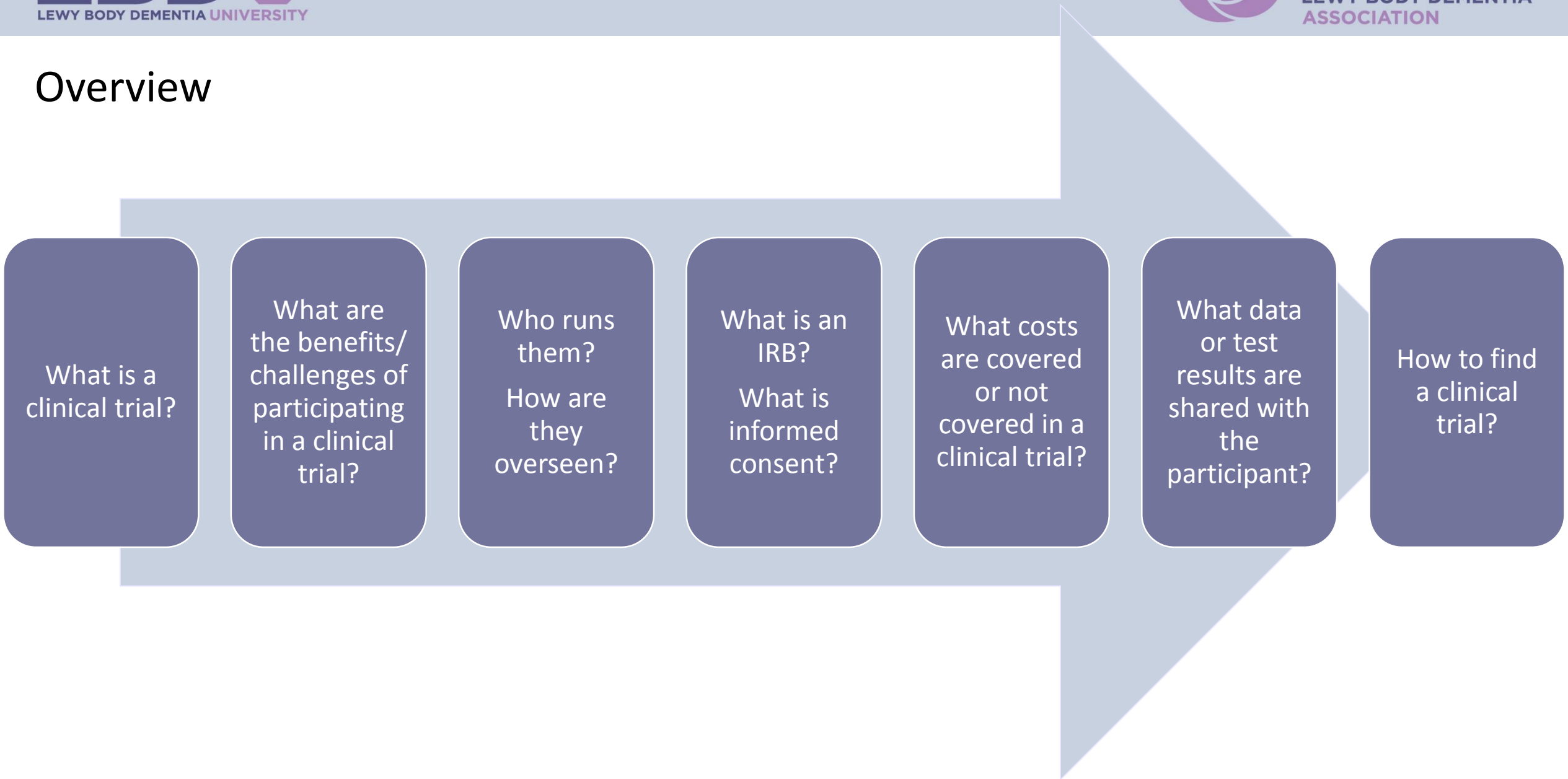
LBDU
LEWY BODY DEMENTIA UNIVERSITY

LBDA
LEWY BODY DEMENTIA ASSOCIATION

An Introduction to Clinical Trials

DANIEL KAUFER, MD
Associate Professor, Neurology and Psychiatry
Division Chief, Cognitive & Behavioral Neurology
Director, Memory Disorders Program
University of North Carolina at Chapel Hill

Overview


What is a clinical trial?
What are the benefits/ challenges of participating in a clinical trial?
Who runs them?
How are they overseen?
What is an IRB?
What is informed consent?
What costs are covered or not covered in a clinical trial?
What data or test results are shared with the participant?
How to find a clinical trial?

How does clinical research differ from clinical care?

Clinical research involves human subjects who participate in a study protocol designed to answer a question that contributes to medical knowledge

Clinical trials are meant for research, not to administer proven effective medical care.

Clinical research is the only legitimate pathway for developing new, safe, and effective treatments for a medical disorder or condition

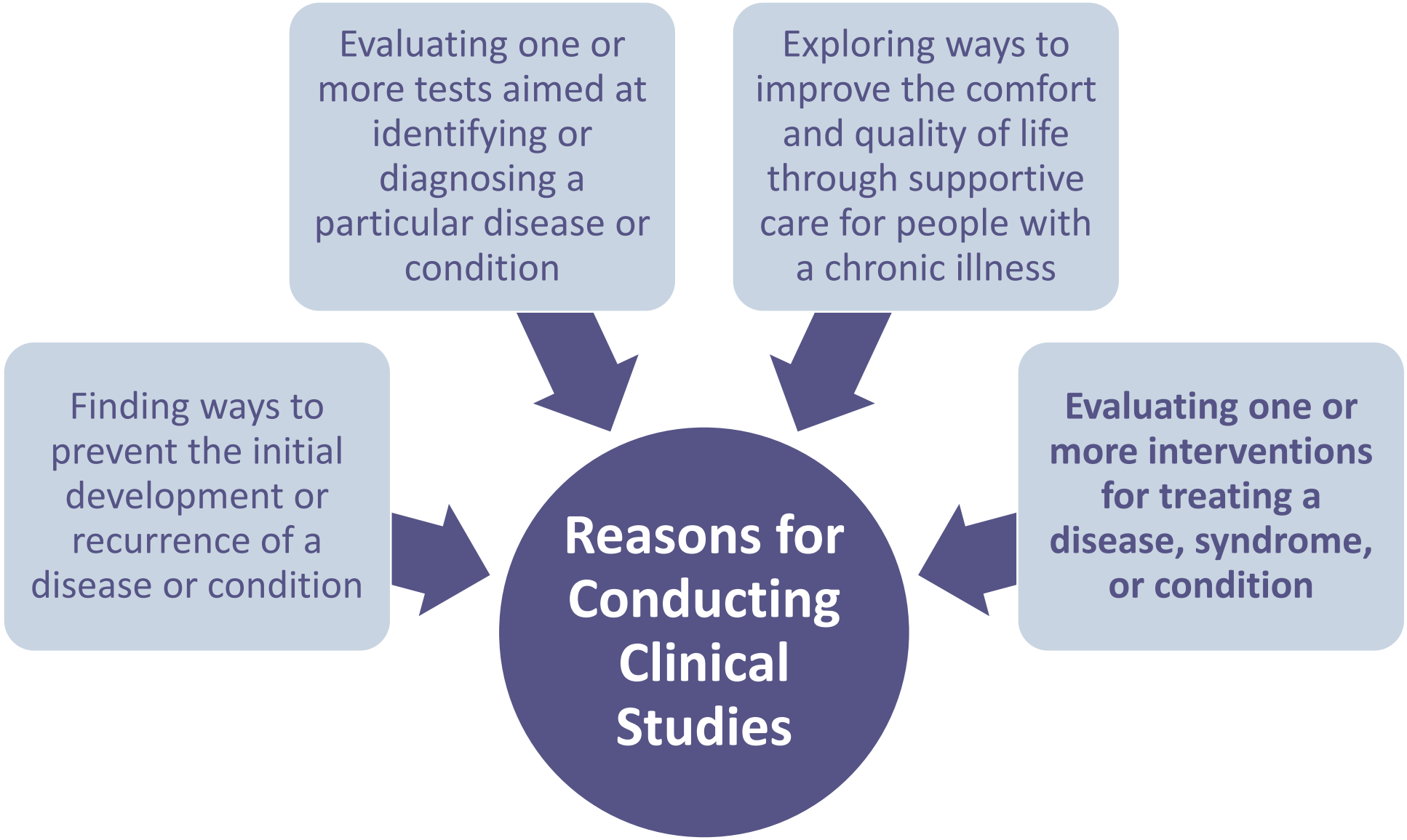
Clinical Research Studies

Observational

- evaluates a health–related outcome that may be done in conjunction with clinical care

Interventional:

- *(also known as a clinical trial)* evaluates or compares one or more therapeutic interventions for safety and potential benefits


Evaluating one or more tests aimed at identifying or diagnosing a particular disease or condition
Exploring ways to improve the comfort and quality of life through supportive care for people with a chronic illness
Finding ways to prevent the initial development or recurrence of a disease or condition
Evaluating one or more interventions for treating a disease, syndrome, or condition
Reasons for Conducting Clinical Studies

Drug Development Process for Human Disease

Preclinical

Clinical
(Average time/$: 12 years / $1.2 billion)

Potential treatment identified based on laboratory studies *(in vitro)*

Proof of concept studies in laboratory animal model *(in vivo)*

Human Testing - Clinical

Drug Development Process for Human Disease: Clinical Phases

Phase 1:

(< 100 subjects)	Is the therapy safe to use in people? (usually tested in normal human subjects)

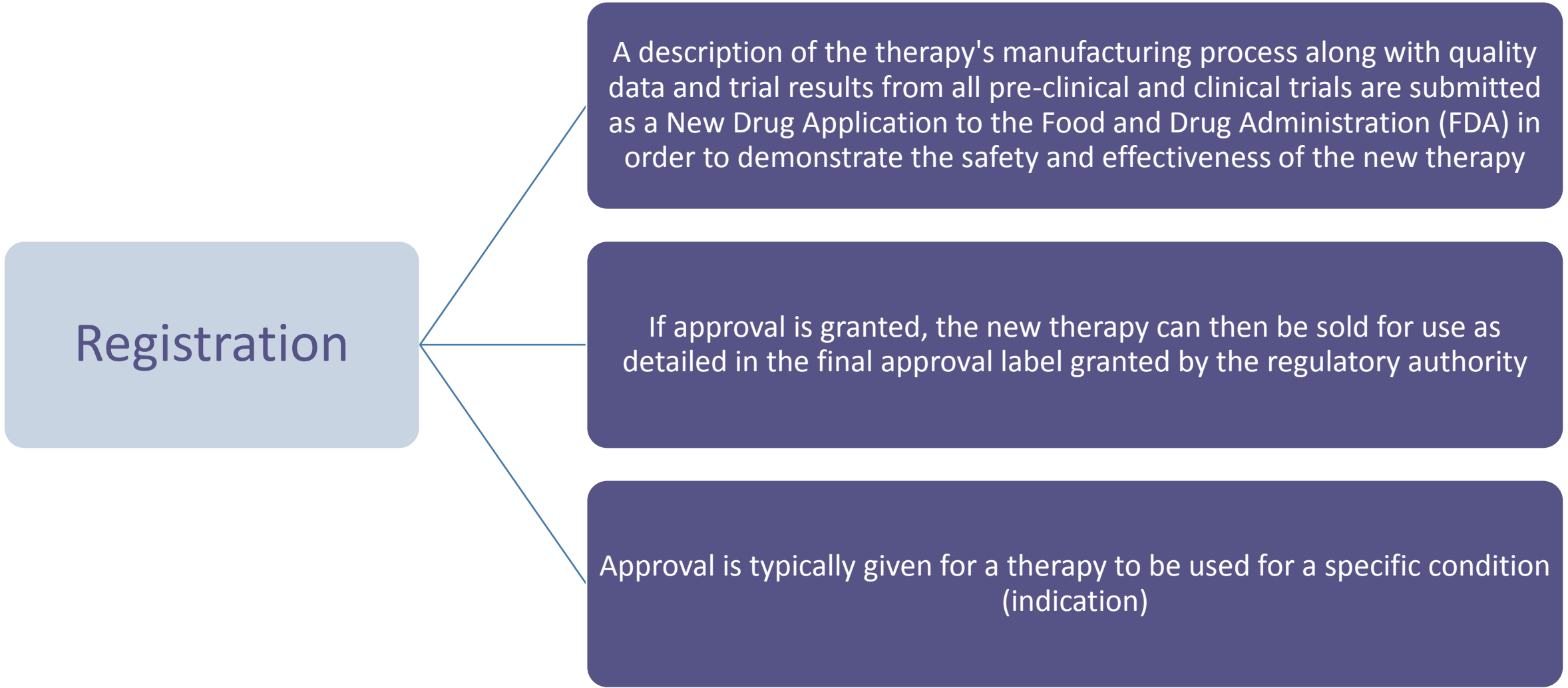
Phase 2:

(100-1000 subjects)	Assess the safety and potential effectiveness of an experimental therapy for a specific medical condition i.e. what dose or delivery method provides the highest benefit and the least amount of risk?

Phase 3:

(100s – 1000s), a.k.a. "pivotal" trial;	**Typically involves testing 1 or more doses of the experimental therapy in a *randomized, placebo-controlled, double-blind* study to determine if the therapy is safe and effective; data from these studies are reviewed by the FDA for regulatory approval**	**Subjects are assigned by chance (randomized) to receive either active treatment or placebo (placebo-controlled), which is not known by either the subject or investigator (double-blind)**

Drug Development Process for Human Disease: Registration



Therapeutic Interventions: Regulatory Tiers

FDA Registered Therapies *(Pharmaceuticals):*

- Requires clinical research protocols that must meet high standards for scientific merit (e.g., double-blind, placebo-controlled), safety, and ethical conduct

Vitamins, Herbal Supplements *(Nutraceuticals):*

- Designation based on Good Manufacturing Practice
- Not intended to treat specific medical conditions
- Not rigorously tested for efficacy or safety

Therapeutic Interventions for Neurodegenerative Disorders

Symptomatic (palliative):

- focus of treatment is ***alleviating*** one or more signs/symptoms associated with the disease or condition
- potential benefit of treatment is not cumulative

Disease-modifying:

- focus of treatment is to ***alter the underlying disease process*** in a way that slows down or halts progression, or reverses decline
- potential benefit of treatment may be cumulative

Who Conducts Clinical Studies?

Every clinical study is led by a principal investigator, typically a medical doctor, and includes a research team that may include doctors, nurses, social workers, and other health care professionals

Clinical studies can be sponsored by pharmaceutical companies, academic medical centers, Federal agencies such as the National Institutes of Health and the U.S. Department of Veterans Affairs

Where Are Clinical Studies Conducted?

Academic research centers, which typically conduct a variety of different research studies, in addition to performing clinical trials and providing clinical care

Community-based clinical trial centers that primarily focus on performing clinical trials with little or no provision for clinical care

Private practices that focus primarily on clinical care but also conduct clinical trials.

Institutional Review Board (IRB)

An IRB is made up of doctors, researchers, and members of the community who review the study protocol.

- Ensure that research risks are minimized and are reasonable in relation to any potential benefits
- Review, approve, and monitor all clinical research studies
- Review the informed consent document to make sure it is understandable and clearly describes the risks and benefits of the study

INFORMED CONSENT

- Provides potential and enrolled participants information about a clinical study
  - Intended to help a person make an informed decision about the risks of, potential benefits of, and alternatives to the study
- A person must sign an informed consent document before participating in a research study
  - Signing the document and providing consent is not a contract
  - Participants may withdraw from a study at any time

Clinical Study Research Plan

A clinical study is conducted according to a **research plan** (protocol) that is designed to answer specific research questions and safeguard the health of participants and covers the following:

- Reason for conducting the study
- Who may participate in the study (eligibility criteria)
- The number of participants needed
- The schedule of tests, procedures, or drugs and their dosages
- The length of the study
- What information will be gathered about the participants

LBDU
LEWY BODY DEMENTIA UNIVERSITY

LBDA
LEWY BODY DEMENTIA ASSOCIATION

WHAT DO YOU NEED TO KNOW?

BASICS

What is being studied?

What is the therapeutic rationale for this treatment?

What do we know about possible treatment effects?

WHAT DO YOU NEED TO KNOW?

ELIGIBILITY

What is the target population?

Inclusion criteria: age, diagnosis, severity, etc.

Exclusion criteria: age, severity, prohibited medications, other medical conditions, etc.

Many studies have fairly strict criteria

WHAT DO YOU NEED TO KNOW?

TREATMENT ARMS

What are the possible interventions (e.g., treatment vs. placebo) that I might receive during the trial?

How will it be determined which intervention I receive (for example, by chance)?

Who will know which intervention I receive during the trial (blinding)?

WHAT DO YOU NEED TO KNOW?

OTHER MEDICATIONS

Can I take my current treatment(s)?

Are there any medications that I am not allowed to take?

Are there other treatment options available?

LBDU
LEWY BODY DEMENTIA UNIVERSITY

LBDA
LEWY BODY DEMENTIA ASSOCIATION

WHAT DO YOU NEED TO KNOW?

STUDY REQUIREMENTS

- What will I have to do to participate?
- Do I need to have a study partner?
- What tests and procedures are involved?
- How often will I have to visit the hospital or clinic?
- Will I have to stay overnight?
- How long will the study last?

WHAT DO YOU NEED TO KNOW?

COST/PAYMENTS

Who will pay for my participation? (experimental vs. standard of care)	Will I be reimbursed for other expenses?	Who will oversee my medical care while I am participating in the trial?	What are my options if I am injured during the study?

LBDU
LEWY BODY DEMENTIA UNIVERSITY

LBDA
LEWY BODY DEMENTIA ASSOCIATION

WHAT DO YOU NEED TO KNOW?

FOLLOW-UP/TERMINATION

What if I decide to withdraw from the study?	What type of long-term follow-up care is part of this trial?	If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?	Will results of the study be provided to me? (e.g., which treatment arm, brain imaging data, genetic testing, etc.)?

RESOURCES

- Comprehensive listing of clinical trials:
  - **clinicaltrials.gov**
- Regulatory guidelines:
  - **FDA.gov**
- Lewy Body Dementia Association:
  - **lbda.org**