



DIA  **2015**

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Data-Driven Study Feasibility Assessment and Impact on Successful Execution of Clinical Trial Protocols

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DIA Session:

***Next Generation Feasibility: How to Predict
the Unpredictable and Plan for Success***

Track: Clinical Operations

June 15, 8:30AM - 10:00AM

Session Number:102

Room Number:145B, Level One North

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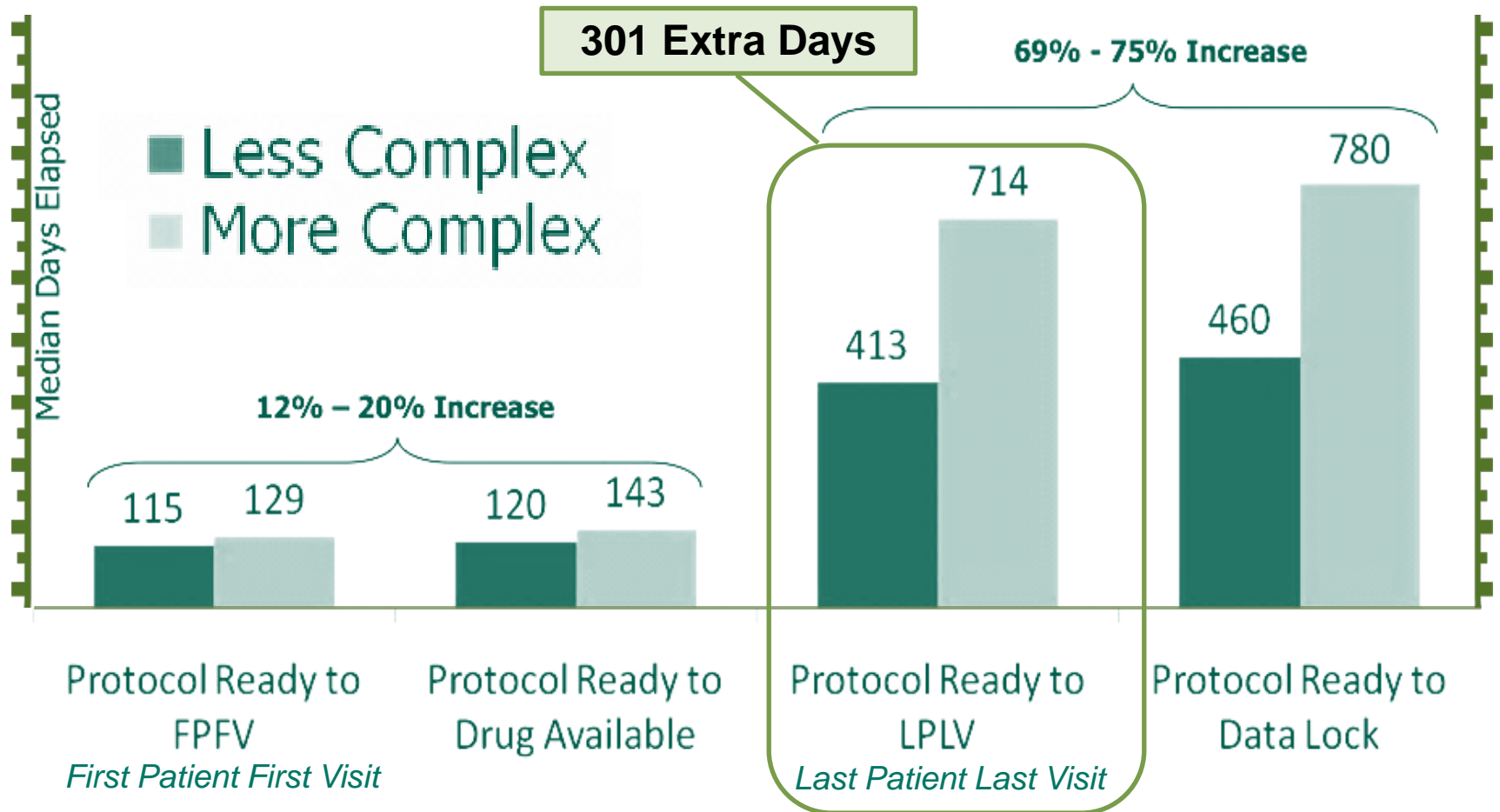


Agenda

- ▶ Industry cost of complexity and finding patients
- ▶ Answer the questions:
 - Do the patients you are looking for exist?
 - How can you find them?
- ▶ Explore new ways to locate your trial patients by combining insurance claims data and clinical data from Electronic Health Records (EHR).
- ▶ Our case study will be on COPD (Chronic Obstructive Pulmonary Disease)



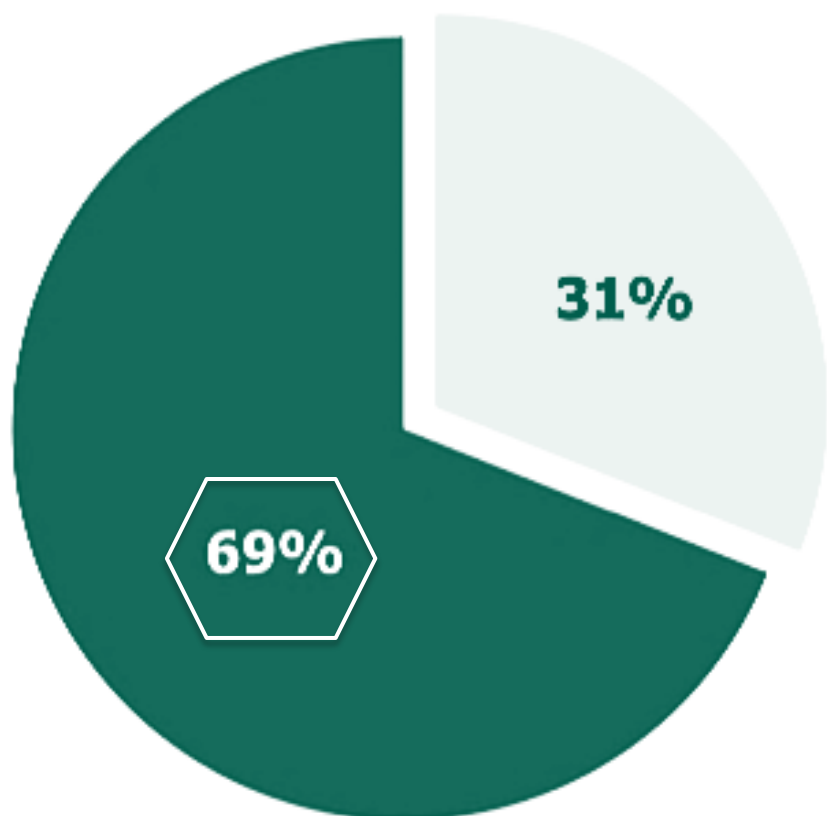
Protocol Complexity Increases Cycle Time



Source: Tufts CSDD (<http://csdd.tufts.edu>), published in *CenterWatch Clinical Trials Data Library*, 2012.

69% of Trials Have Amendments

■ No Amendments ■ At least One Amendment



Protocol phase	Number of amendments*	Number of changes per amendment
Phase I	2.0	5.6
Phase II	2.6	6.8
Phase III	3.6	8.5
Phase IIIb/IV	2.3	8.3
All protocols	2.4	6.9

* All values are means

2.4 amendments per protocol

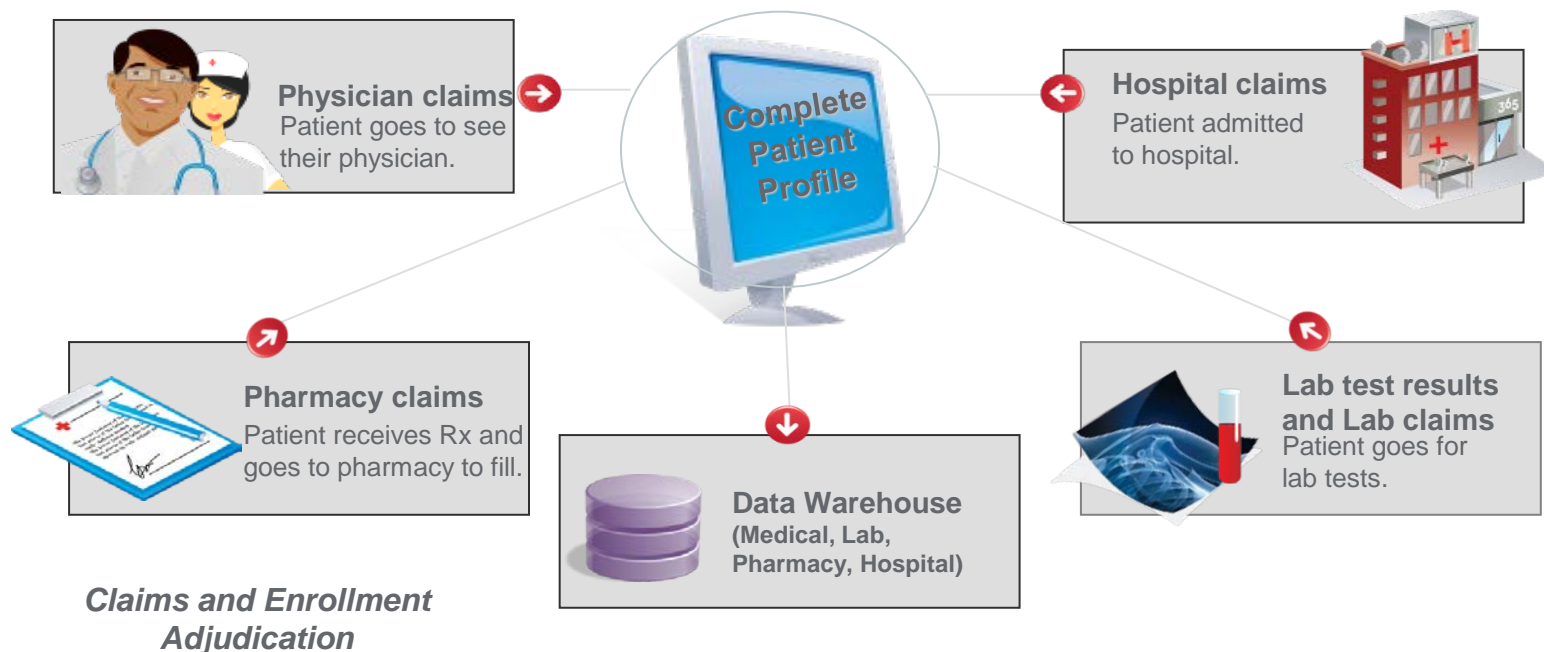
- **\$450,000+**
- **61 days**

Source: Tufts CSDD, <http://csdd.tufts.edu>, published in CenterWatch Clinical Trials Data Library, 2014.

Insurance Claims Data Source

Will Be Important for Today's Case Study

- ▶ UnitedHealth Group (UnitedHealthcare®), is largest insurer, \$134.5 billion.* Has 15% - 20% of commercial market.
- ▶ 25% of Medicare Part D population (largest payer)
- ▶ Person-level data allows for accurate statistics with no double counting.
- ▶ De-identified data for statistics are done by Optum.



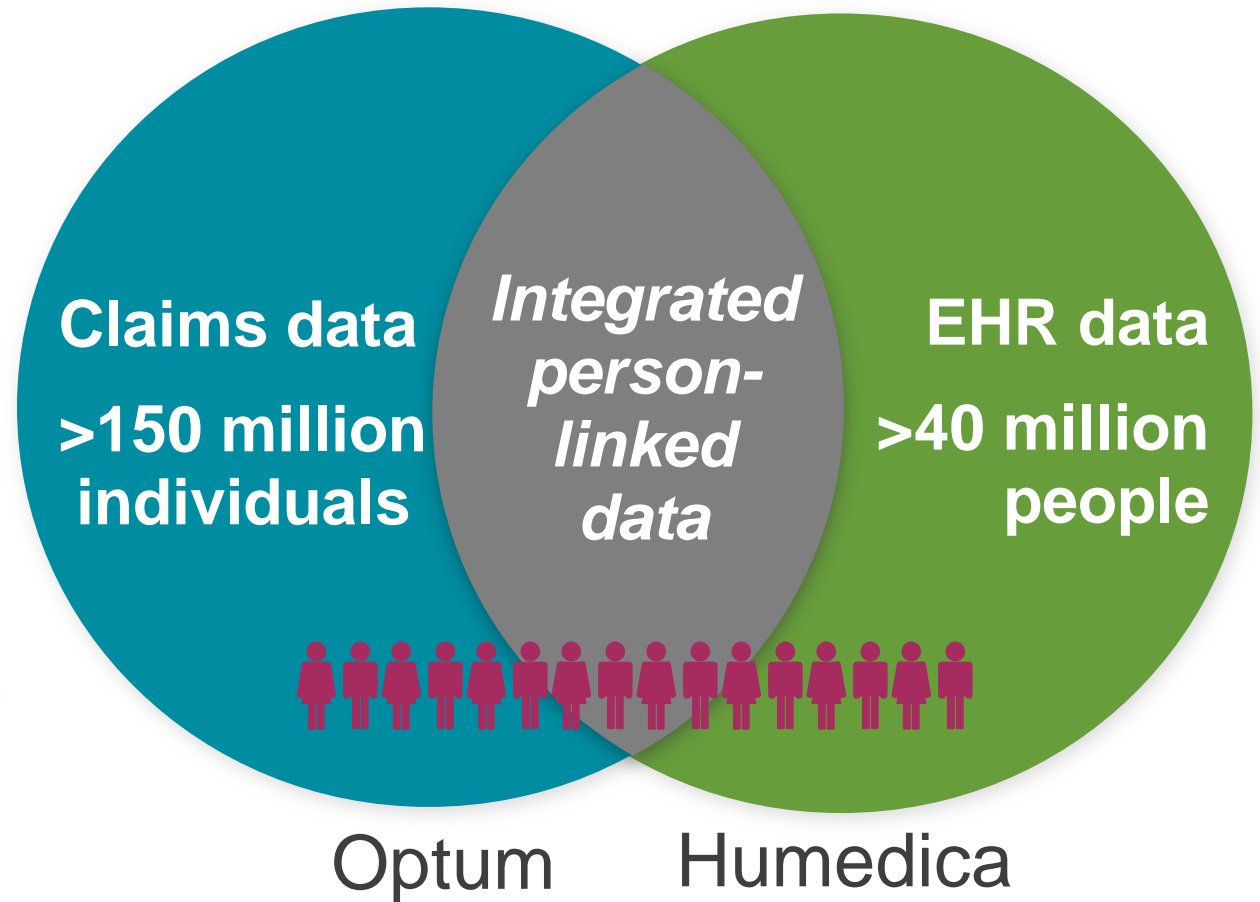
* 12- Month Revenue in Billions: UnitedHealth Group (UNH) \$134.5, Anthem (ANTM, Blue Cross) \$75.1, Aetna (AET) \$56.1. From *Morningstar*, 5/22/2015.

Claims are linked with Electronic Health Records (EHR) for today's case study.

A new class of data: Integrated and person-linked.

Enables powerful insight into quality standards, economics, outcomes, and clinical practice.

We will use today to assess patient availability.



*Based primarily on membership in the UnitedHealthcare affiliate single-payer database, as well as a non-affiliate multi-payer database

Case Study:

Chronic Obstructive Pulmonary Disease

- ▶ COPD refers to lung diseases that block airflow.
- ▶ COPD is a leading cause of death.
- ▶ Most COPD is caused by long-term smoking.
- ▶ Damage to lungs cannot be reversed and is usually progressive.
- ▶ Treatment is controlling symptoms and minimizing further damage.

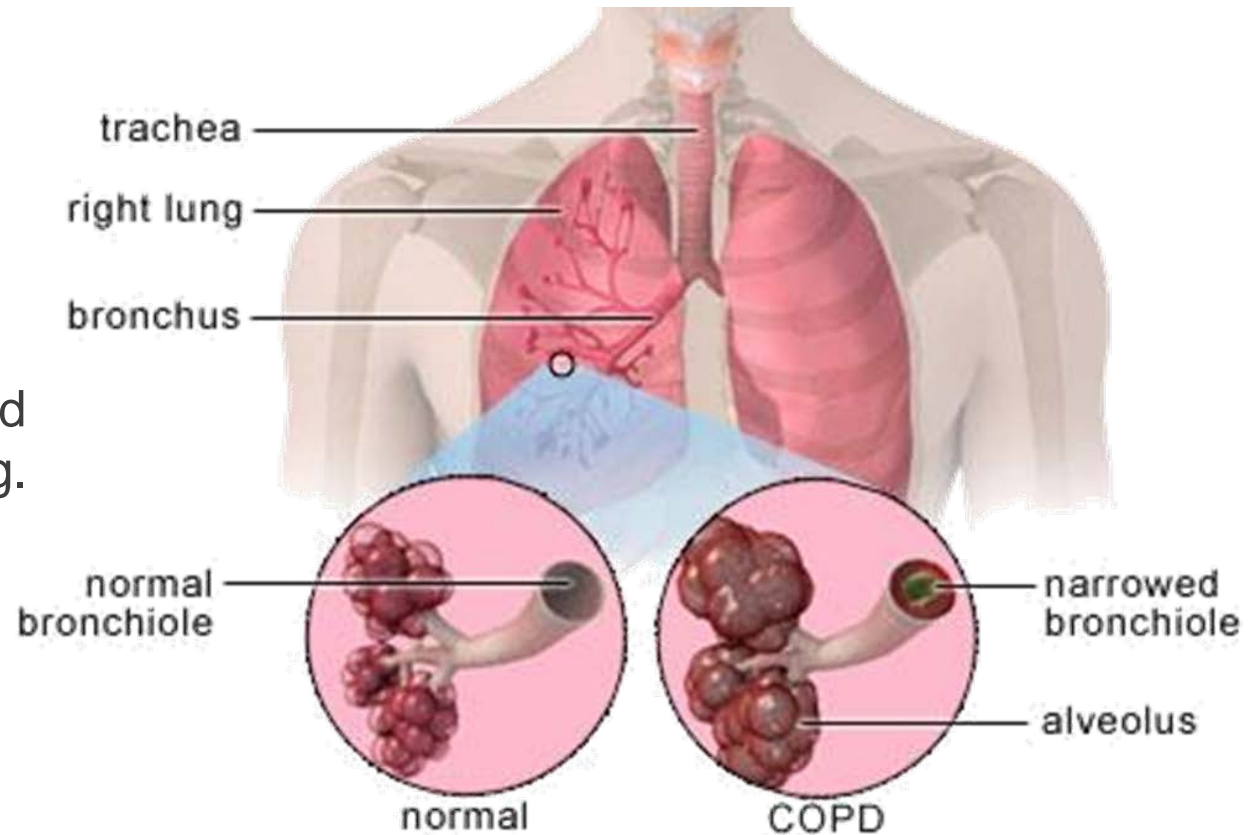


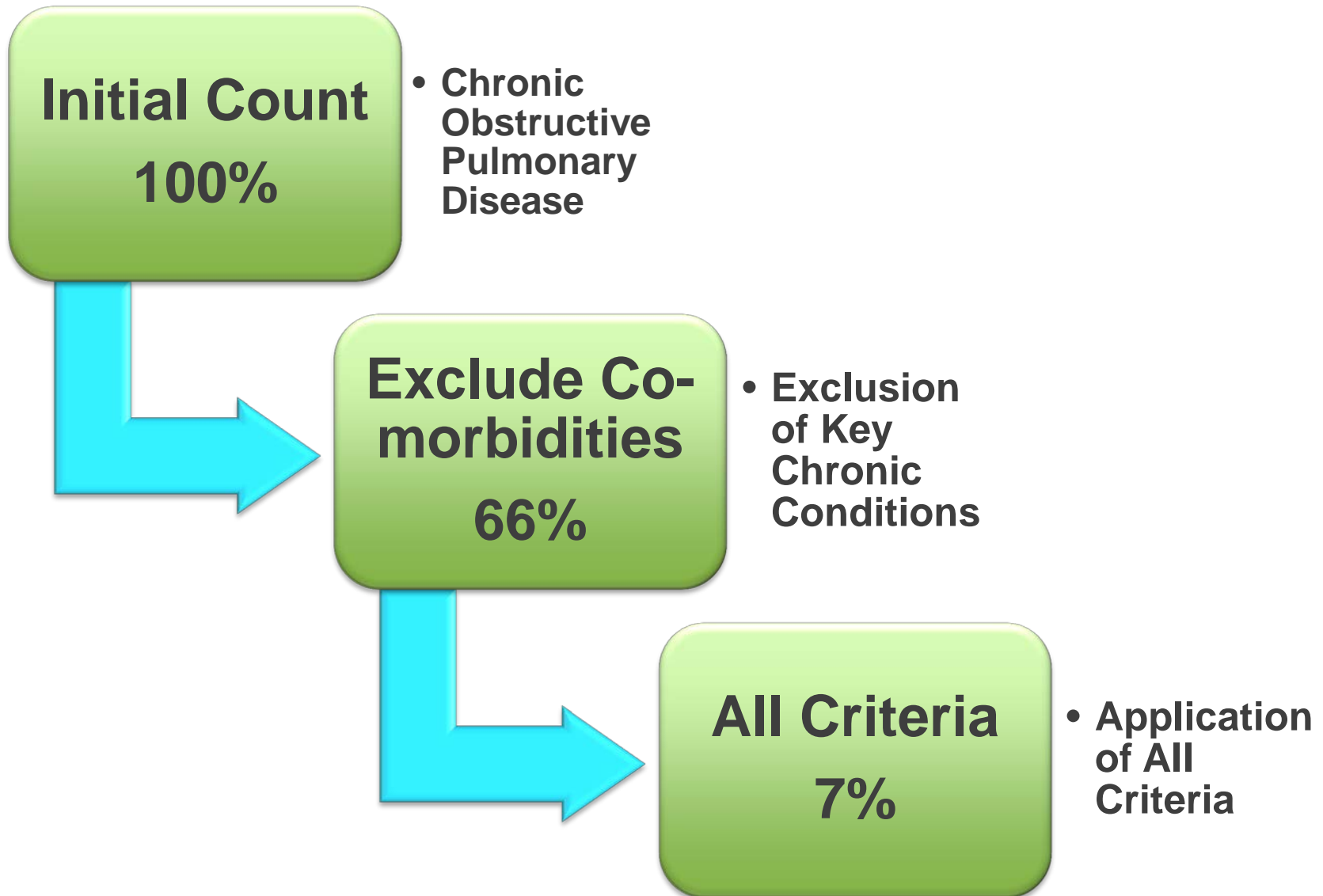
Image from Ultimate Health Fitness, 5/2013,
<http://www.ultimate-health-fitness.com/wp-content/uploads/2011/05/copd.jpg>

Study Design

- ▶ Study shows national percentage of patients lost and retained for each specification.
- ▶ A specification can be an inclusion or exclusion criterion, or it can be a “what if” question like a different definition of exacerbation.
- ▶ Static tables show each specification, one at a time, and the numbers for each.
- ▶ Dynamic tables have on/off switches for each specification and show net result of all specifications simultaneously.



The Patient Attrition Funnel



Static Table Illustration

	# Retained	% Retained	# Lost	% Lost
Total Patients	604,657	100%	0	0%
Example Flag: Ischemic Heart Disease	512,244	84.7%	92,213	15.3%



COPD Feasibility Conclusions from Claims

- ▶ With insurance claims integrated with pharmacy, the patient is not counted if he or she does not fill the script, and the numbers get lower.
 - Client was surprised that few patients complied with standard of care.
 - Behavior was poor until two hospitalizations.
- ▶ For trial recruitment, it forced loosening of criteria. Loosening greatly improved trial efficiency.
- ▶ The client was frustrated with limited measures, so **we added Electronic Health Records . . .**



Electronic Health Records better identify smoking & obesity. However, claims are still best for drug compliance.

Criteria	Claims		Clinical	
	%	Source Notes	%	Source Notes
Number of Patients with COPD	100%	Pts with 1+ ICD9 in past 12 mo.	100%	Pts with 1+ ICD9 in past 12 mo.
% Current or Former Smokers	11%	ICD9 only	70%	ICD9 and NLP
% Obesity	4%	ICD9 only	35%	ICD9 and BMI>30
Patient must be on ANY of these drugs: Advair, Symbicort, Spiriva	27%	Must fill script to make claim count.	40%	Any Rx counts, filled or not.

- **What to believe? The yellow boxes.** EHR is better chart capture. However, claims measure if patient filled the script. Next, we'll turn to test values.
- **Abbreviations:** ICD9 = ICD9 Diagnosis Code. NLP = Natural Language Processing of EHR, Electronic Health Records. BMI = Body Mass Index.

Spirometer Breathing Test

Protocol required using test scores to count available patients.

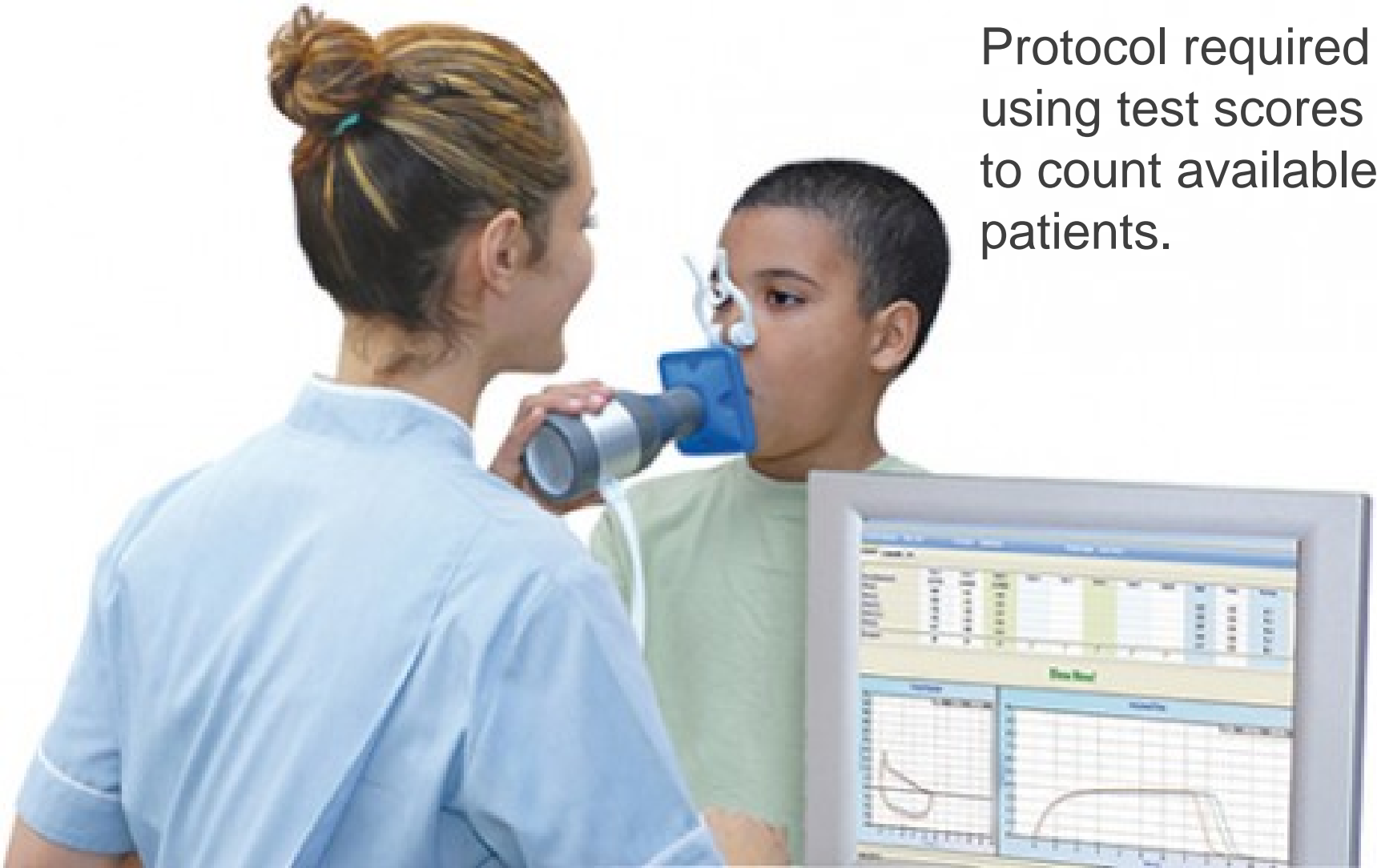


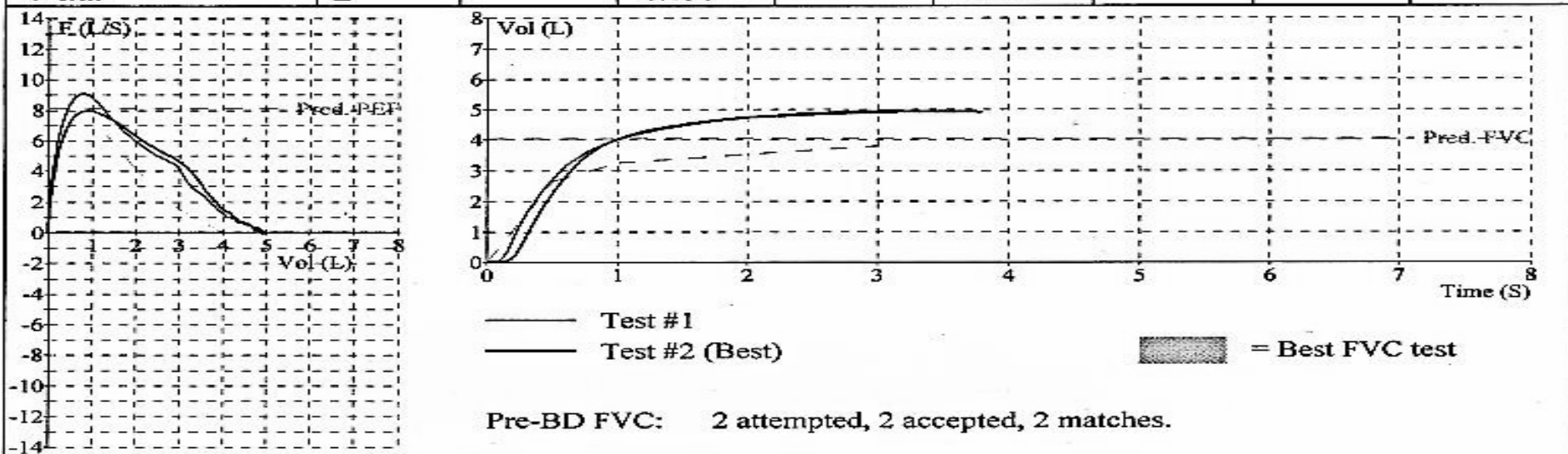
Image from RTM Web Site, <http://www.rtmagazine.com/2014/08/market-analysis-spirometry/>



Spirometer (Breathing Test): One Five-Minute Test on One Patient: 10 Data Rows, 44 Numbers, 2 Graphs

Spirometer Printout
 Healthy Optum Volunteer
 11/2014

Measurement	Units	Predicted	Pre-Bronchodilator Trial					
			1		2		Actual	% Pred.
			Actual	% Pred.	Actual	% Pred.		
FVC	L	4.008	4.880	122%	4.918	123%		
FEV1	L	3.219	4.124	128%	4.241	132%		
FEV1/FVC	%	80 %	85 %	105%	86 %	107%		
FEF25%	L/S	7.481	7.156	96 %	6.466	86 %		
FEF50%	L/S	4.077	4.207	103%	4.598	113%		
FEF75%	L/S	1.492	1.745	117%	1.972	132%		
FEF25-75%	L/S	3.305	4.436	134%	4.918	149%		
PEF	L/S	8.143	9.171	113%	8.029	99 %		
Exp. Time	Sec.		3.033		2.917			
V ext.	L		0.138		0.139			



Interpretation: Normal spirometry.

Focus on the Key Measure in the Protocol's Inclusion/Exclusion Criteria

- ▶ **Spirometry** – Performed by inhaling and forcefully exhaling into a spirometer.
- ▶ **Actual** – Actual results, which can be compared to predicted results.
- ▶ **Predicted** – Knudson formulas that predict normal values based on height, gender, and age. If actual values are far below 100% of predicted, there is impairment.
- ▶ **FVC** – Forced Vital Capacity (in liters): the total volume of air that can be exhaled following a deep inhalation.
- ▶ **FEV1** – The Forced Expiratory Volume at one second. This is a measure of how much air can be exhaled in one second following a deep inhalation.

- ▶ **FEV1/FVC** – Key ratio of two measures. The normal value for the FEV1/FVC ratio is 70% (and 65% in persons older than age 65). When compared to the reference value, a lower measured value corresponds to a more severe lung abnormality.
- ▶ **FEF 25%, FEF 50%, FEF 25%-75%** – Forced Expiratory Flow rate at certain points of completion in exhaling.
- ▶ **PEF** – Peak Expiratory Flow (maximum exhale rate). Patient can use a small plastic meter to measure PEF.
- ▶ **Exp. Time** – Expiratory Time, time spent exhaling, in seconds.
- ▶ **V ext.** – Volume of air from the beginning of expiration to the zero point of the FVC due to back Extrapolation.

What Did the Protocol Want?

- ▶ The inclusion/exclusion criteria of the protocol wanted patients **FEV1/FVC < 70%**. The lower the percent, the more impaired the breathing.
- ▶ We used **NLP, Natural Language Processing**, to turn notes from medical charts in Electronic Health Records into uniform and standardized statistics for tabulation.
- ▶ The best use of NLP is done in advance to create menus of key measures. FEV1/FVC was already in Optum's menu.



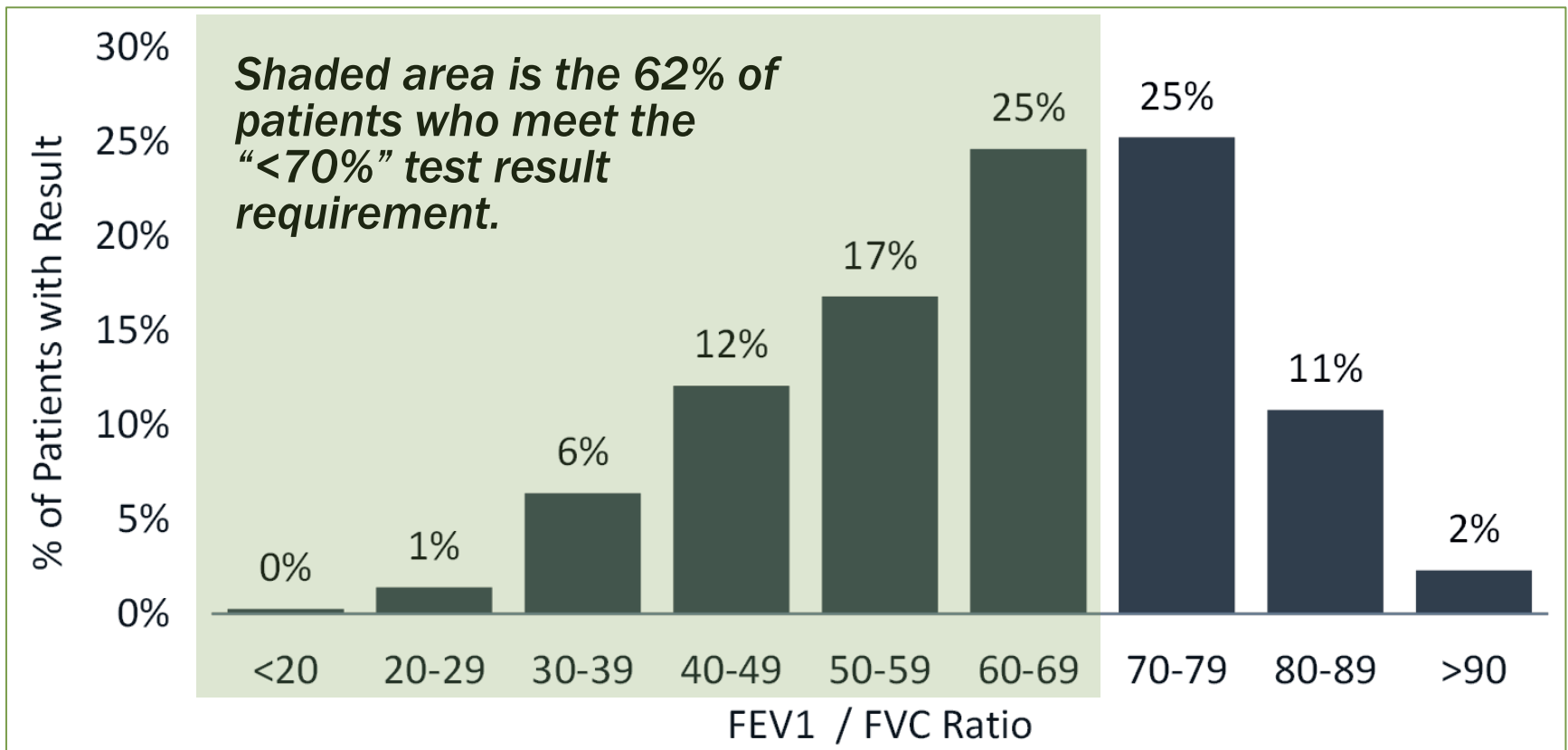
What Percent of COPD patients qualify at “<70%”? Answer: 62%. The rest would be a Screen Failure Rate.

Criteria and Simple Attrition (% of Total) Natural Language Processing of Electronic Health Records	Count	%
% with FEV1 / FVC result (COPD Patients with Spirometer Results)	15,394	4%
% with FEV1 /FVC result < 70% (Percentage of the 15,394 Available)	9,473	62%



For the effect of a threshold other than <70%, we have the frequency distribution of results.

Criteria and Simple Attrition (% of Total)	Count	%
Natural Language Processing of Electronic Health Records		
% with FEV1 /FVC result < 70% (Percentage of the 15,394 Available)	9,473	62%



Integrated Claims & Clinical for Protocol Feasibility Based on Patient Counts

Criterion #1

Criterion #2

DYNAMIC TABLE

On/Off Switch for Each
Inclusion/Exclusion

Table Instantly
Recalculates Patients



Criterion #3

Criterion #4



Statistical Projections And Physician & Investigator Counts

Patient Definition (Age 18+)	Projected Patient Count (Projection of <u>All</u> U.S. Patients Including the Uninsured)	Investigator Count (Matching Out of 128,000 in U.S.)	Physician Count (Matching Out of 1.2 Million in U.S.)
COPD	10,373,867	25,002	175,363
Prevalence Rate	4.3%*	n/a	n/a

* 10.3 million patients is 4.3% of the 242.7 million U.S. adults aged 18+.

Source: *Optum Clinformatics[®] for Clinical Trials, 2013 U.S. Population*

Finding the Patients: Fish Where the Fish Are



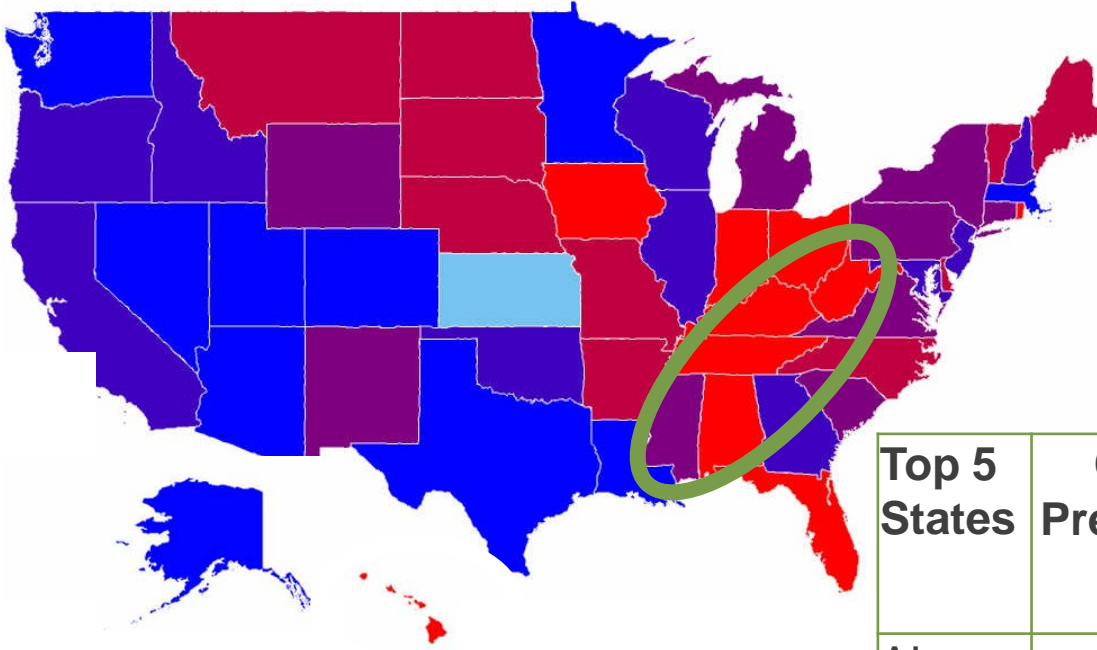
Insurance claims can locate patients with these:

1. Geographical targeting on disease prevalence
2. Investigator profiling with patient counts
3. Physician profiling for referrals, with patient count and distance from sites



COPD Area Ranking

Top 5 States on Prevalence Rate Are Circled and Appear in Table



Top 5 States	COPD Prevalence Rate	COPD Patients (18+)	Total Population (18+)
AL	7.5%	279,151	3,732,391
WV	7.4%	109,071	1,478,410
HI	7.3%	80,078	1,093,475
KY	6.8%	230,462	3,399,813
TN	6.3%	314,682	5,016,736
USA	4.3%	10,373,867	242,707,499

Prevalence Rate =
Patients Divided by Population
Can go down to county level.

Source: *Optum Clinformatics for Clinical Trials, 2013 Population Data*

Finding the Best Investigators

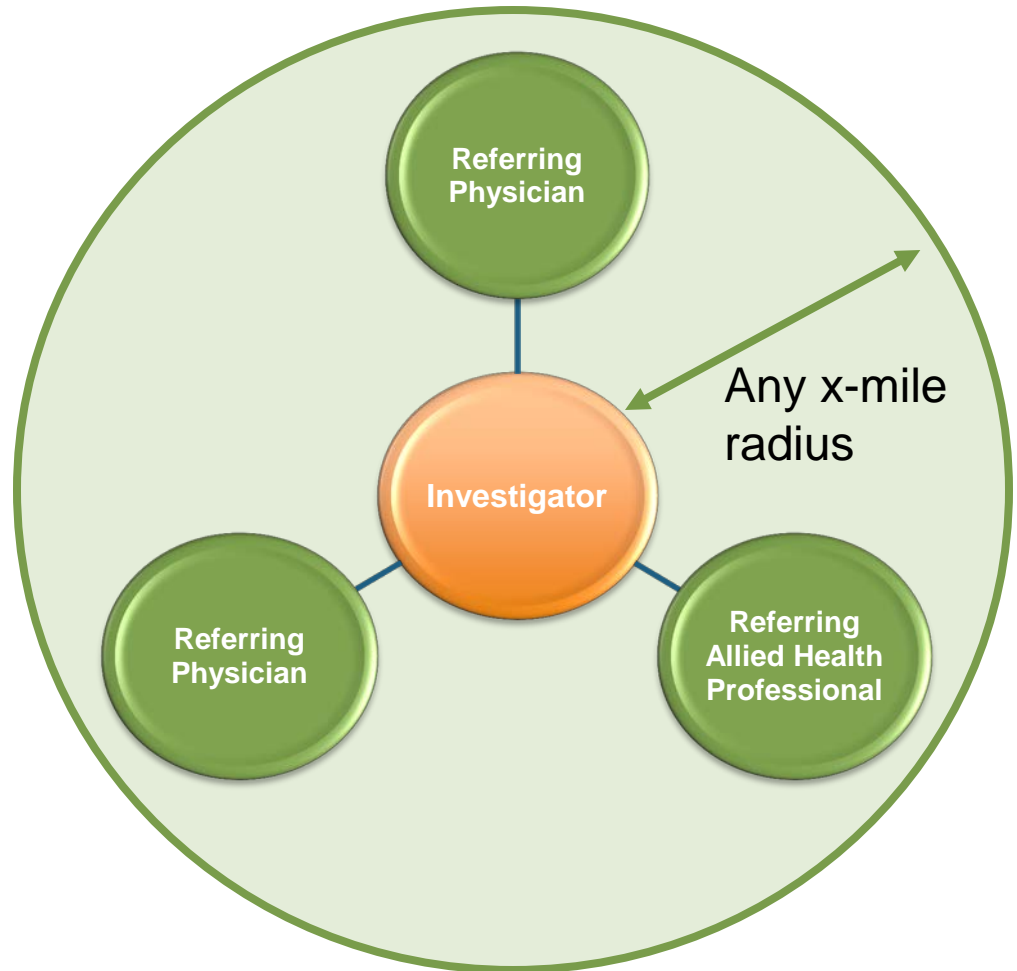
Patient Definition	Investigator Count (Investigators With Patients Matching the Criteria)
COPD	25,002

- ▶ Rank investigators on patient count.
- ▶ Filter on specialty:
 - The majority are internal medicine.
 - Only a few are pulmonary medicine.
- ▶ Also rank on:
 - Past trial experience (number of 1572 forms filed at FDA – this form is required for each trial)
 - Date of Last Trial (More Recent is Better)
 - Publication History (Identify KOLs – Key Opinion Leaders)

Source: *Optum Clinformatics™ for Clinical Trials*, Current Year

Finding Referral Physicians

- ▶ We found 175,363 who treat COPD.
- ▶ Filter the list to physicians within 50 miles of a site
- ▶ Rank everyone on:
 - Patient Count
 - Mileage from Site



Source: *Optum Clinformatics for Clinical Trials*, Current Year

Hub and Spoke Report for Referrals

What Should You Do?



- ✓ **Incorporate objective metrics into early planning.**
 - Avoid the infamous “rescue mode.”
 - If you are a sponsor, do not rely on epidemiology studies and investigator questionnaires as the only sources for protocol feasibility.
 - If you are a site, use EHR if you have it, or pull a few charts if not. Don’t guess – your guess bias is 2X to 10X of those available.
- ✓ **Use large national databases of insurance claims and EHR data, for best precision.**
- ✓ **Use data suppliers for EHR that pre-format desired results or who can data-mine for you.** If you license raw files, have analytic resources.
- ✓ **If feasibility data have bad news, suggesting a high screen failure rate, plan on enough sites and outreach.**
- ✓ **Rank investigators on patient count.** Investigators with the most patients enroll patients at least twice as fast.
- ✓ **Do not expect sites to enroll their whole quota using only site data.** There must be outreach. We showed *Hub & Spoke Report for Referrals*.



Data for Your Disease of Interest



- ▶ What are numbers for *my* disease?
- ▶ I will customize the insurance claims part of the speech for anyone.
- ▶ Free summary data will have a format like the COPD data.
 - Raw number of patients
 - Projected national number of patients
 - U.S. “Heat Map” of patient concentration
 - Number of treating investigators
 - Number of treating physicians
- ▶ Please give me your card with disease on back, come by the Optum booth (#1826), or send an e-mail.



Thank You

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