INTRODUCTION:** Low productivity challenges the pharmaceutical industry. Achievements in drug discovery typically falter during clinical drug development. Improve productivity with four main scientific steps.

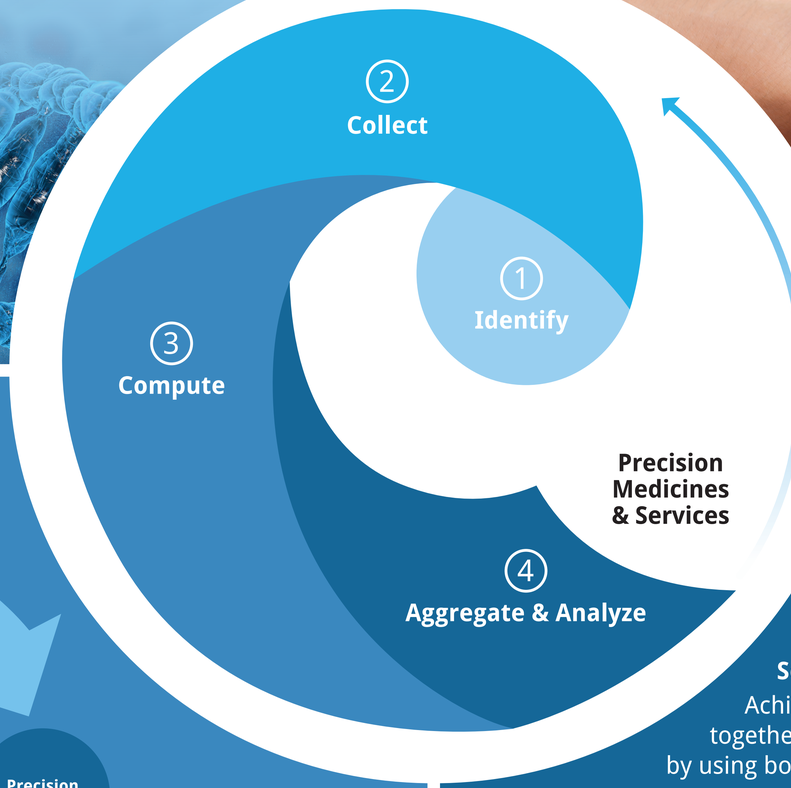
## STEP 1: Identify Each Individual: Genotype or Sequence

**Best guess target population**
- Indications
- Contra-indications

**Start broad,** funnel targeting from first person on drug forward

**Genotype or whole genome sequence each**
- Person
- Cancer

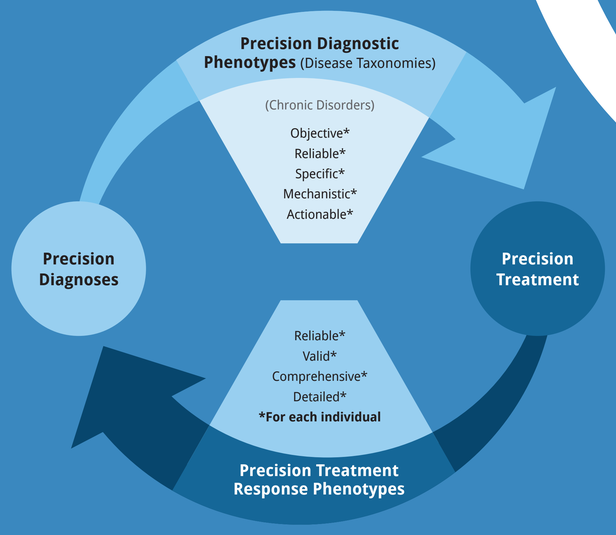





## STEP 2: Collect Multivariate Time Series (Streaming Data)

- Many time series for more holistic systems science
- Randomize doses over time for validity
- Many repeated measurements for reliability and power


## STEP 3: Compute Precision Quantitative Phenotypes

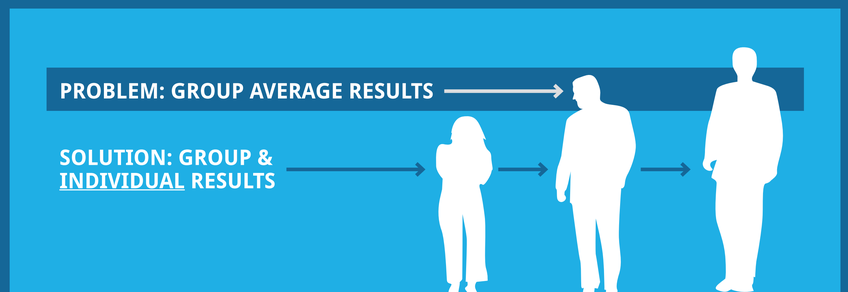



Compute these phenotypes by applying Science of Individuality Measurement Algorithm (SIMA)—see sidebar—from DataSpeaks, Inc. to multivariate time series.

## STEP 4: Aggregate & Analyze with Statistics

**Problem:**
Parallel groups studies based on statistics yield only group average results. However, clinicians treat individuals.

**Solution:**
Achieve both individual and group average results—together with additional advantages in the SIMA sidebar—by using both SIMA and statistics.




## The Science of Individuality Measurement Algorithm (SIMA)

**Limits:** SIMA is limited to time fluctuating variables as for chronic disorders that account for 85% of annual health care expenditures of over $3 trillion in the U.S. alone.

**SIMA measures:** Interactions over Time (e.g., functional connectivity, edges for time series nodes, benefit and harm)

**Clinical Trials**
- Use within-person randomized dose titration
- Null hypothesis rejection in the positive or beneficial direction indicates benefits outweigh harms
- Rejection in the negative direction indicates harms outweigh benefits

**Analogy:** SIMA's measures of ***benefit and harm*** are analogous to how ***dollars*** pay for diverse goods and services. Both are common metrics.

**Target Discovery & Mechanisms:** Identify measures of Interaction over Time that can be up- or down-regulated by treatment.

**Nonlinearity:** SIMA can, for example, quantify benefit and harm as nonlinear functions of dose, response variable level, delay and persistence of response.

**Boolean Events:** SIMA uses Boolean events to account for drug-drug interactions, combination treatments, and syndromes.

**Emergent Properties:** SIMA can measure coordinated action as an emergent system property.

**Levels of Investigation:** SIMA can help integrate across levels of investigations such as molecular, biological, psychological, and social.

**Causality:** SIMA assesses causality over time within individuals as distinct from group comparisons.

**Ethics:** SIMA has an ethical advantage—subjects become persons again.

**Scientific rigor:** SIMA improves scientific rigor by measurement.

**Statistics:** SIMA's scores are well suited for statistical analyses
- Describe groups
- Make inferences
- Identify predictors

**Translation:** SIMA helps obviate the translation problem from research to practice.

**Some Nuts & Bolts:**
- Digitize each transformed time series.
- Add digital series to account for delay and persistence of response, additional analysis parameters, Boolean events, etc.
- Cross-classify digital series to form arrays of 2 x 2 tables.
- Repurpose simple statistical tools to compute raw interaction-over-time and benefit and harm scores.
- Standardize scores within individuals by identifying all scores that are possible given observed 2 x 2 table marginal frequencies together with their hypergeometric probabilities.
- Summarize score arrays as functions of analysis parameters.
- Compute within person-specific overall benefit and harm scores for evaluations that account for clinical significance and personal preferences.

**Opportunity:** SIMA, a product of serendipity, offers a positive black swan opportunity—a highly improbable and unpredicted advancement—in software engineering.

**Commercialization:** DataSpeaks seeks help to commercialize SIMA.

**Michigan** can be a world leader in precision drug discovery and development.

**Contact**
Curtis A. Bagne, Ph.D.
cbagne@DataSpeaks.com
(248) 854-6816 (mobile)

**MORE INFORMATION & THIS POSTER AT:**
www.DataSpeaks.com