State of Diabetes-Related Trials in the ClinicalTrials.gov Dataset

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Duke Clinical Research Institute

Disclosures

- **Dr. Green receives institutional grant support for research from Merck and Amylin, and has received honoraria from Merck and Takeda for lectures.**
- Dr. Lakey receives funding from Amarin and Janssen
- Dr. Batch has participated in CME activities funded by Sanofi-Aventis
- Dr. Bethel receives institutional research support from Merck, Amylin, Eli Lilly, and Bristol Myers Squibb. She receives individual research support from Novartis and Bayer.
- Drs. Barnard, Chiswell, and Tasneem have no activities to disclose.

Background

- **The goal of this project is to characterize the diabetes-related clinical trials registered in the ClinicalTrials.gov dataset**
  - A collaboration between the US FDA and Duke University through the Clinical Trials Transformation Initiative (CTTI)

ClinicalTrials.gov History Overview

Date	Event	Description
Nov 21, 1997	Food and Drug Modernization Act of 1997 (FDAMA) section 113 enacted	Mandated the creation of the clinicaltrials.gov registry for efficacy trials in serious and life-threatening conditions and interventions regulated by the FDA
Feb 29, 2000		First version ClinicalTrials.gov publicly available
September 2004	International Committee of Medical Journal Editors' (ICMJE) policy established	Required studies published in their journals be registered in Clinicaltrials.gov or other equivalent publicly available registries.
September 27, 2007	**US Public Law 110-85 FDA Amendments Act (FDAAA) section 801 enacted**	**Created a legal requirement for the registration of trials of drugs, biologics, and devices**
September 23, 2008		Results reporting launched
September 28, 2009		Adverse Event reporting launched

Methods

- A dataset of 96,346 studies was downloaded from ClinicalTrials.gov on September 27, 2010
- A database for the Aggregate Analysis of ClinicalTrials.gov (AACT) was created to facilitate analysis
- The subset of interventional trials corresponding to the FDA enactment of mandatory registration in 2007 was identified

Creation of the Diabetes Trials Dataset

- **Condition terms identified from:**
  - *Selected disease nodes of the 2010 MeSH thesaurus*
  - *Non-MeSH (free-text) terms appearing in ≥ 5 studies*
- **MeSH and non-MeSH terms were reviewed by specialists at Duke University and annotated for relevance to Endocrinology**
- **Terms further classified to identify those with relevance to diabetes or diabetes-related complications**

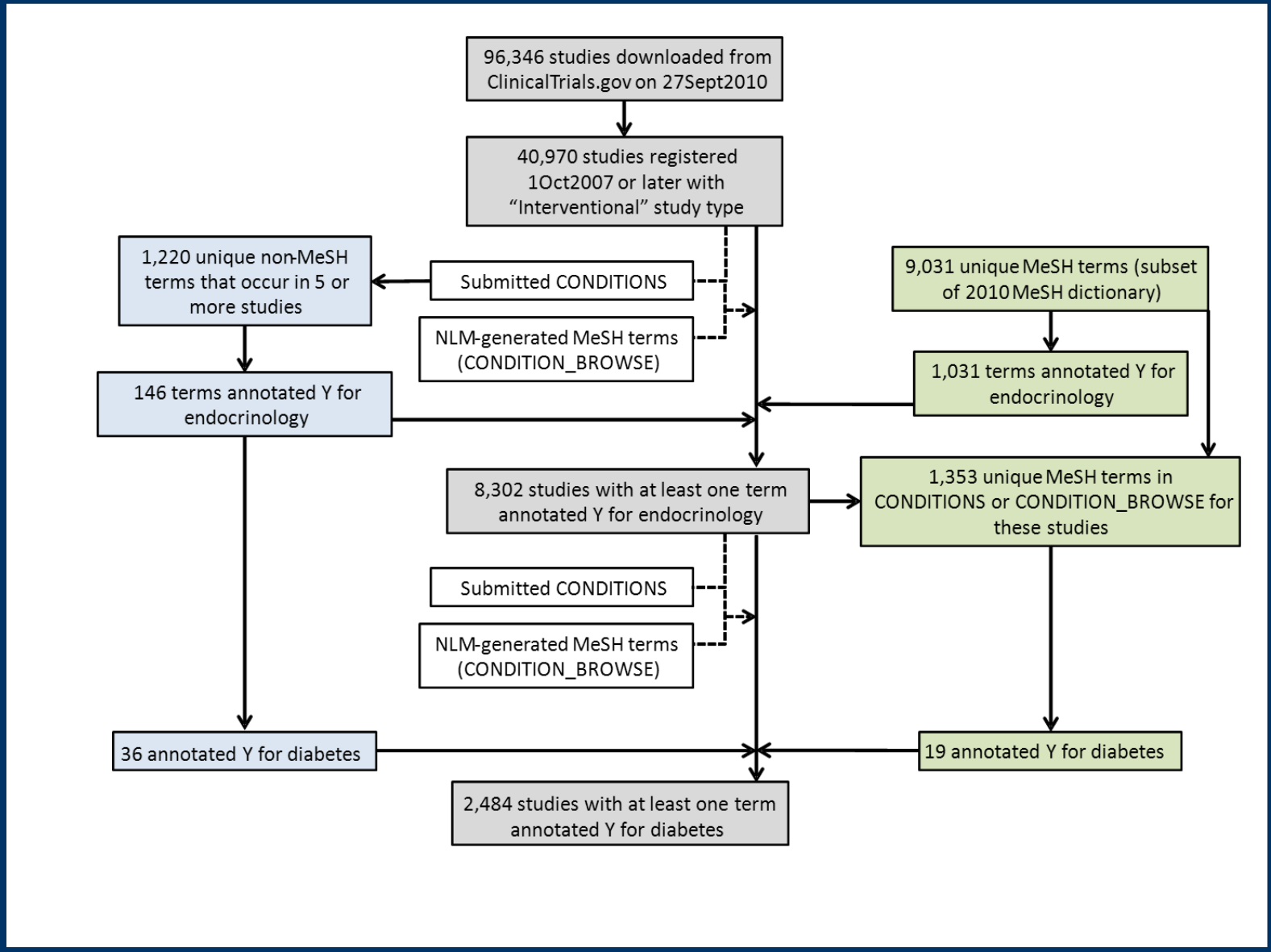
Creation of the Diabetes Trials Dataset

MeSH terms
Insulin Resistance
Islets of Langerhans Transplantation
Diabetes Complications
Diabetes Mellitus
Diabetes Mellitus, Type 1
Diabetes Mellitus, Type 2
Diabetes, Gestational
Diabetic Foot
Diabetic Ketoacidosis
Diabetic Nephropathies
Diabetic Neuropathies
Diabetic Retinopathy
Foot Ulcer
Glucose Intolerance
Glucose Metabolism Disorders
Hyperglycemia
Hyperinsulinism
Prediabetic State
Pregnancy in Diabetics

Non-MeSH terms
Diabetes
Diabetes Mellitus Type 2
Diabetes Mellitus, Non-Insulin-Dependent
Diabetes Mellitus, Type I
Diabetes Mellitus, Type II
Diabetes Prevention
Diabetes Type 2
Diabetes, Type I
Diabetic Foot Ulcer
Diabetic Foot Ulcers
Diabetic Gastroparesis
Diabetic Macular Edema
Diabetic Nephropathy
Diabetic Neuropathy
Diabetic Neuropathy, Painful
Diabetic Peripheral Neuropathy
Diabetic Polyneuropathy

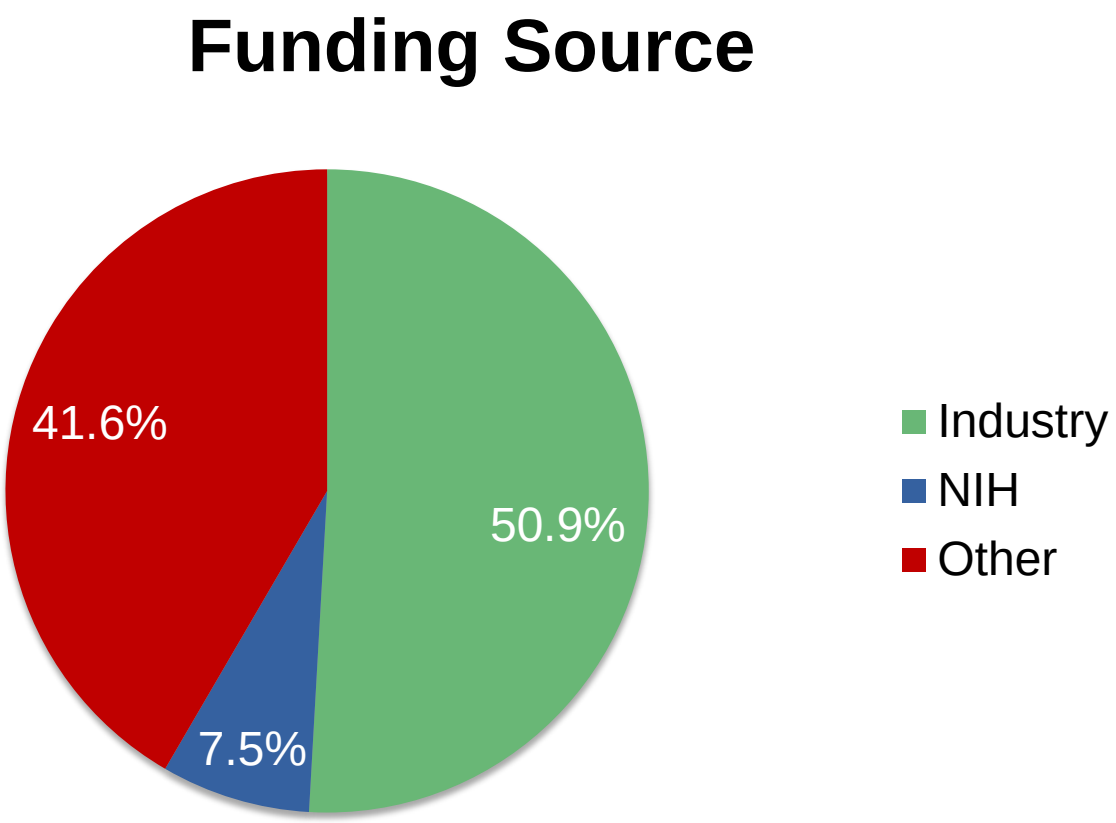
Non-MeSH terms
Foot Ulcer, Diabetic
Gestational Diabetes
Gestational Diabetes Mellitus
Glucose Metabolism
Glycemic Control
Impaired Fasting Glucose
Impaired Glucose Tolerance
Insulin Sensitivity
Painful Diabetic Neuropathy
Pre-diabetes
Prediabetes
Proliferative Diabetic Retinopathy
Type 1 Diabetes
Type 1 Diabetes Mellitus
Type 2 Diabetes
Type 2 Diabetes Mellitus
Type 2 Diabetes Mellitus (T2DM)
Type II Diabetes
Type II Diabetes Mellitus

Creation of the Diabetes Trials Dataset



RESULTS

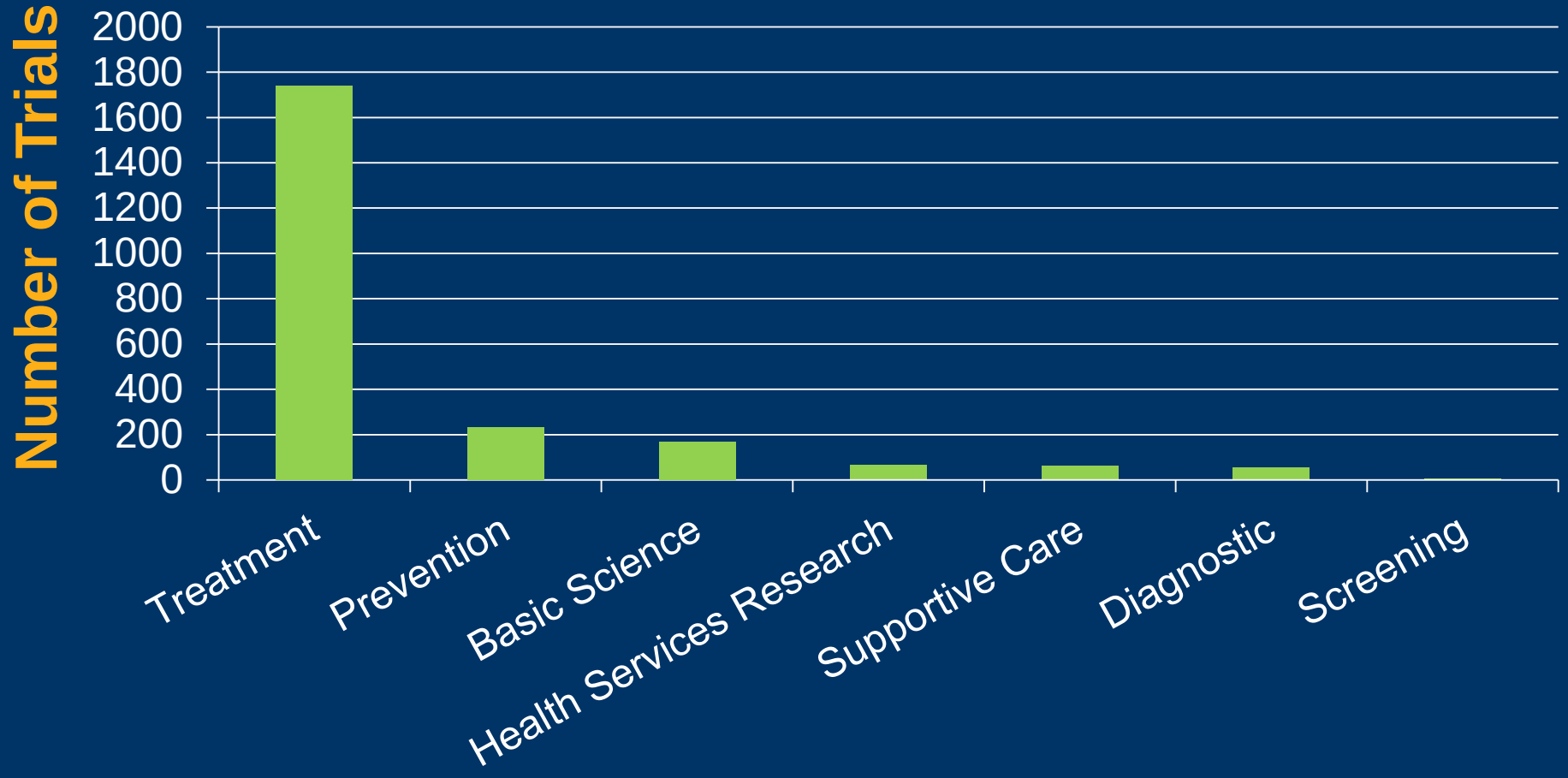
Characteristics of Diabetes-Related Trials



Funding source derived from lead sponsor and collaborator data

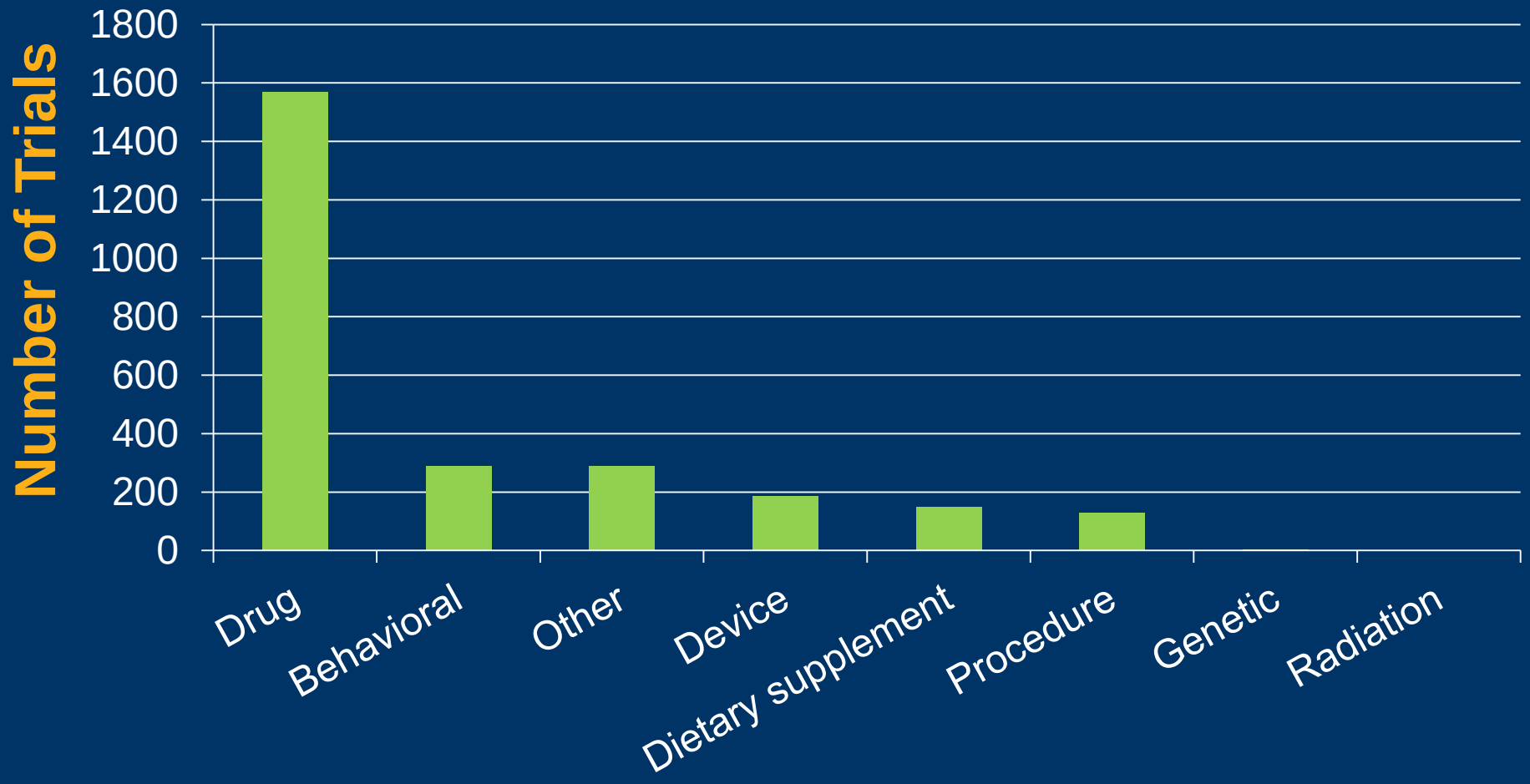
n = 2,484

Primary Purpose of Diabetes-Related Trials



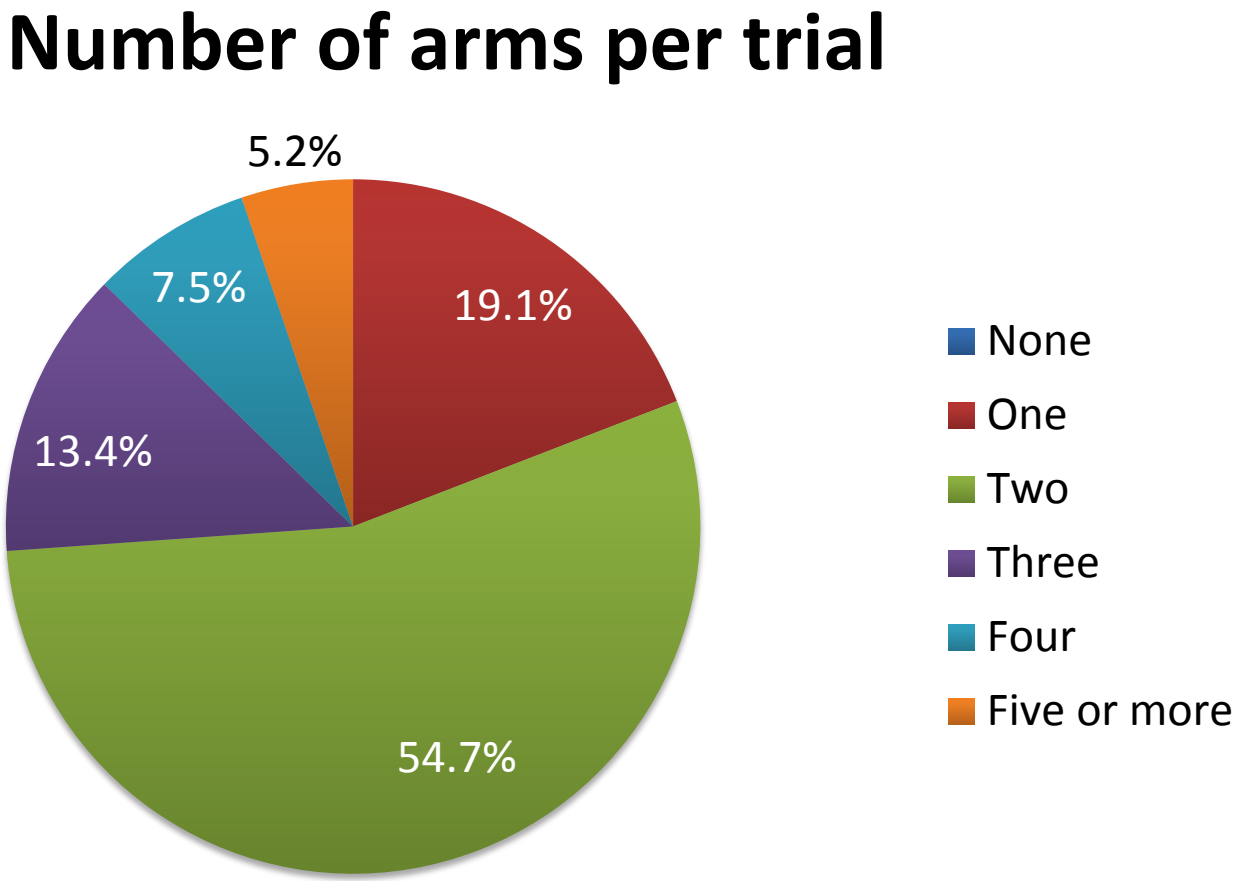
Total n = 2327

Types of Interventions in Diabetes-Related Trials



Total n = 2484

Characteristics of Diabetes-Related Trials



n = 2,351

Characteristics of Diabetes-Related Trials

Number of Participants in Trials

Percent of Trials	Planned enrollment
91%	≤ 500 subjects
58.6%	≤ 100 subjects
38.4%	≤ 50 subjects

n=2,449

Characteristics of Diabetes-Related Trials

Duration of trials

Mean +/- SD	1.8 +/- 1.48 years
Median (25^{th}, 75^{th})	1.4 (0.8, 2.3) years
Min, Max	0.0, 12.1 years

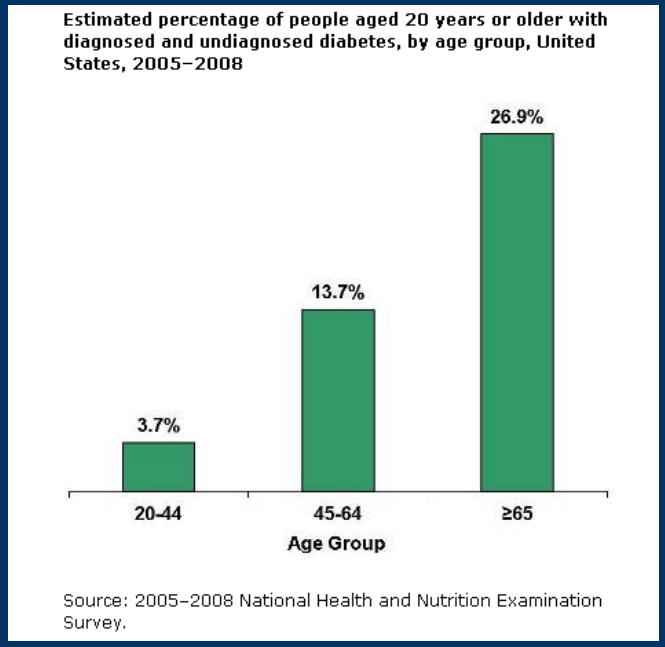
Duration defined as years from study start date to date when f/u for primary endpoint complete

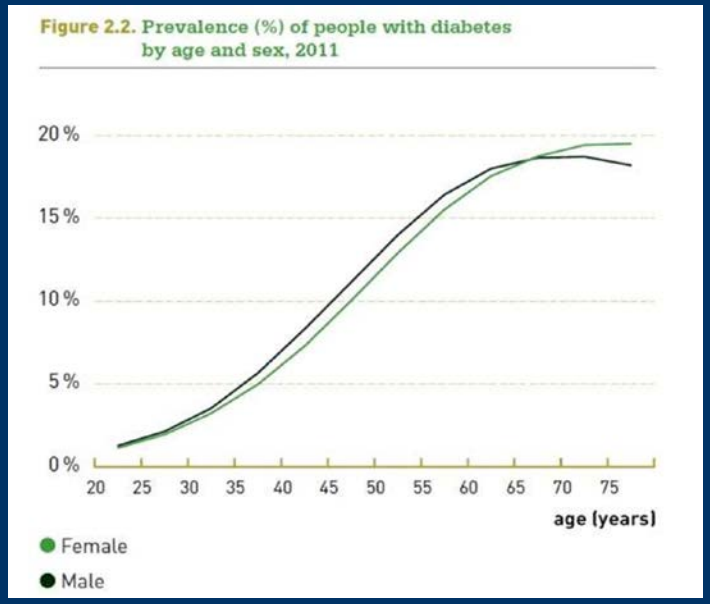
n=2,295

Characteristics of Diabetes-Related Trials

Ages of Participants	Number of Trials (%)
Maximum age ≤ 18 years	92 (3.7)
Minimum age ≥ 18 years	2225 (89.6)
Excludes ages > 65 years	764 (30.8)
Excludes ages > 75 years	1364 (54.9)
Minimum age ≥ 65 years	15 (0.6)
Minimum age ≥ 75 years	1 (0.0)

Total n = 2,484

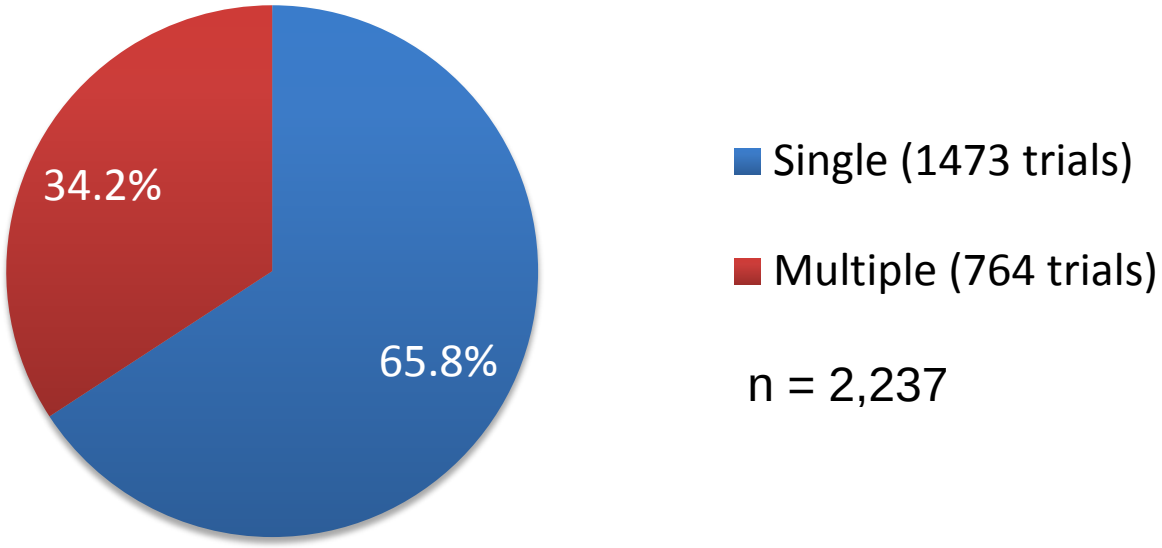




http://www.idf.org/diabetesatlas/5e/diabetes

Characteristics of Diabetes-Related Trials

Number of Trial Sites



Number of Sites (Multiple Site Trials)

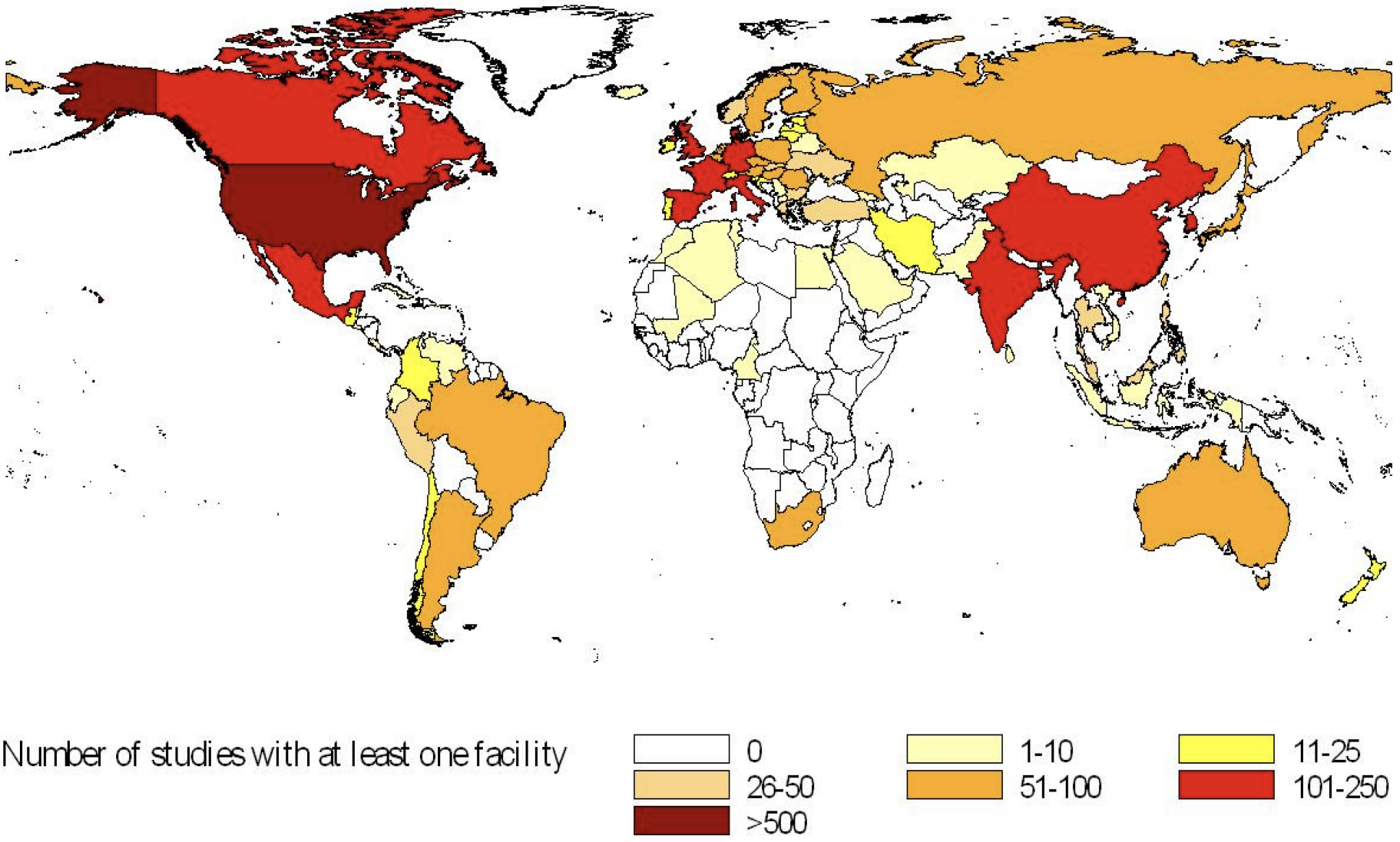
Mean +/- SD	**34.6 +/- 60.25**
Median (25^{th}, 75^{th})	**11.0 (3.0, 44.0)**
Min, Max	**2, 741**

Characteristics of Diabetes-Related Trials

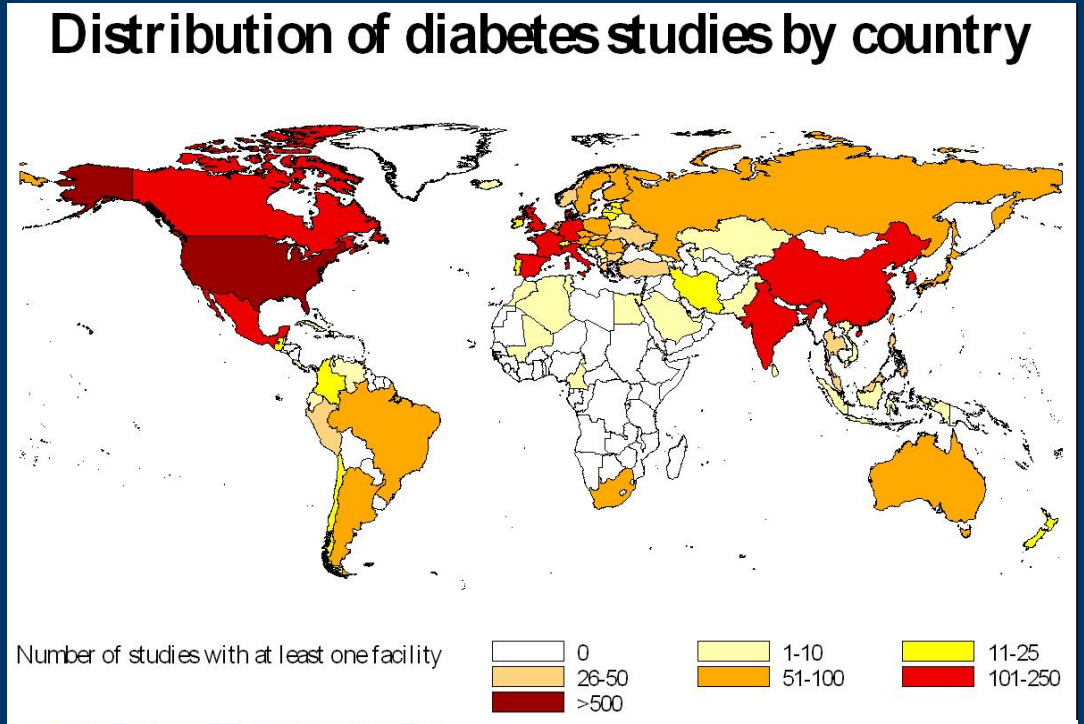
Locations of Trial Facilities	Number of Trials (%)
US only	907 (40.5)
Outside US only	1111 (49.7)
Both US and Outside US	219 (9.8)

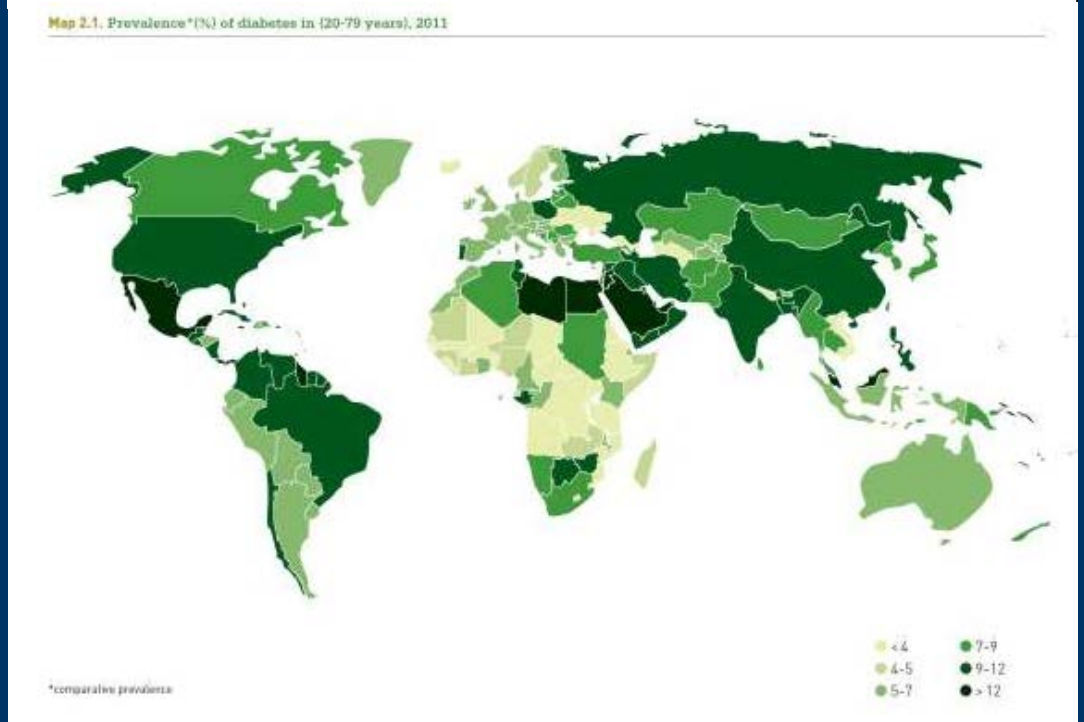
Total n = 2,237

Distribution of diabetes studies by country

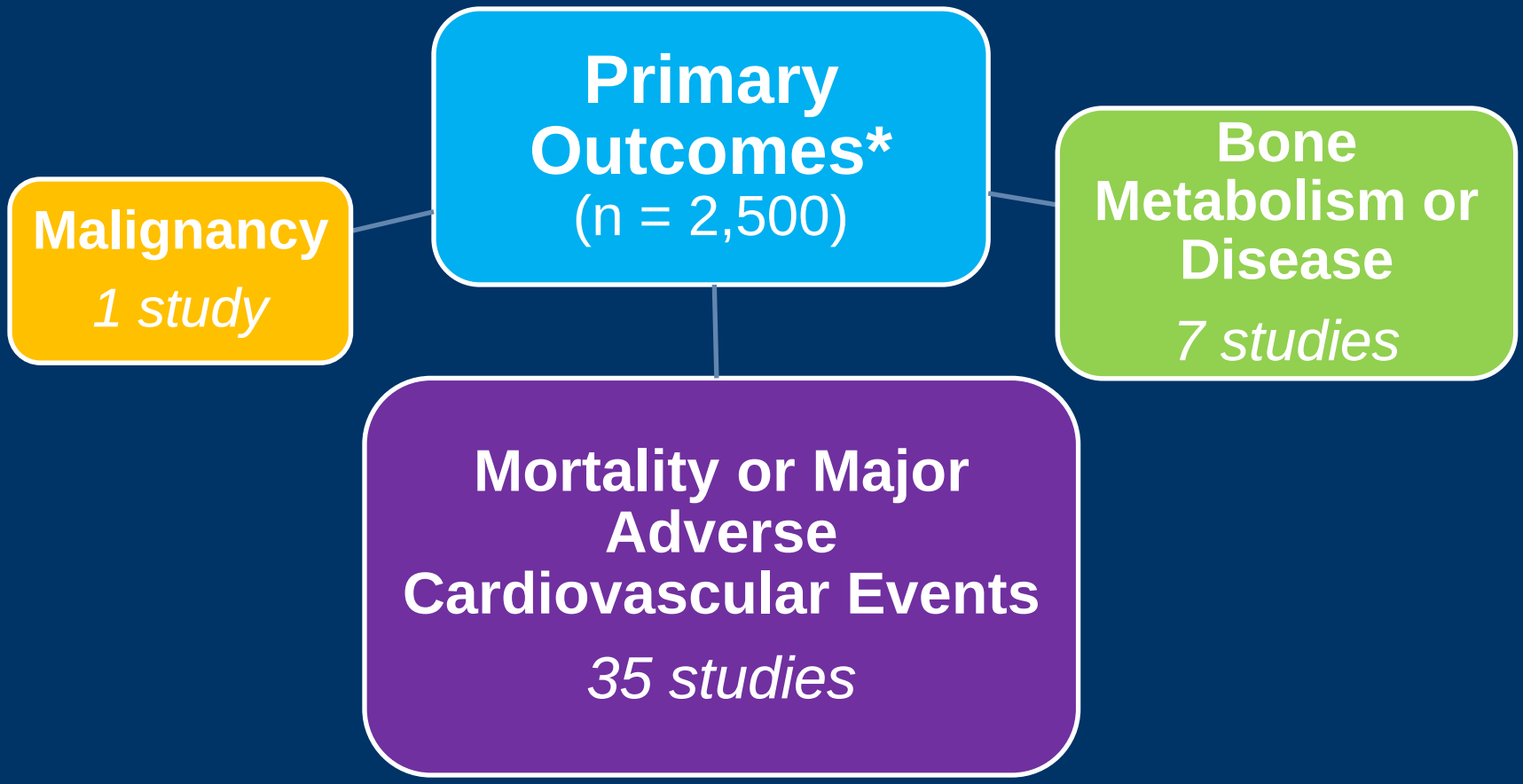


Trials distribution as compared to 2011 IDF estimates of disease prevalence





Characteristics of Diabetes-Related Trials



*Derived from manual review of free-text outcomes descriptions
No trials listed a primary outcome related to pancreatitis

Conclusions

The majority of diabetes-related trials:

- Are funded by industry
- Have a therapeutic rather than preventive, supportive or diagnostic purpose
- Involve drug therapy rather than behavioral or non-drug interventions
- Compare few interventions

Conclusions

The majority of diabetes-related trials:

- Include relatively small numbers of patients
- Take place at a single site
- Exclude those at extremes of age
- Do not focus upon clinically significant cardiovascular complications

Trial distribution does not correlate with the prevalence of diabetes in many locations

Conclusions

Recently registered trials may not sufficiently address important diabetes care issues or involve affected populations

Information available from this analysis may be meaningful in the allocation of future research activities and resources

Limitations

ClinicalTrials.gov

- Does not include information for all studies worldwide
- Data collection
  - *Has changed over time*
  - *Completeness and quality variable across trials*
  - *Some data may be entered as “other” or in free text*
- Difficult to fully assess proportionality of trial activity within given areas

Limitations

Methods

- Annotation of terms and classification of trials not independently validated
- Data presented do not reflect changes in trial characteristics over time

Acknowledgments

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