

# UNRAVELING THE POWER OF ESTIMANDS

## IN DERMATOLOGY RESEARCH

Kelly Van Lancker

# ESTIMAND?

# CLINICAL TRIALS: ESTIMAND

What precisely are we **aiming**  
to calculate and **find out**?



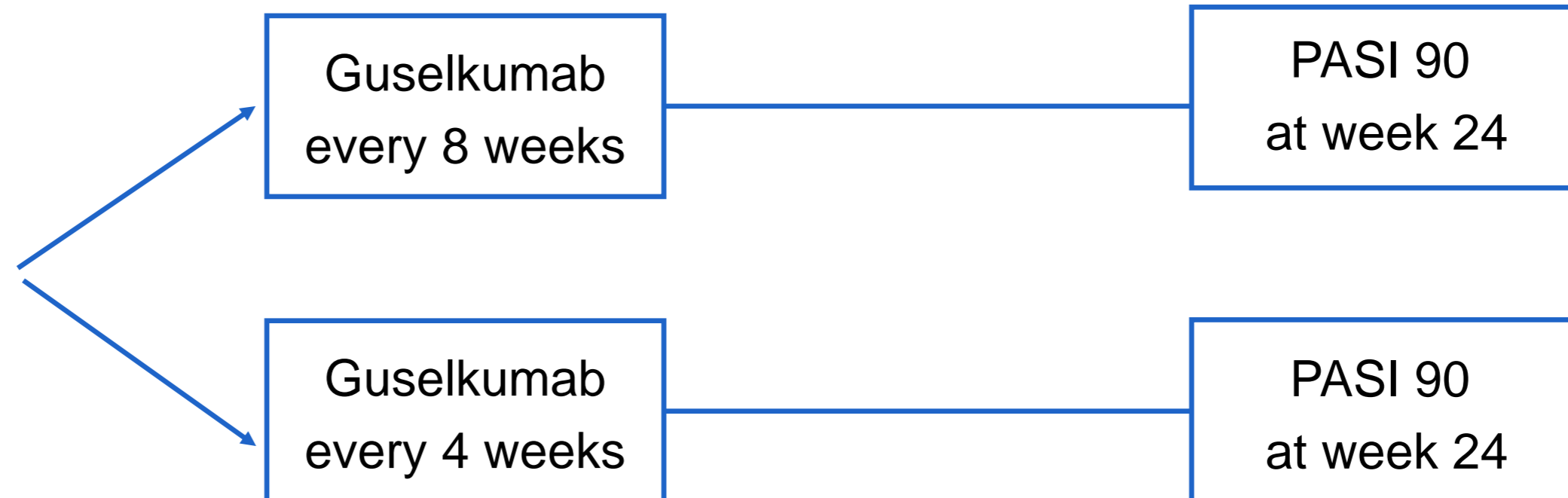
# DIFFERENT QUESTIONS CAN BE ASKED

- What is the treatment effect when **all patients adhere** precisely to the treatment instructions?
- What is the treatment effect for all patients, **regardless of strict adherence** to instructions?
- For **patients who could tolerate the treatment**, what is the treatment effect?

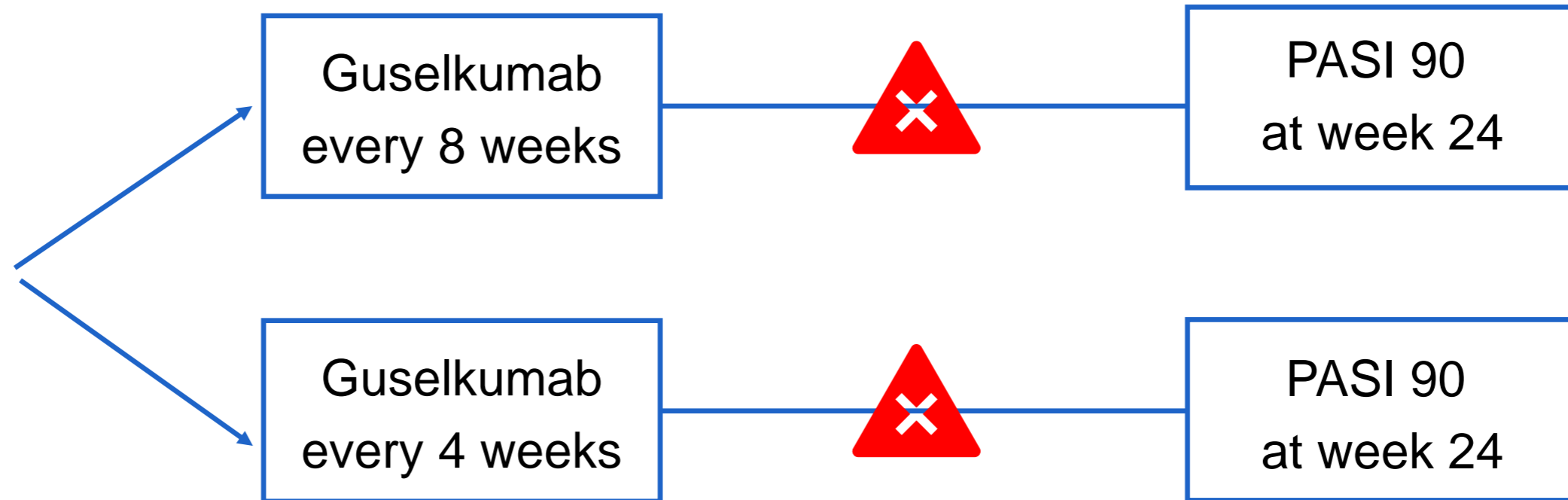
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# HYPOTHETICAL EXAMPLE: PSORIASIS RCT



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Treatment discontinuation

# DIFFERENT CONCLUSIONS?

- What was mean difference in PASI 90, for patients receiving Guselkumab every 8 weeks versus every 4 weeks...



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- What was mean difference in PASI 90, for patients receiving Guselkumab every 8 weeks versus every 4 weeks...  
  
... **regardless** of treatment discontinuation?

# DIFFERENT CONCLUSIONS?

– What was mean difference in PASI 90,  
for patients receiving Guselkumab  
every 8 weeks versus every 4 weeks...

... **regardless** of treatment discontinuation?

... if all patients had **hypothetically** adhered to  
assigned treatment regimen?

# ESTIMAND



## Estimand

= A **precise** description of exactly **what treatment effect** you are **aiming to find out**

# ICH E9 (R1) ADDENDUM



17 February 2020  
EMA/CHMP/ICH/436221/2017  
Committee for Medicinal Products for Human Use

## ICH E9 (R1) addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials

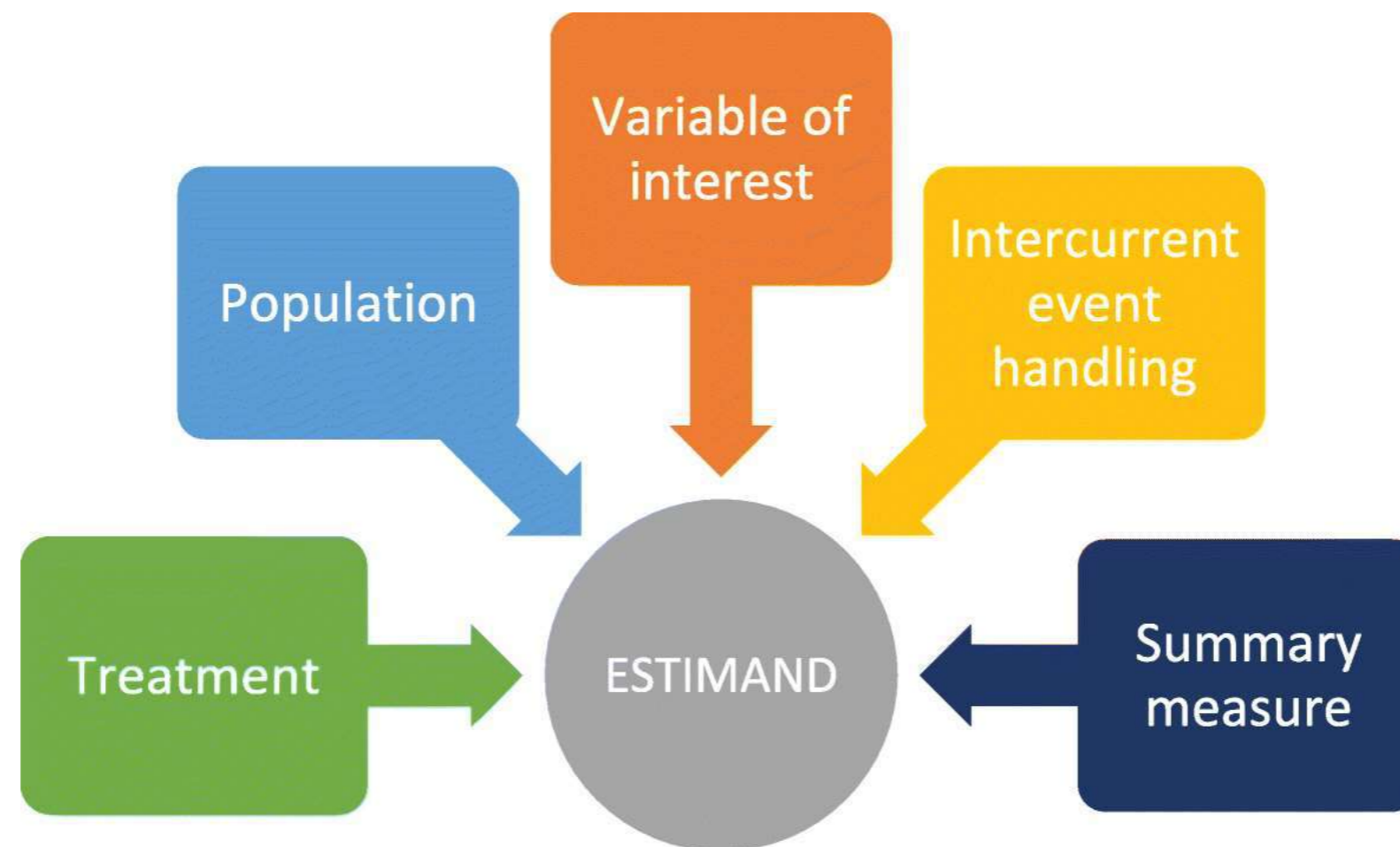
### Step 5

Transmission to CHMP	July 2017
Adoption by CHMP for release for consultation	20 July 2017
Start of consultation	31 August 2017
End of consultation (deadline for comments)	28 February 2018
Final adoption by CHMP	30 January 2020
Date for coming into effect	30 July 2020

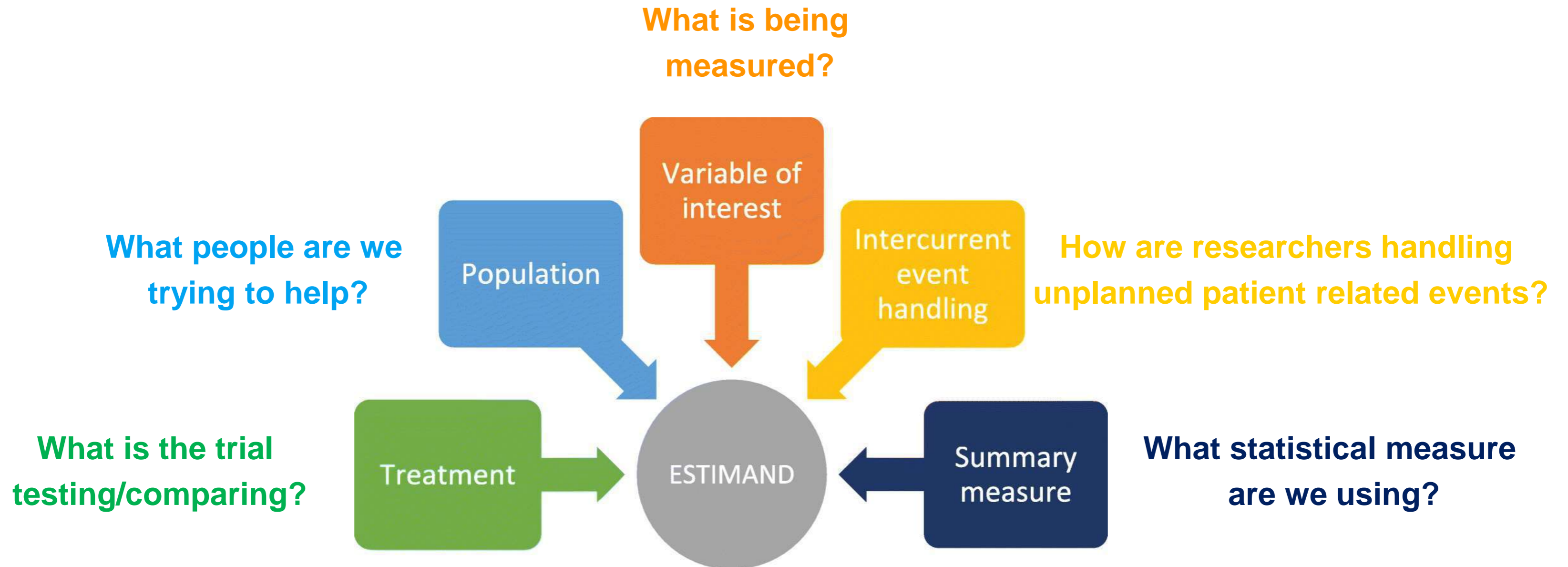
# ICH ADDENDUM

- Key point: multiple, different treatment effects can be considered.
- Addendum:
  - A basis for **describing different treatment effects**, and
  - some **points** to consider for **design and analysis** of trials to give estimates of treatment effects that are **reliable for decision making**.

# ESTIMAND ATTRIBUTES

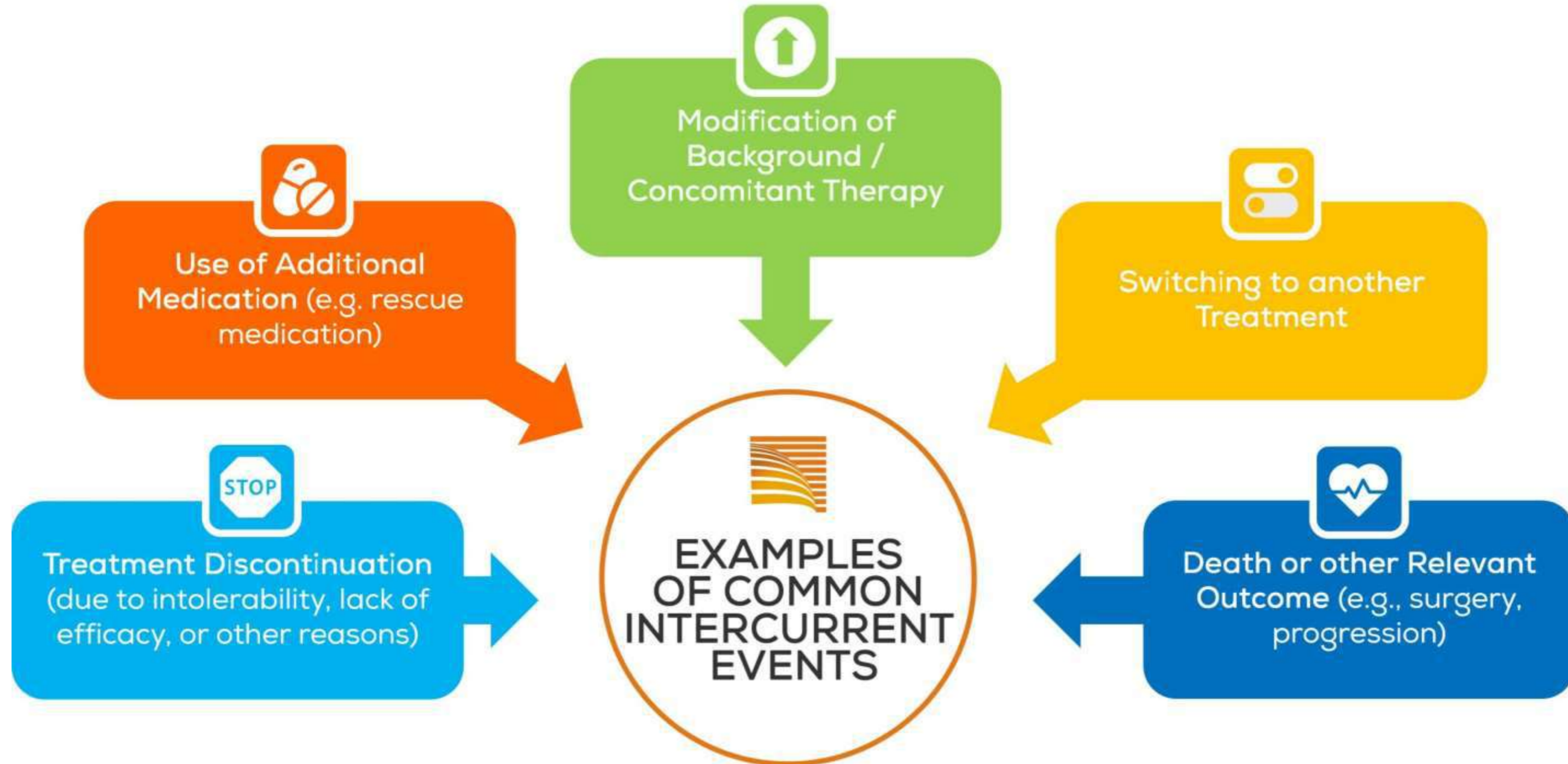


# ESTIMAND ATTRIBUTES





# INTERCURRENT EVENTS



# HANDLING OF INTERCURRENT EVENTS

Intercurrent event: 'Intake of additional medication'

**Treatment policy:** Treatment effect regardless of the intercurrent event

- 'Drug, plus additional medication as needed' vs. 'Placebo, plus additional medication as needed'

**Composite:** Occurrence of intercurrent event included in the endpoint definition

- 'Intake of additional medication is considered a treatment failure'

**Hypothetical:** Treatment effect if the intercurrent event did not occur

- 'Effect of Drug vs Placebo if additional medication had not been taken'

**Principal stratum:** Treatment effect in a population without the intercurrent event

- 'Effect of Drug vs Placebo on patients who do not take additional medication'

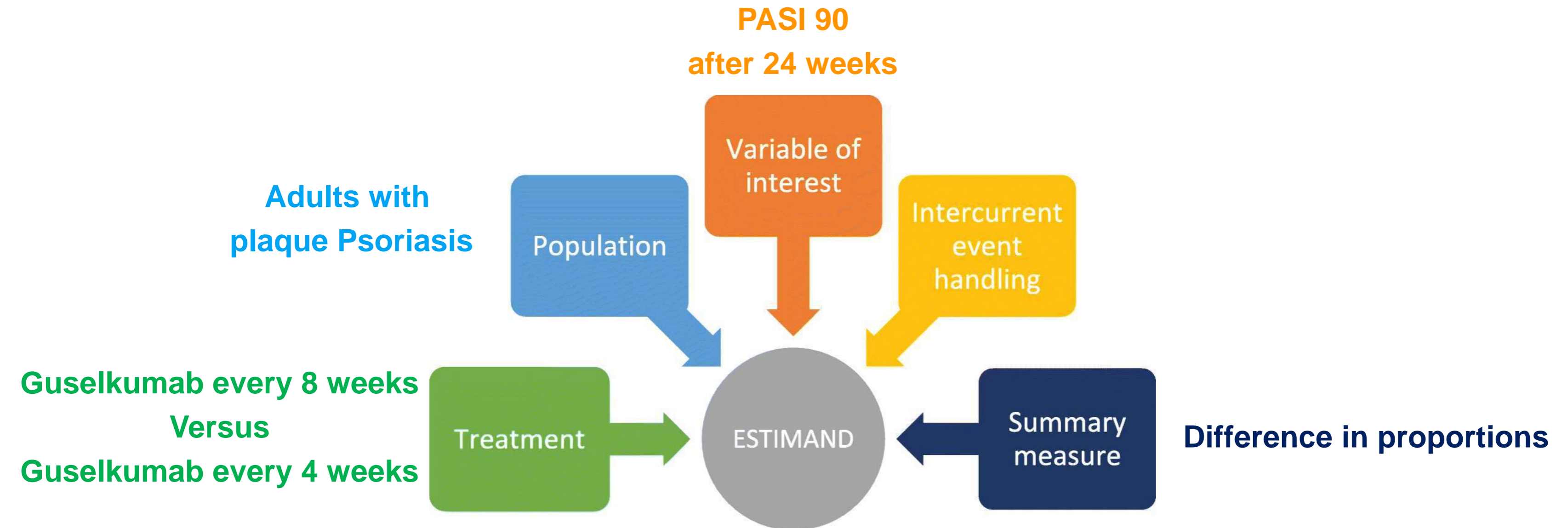
**While on treatment:** Treatment effect before the occurrence of the intercurrent

- 'Effect of Drug vs Placebo before additional medication is taken'

# OUR HYPOTHETICAL EXAMPLE

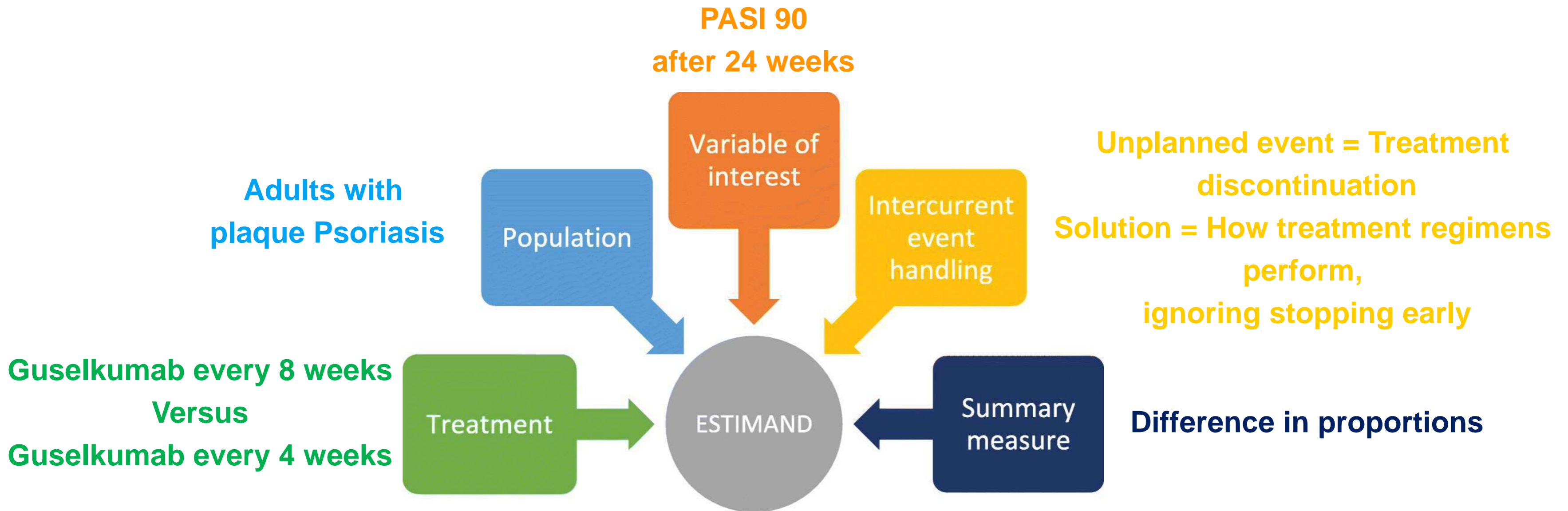
# POTENTIAL RESEARCH QUESTION 1

How does “Guselkumab every 8 weeks” compares against “Guselkumab every 4 weeks”, **even if not all of the treatment is received**, for adults with Psoriasis in terms of PASI 90 after 24 weeks?



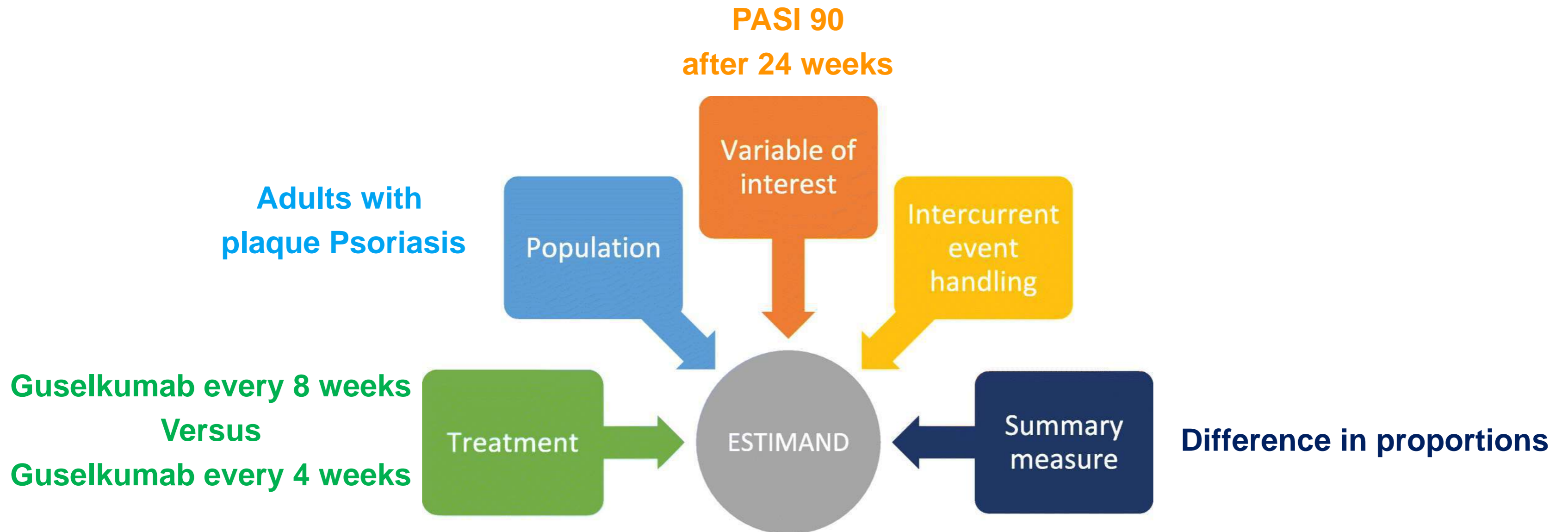
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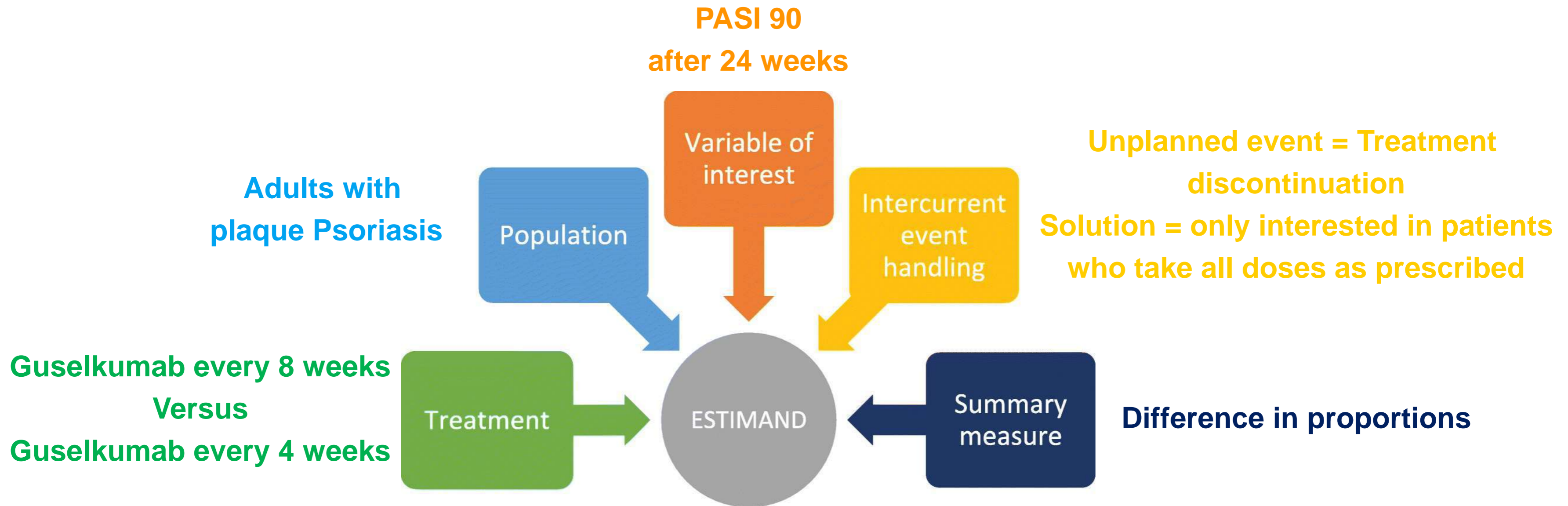
# POTENTIAL RESEARCH QUESTION 2

How does “Guselkumab every 8 weeks” compares against “Guselkumab every 4 weeks”, for adults with Psoriasis **who take all doses as prescribed**, in terms of PASI 90 after 24 weeks?



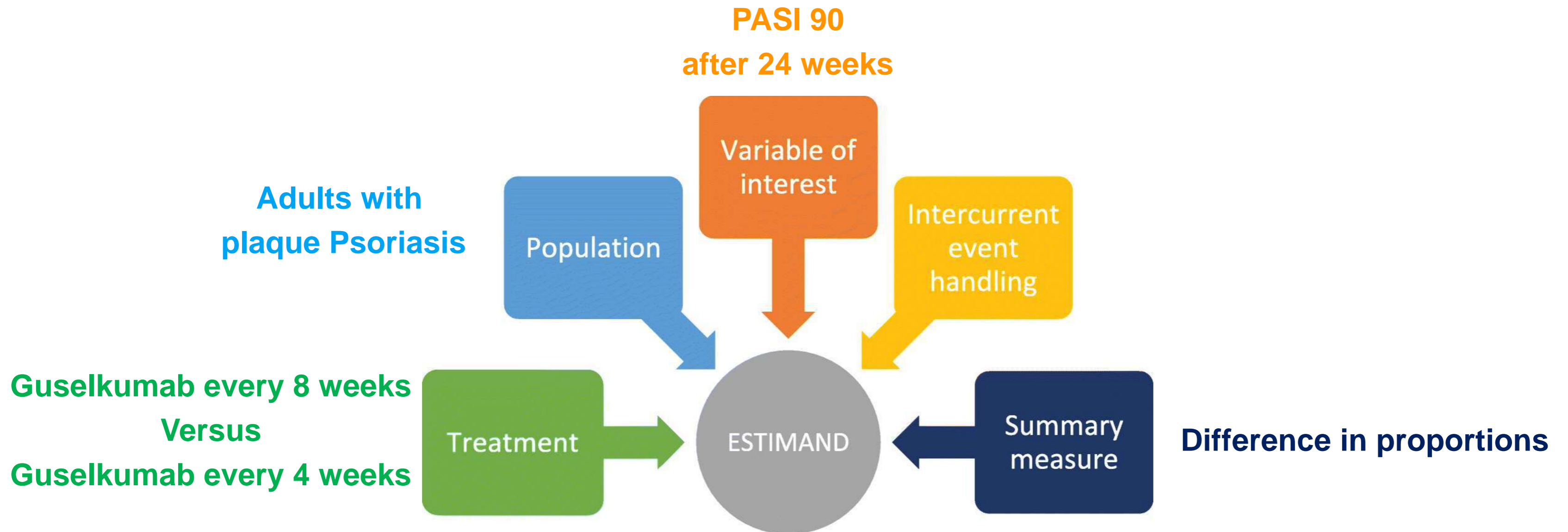
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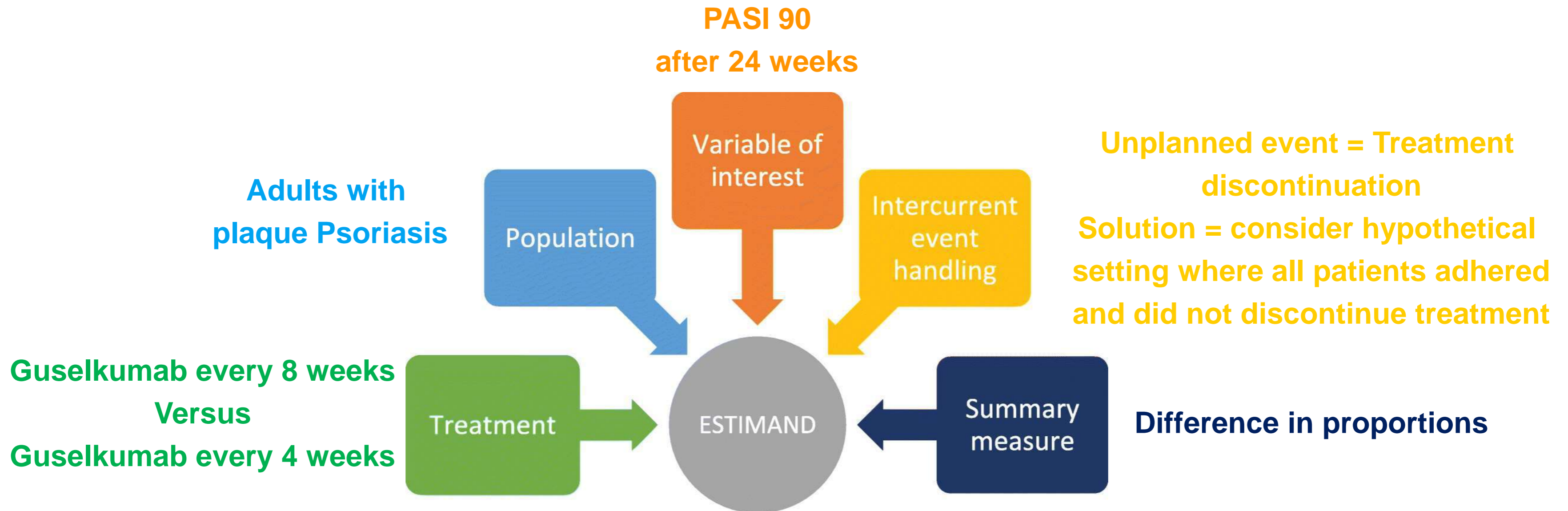
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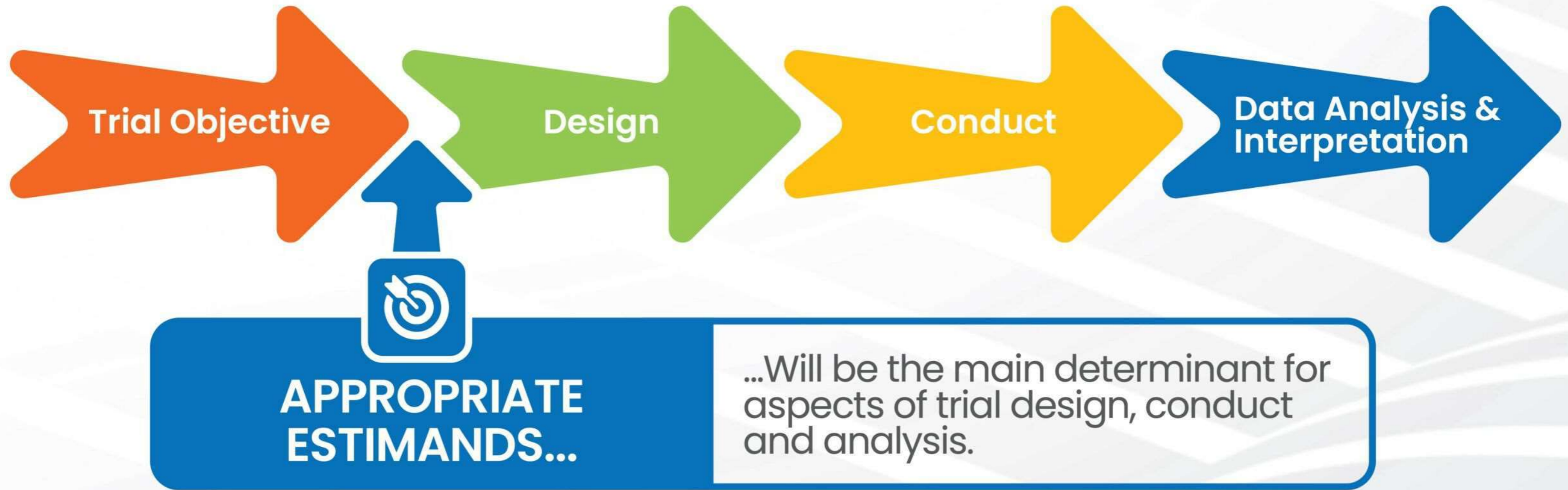
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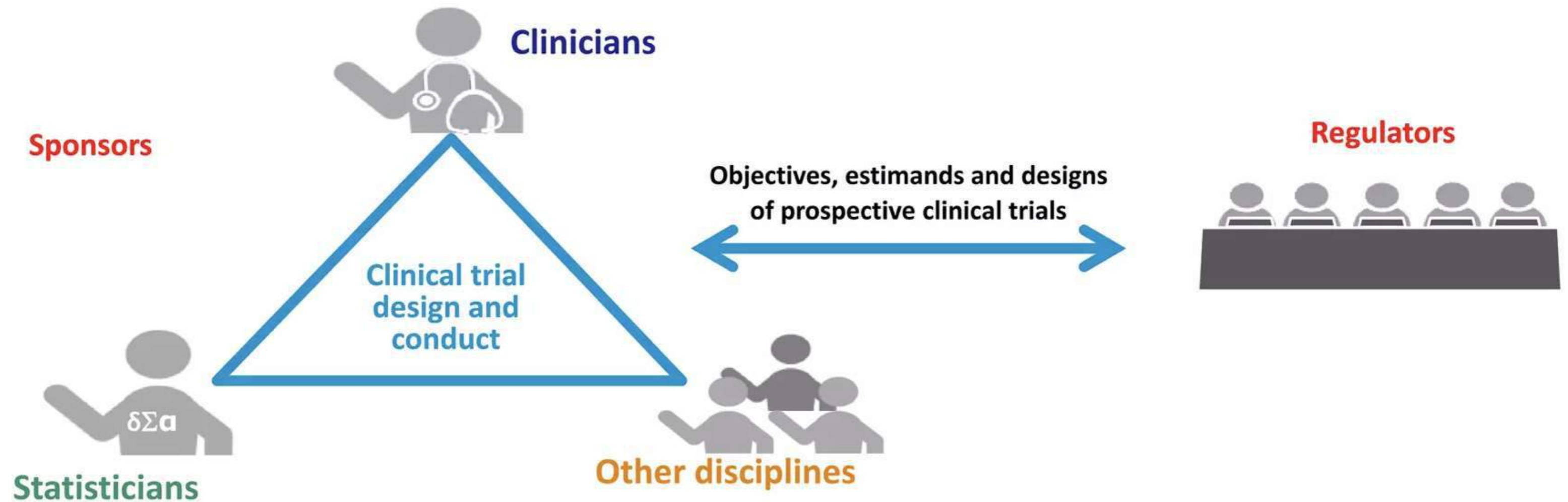


# WHY RELEVANT FOR NON-STATISTICIANS?

# A NEW FRAMEWORK FOR CLINICAL TRIALS



# MULTI-DISCIPLINARY TASK



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