One2Treat

Beyond traditional endpoints: a patient-focused approach to enhancing rare disease trials.

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CMO

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CEO

90+% of clinical trials estimate treatment effects based on one single outcome

It’s time to better address patient needs and leverage more of the data collected in clinical trials

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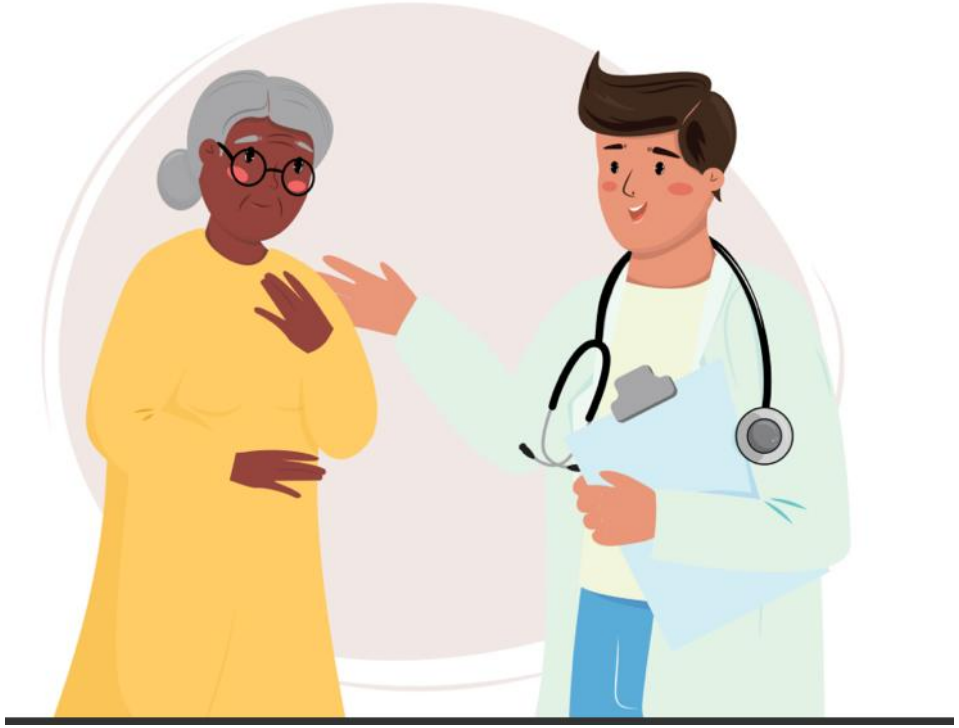
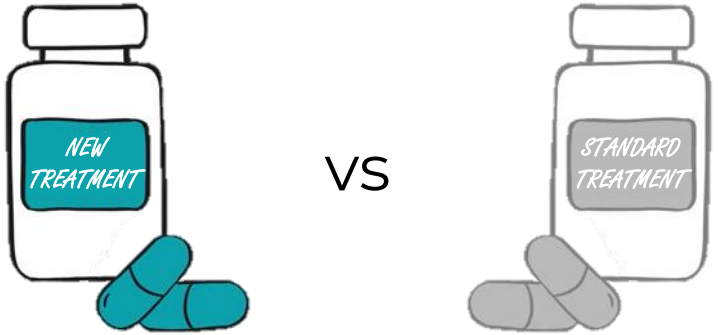
Randomized clinical trials?

Demonstrate that one treatment is better*





* **“better”** needs to be prespecified

One2Treat founder Marc Buyse developed a robust statistical solution

Incorporating multiple outcomes within a single treatment assessment

Comprehensively evaluate
Net Treatment Benefit

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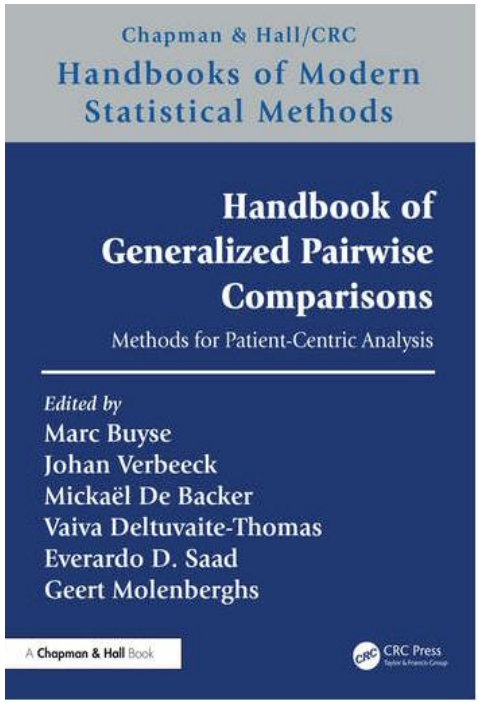
50+ peer-reviewed publications
1 methodological handbook



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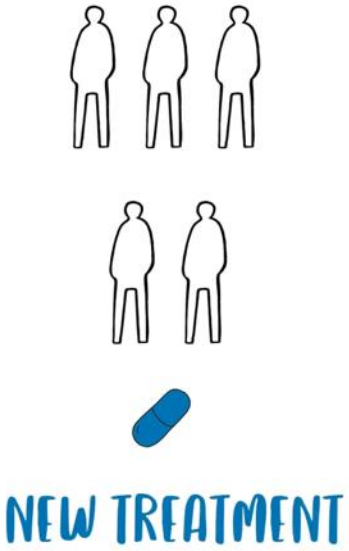
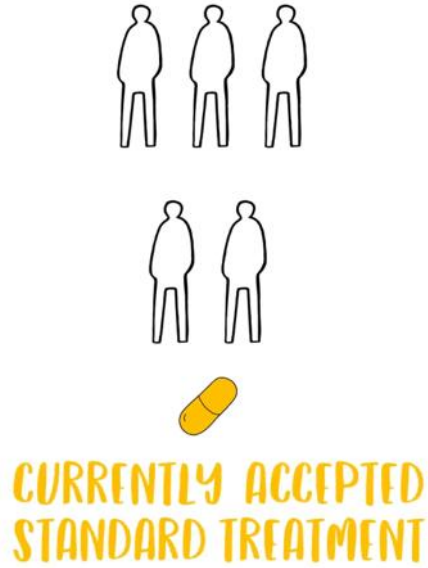
The Net Treatment Benefit (NTB)

in a randomized clinical trial (RCT)





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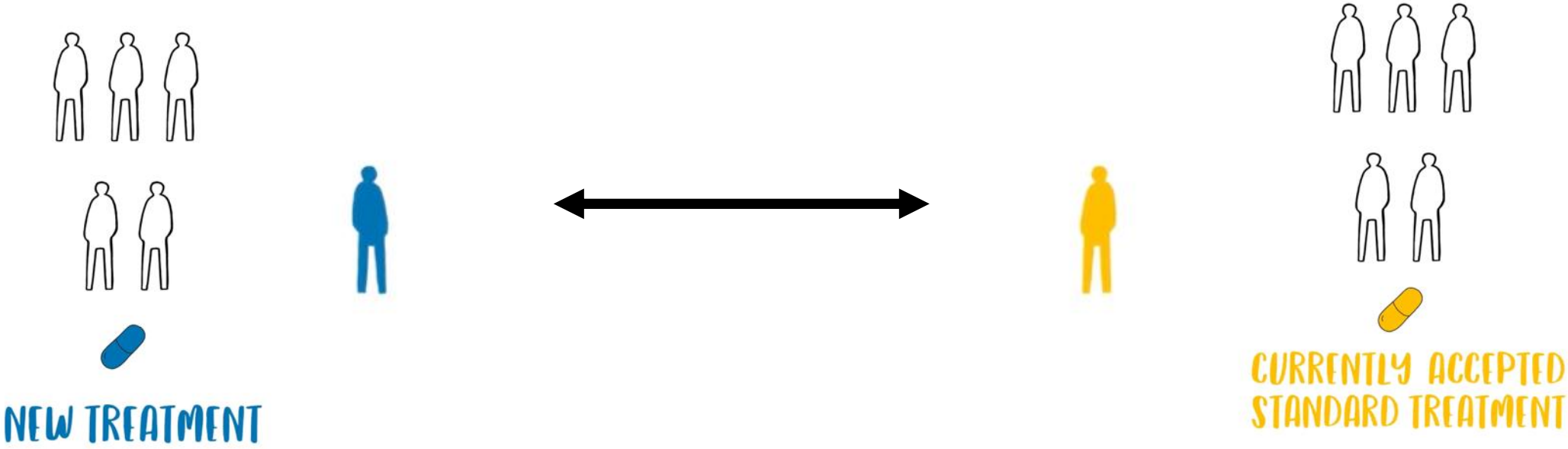

- **Pairwise patient comparisons**: Each patient in one treatment arm is compared to each patient in the other arm *(forming all possible pairs between the two groups)*

The Net Treatment Benefit (NTB)

in a randomized clinical trial (RCT)

- **Pairwise patient comparisons**: Each patient in one treatment arm is compared to each patient in the other arm *(forming all possible pairs between the two groups)*
- **Holistic treatment assessment**: Simultaneously evaluate multiple clinically relevant outcomes in randomized controlled trials (RCTs)

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The Net Treatment Benefit (NTB)

in a randomized clinical trial (RCT)

For this pair of patients, which treatment shows a greater benefit—the new treatment or the standard ?

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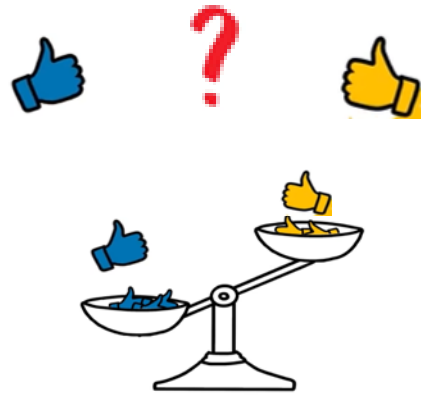
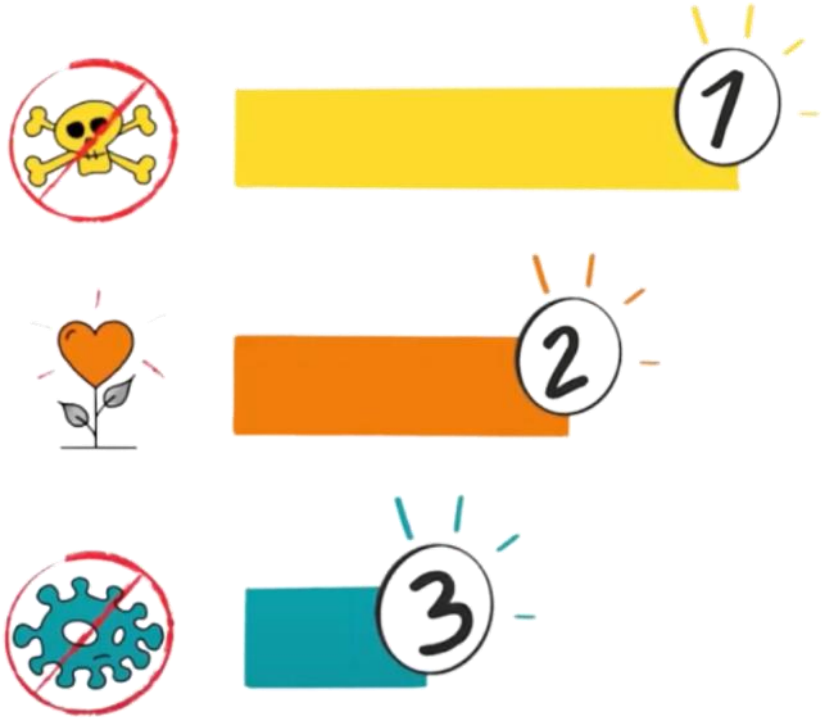
The Net Treatment Benefit (NTB)

in a randomized clinical trial (RCT)



- For each treatment arm, sum all pairwise scores and divide by the total number of patient pairs, then compute the difference between the resulting probabilities.
- The **Net Treatment Benefit** represents the net probability that a random patient in the new treatment group has a better outcome than a random patient in the control group

PATIENT PRIORITIES



One2Treat has developed patented software solutions for pharma & academic sponsors to capture and prioritize patient preferences

Engage with patient advocates and clinicians in a data-driven way

Redefine clinical trial designs to better meet regulatory guidance & reduce sample size

Bring innovative treatment to patients faster & reduce clinical budgets

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Rare disease case study - **Sjögren’s syndrome**

Sjögren's syndrome is a disorder of the immune system, where the **glands that produce fluid**, such as tears and saliva, **stop working properly**.

Common **symptoms** of Sjögren's syndrome include:

dry eyes; a dry mouth; aching muscles and joint; tiredness; dry skin...

There's currently **no cure** for Sjögren's syndrome, but there are treatments that can **help manage symptoms**.

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How to **choose** & **prioritize multiple outcomes**?

While **numerous endpoints** have been used in **Sjögren trials**...

ESSDAI

Physician Global Assessment of Disease Severity (PhGA)

Safety assessments

Sjögren's Tool for Assessing Response (STAR)

Serum immunoglobulin levels

ClinESSDAI

Sjögren's Symptoms Tool

Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS)

Disease Activity Level (DAL)

European League Against Rheumatism Sjögren's Syndrome Patient-Reported Index (ESSPRI)

MFI-20 (Multidimensional Fatigue Inventory)

Quality of life measures

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Choosing & ranking outcomes: A patient-centered approach

One2Treat Voice®: a solution to prioritize what matters most

- Clear and transparent tool **capturing patient and clinician** preferences
- Enables the formalization of what is considered ***"best for patients"*** *when receiving a treatment*
- Leads to a more holistic treatment assessment through prioritized composite endpoints

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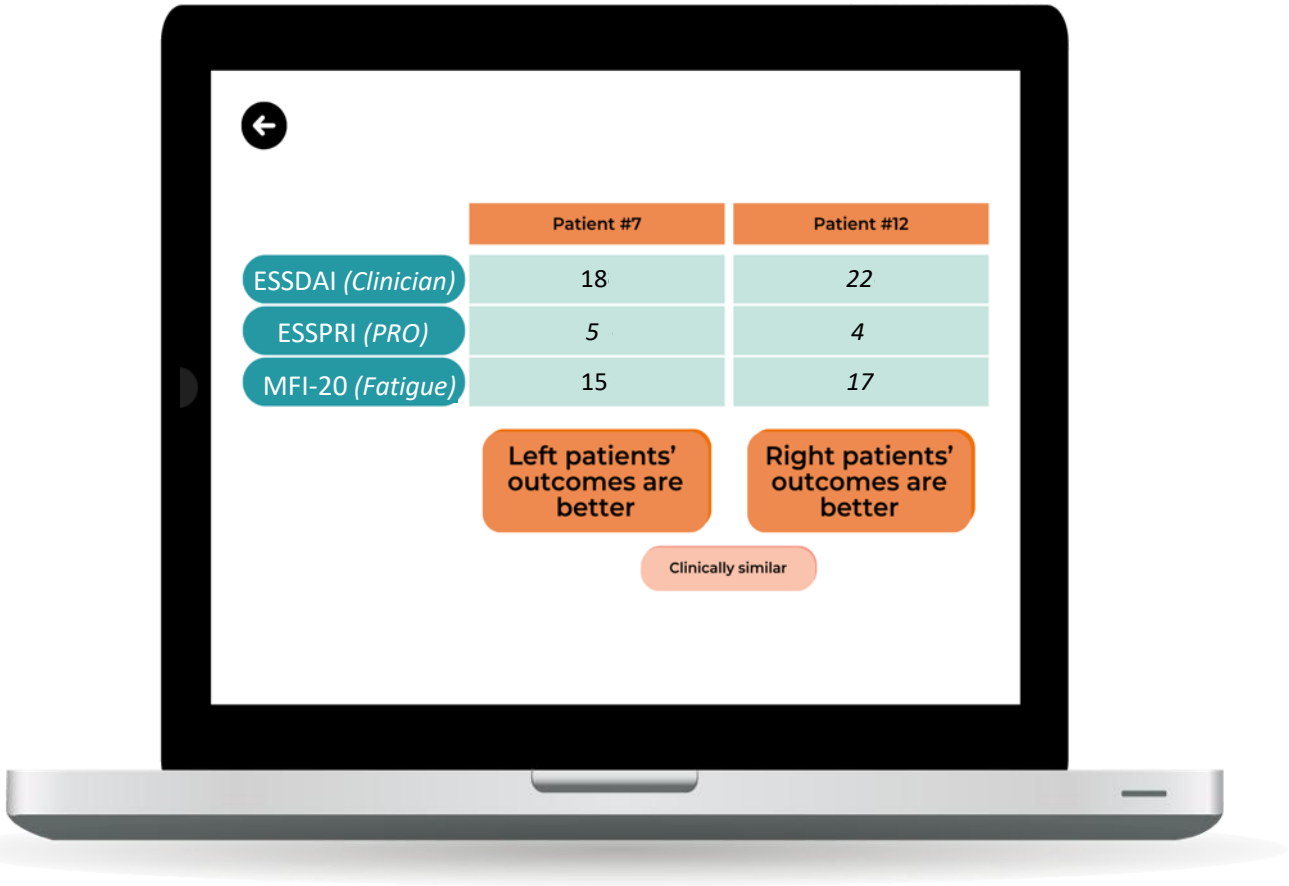
Choosing & ranking outcomes: A patient-centered approach

One2Treat Voice®: a solution to prioritize what matters most



- Simple questions asked to patient advocates / clinicians, regarding patient outcomes
- Pairs of patients are displayed, user selects the preferred option
- Answers processed by an AI algorithm to extract and quantify the clinical outcomes preferences

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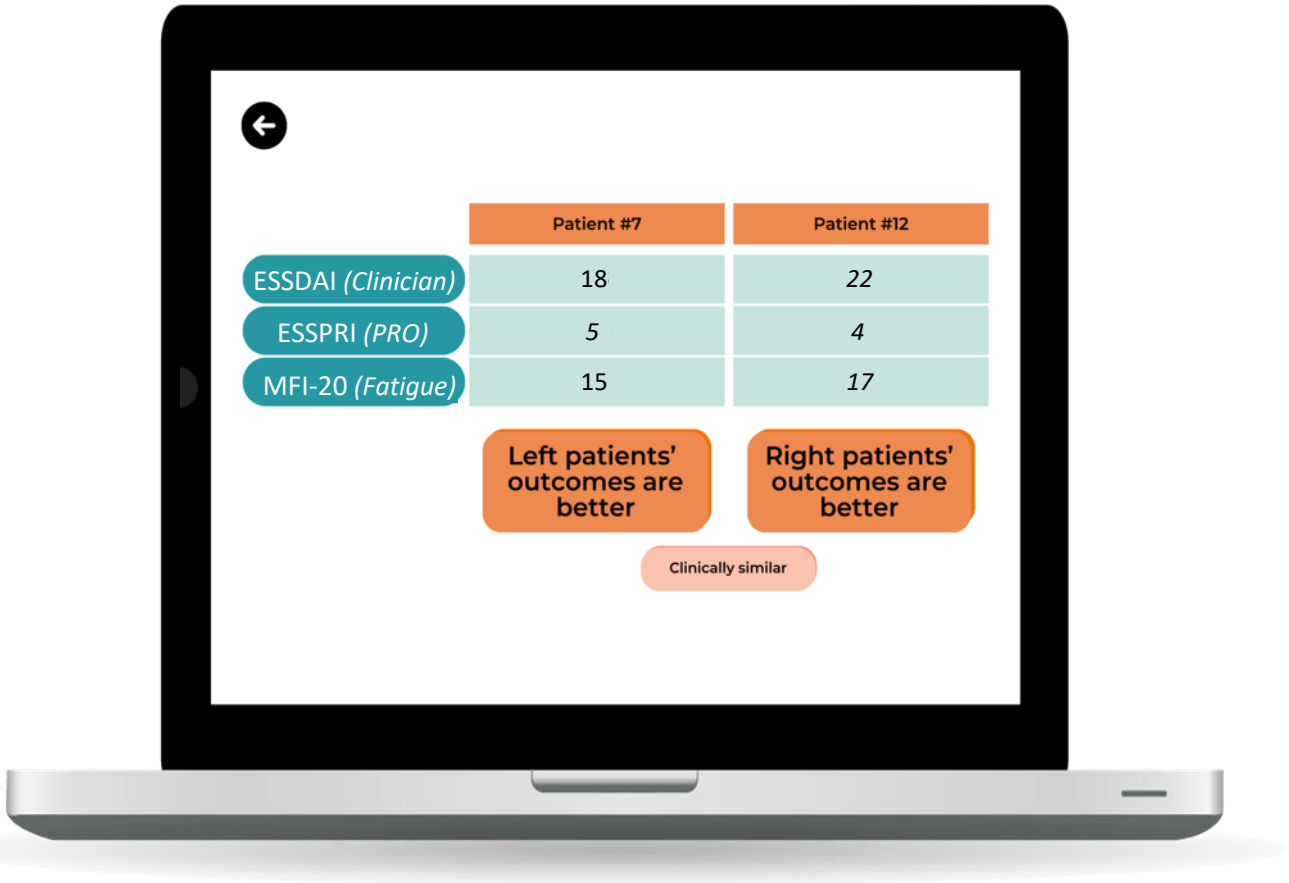
Choosing & ranking outcomes: A patient-centered approach

One2Treat Voice®: a solution to prioritize what matters most



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Help trial's sponsor to define a **list of prioritized outcomes** and **thresholds of clinical relevance**

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List of prioritized outcomes defined - *illustration*

Definition of the trial's primary endpoint

- First outcome: **ESSDAI**
  (with at least 3 points index difference to be clinically meaningful)
- Second outcome: **ESSPRI**
  (with at least 2 points index difference to be clinically meaningful)
- Third outcome: **MFI-20 Fatigue**
  (with at least 2 points index difference to be clinically meaningful)
- Fourth outcome: **Adverse event Grade 3/4** (yes/no)

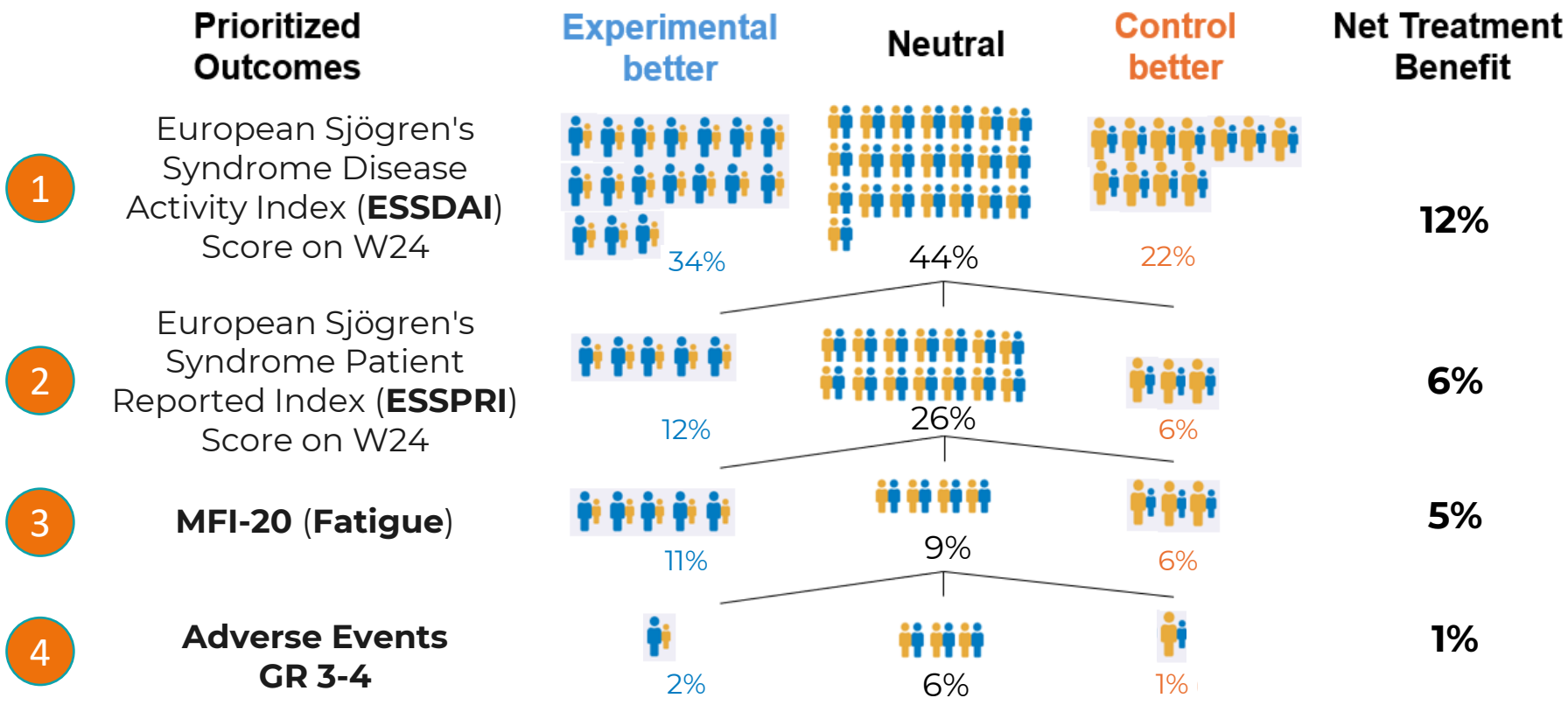
NTB - an efficient composite primary endpoint

Main advantages for rare disease trials

- Defined by patient advocates / clinicians (e.g. KOLs)
- Better reflects what matters most to patients
- Aligns clinical trial objective with patient needs
- Leverages more of the collected data *(to assess trial success)*
- Reduces *(significantly)* trial sample size *(key in rare disease)*

Sjögren's syndrome clinical trial designed with NTB

Final analysis illustration *(post-trial, 4 outcomes)*



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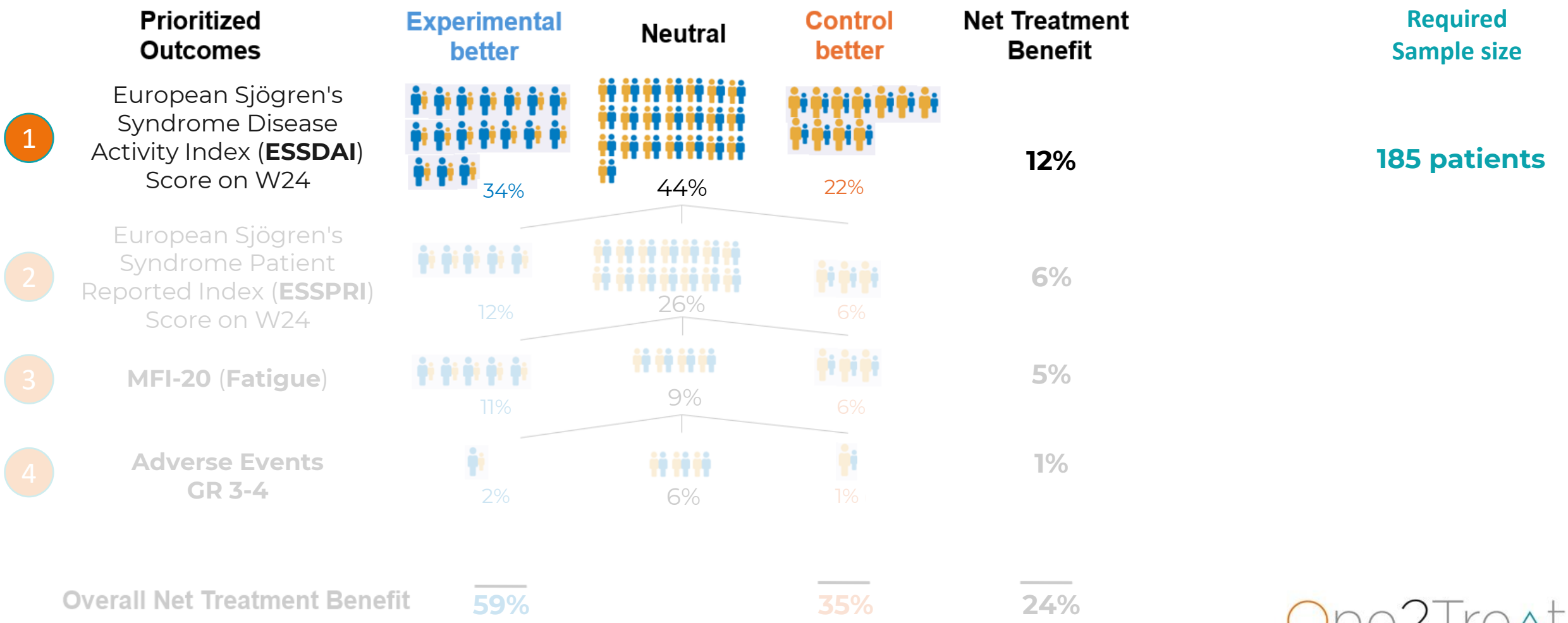
Sjögren's syndrome trial designed with 1 outcome

Final analysis illustration *(post-trial, 1 outcome)*



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Sjögren's syndrome trial designed with 1 outcome

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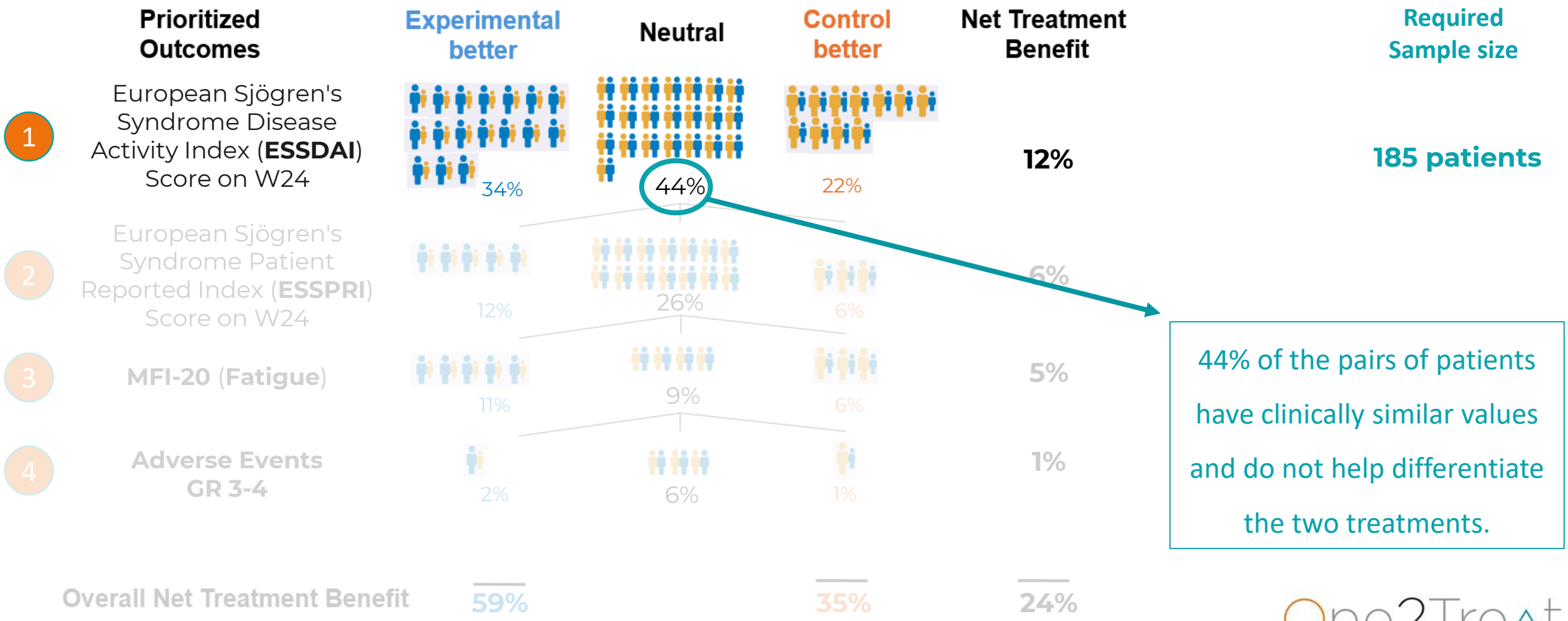

44% of the pairs of patients have clinically similar values and do not help differentiate the two treatments.

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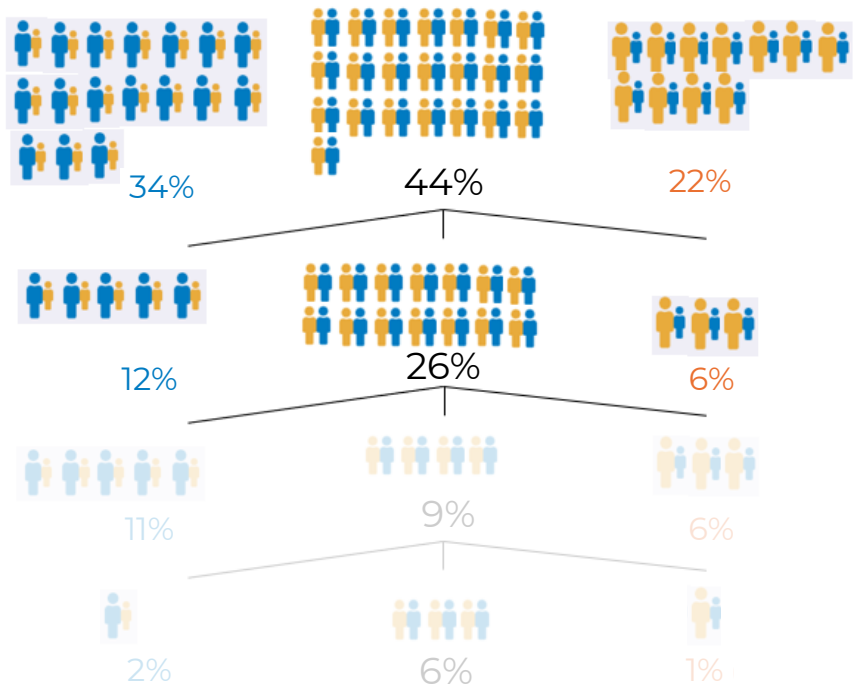
Sjögren's syndrome trial designed with NTB

Final analysis illustration *(post-trial, 2 outcomes)*

	Prioritized Outcomes	Experimental better	Neutral	Control better	Net Treatment Benefit	Cumulative NTB	Required Sample size
1	European Sjögren's Syndrome Disease Activity Index (**ESSDAI**) Score on W24	34%	44%	22%	**12%**	**12%**	**185 patients**
2	European Sjögren's Syndrome Patient Reported Index (**ESSPRI**) Score on W24	12%	26%	6%	**6%**	**18%**	
3	MFI-20 (Fatigue)	11%	9%	6%	**5%**		
4	Adverse Events GR 3-4	2%	6%	1%	**1%**		
	Overall Net Treatment Benefit	59%		35%	**24%**		



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3	**MFI-20** (**Fatigue**)	11%	9%	6%	**5%**	23%	
4	**Adverse Events GR 3-4**	2%	6%	1%	**1%**	24%	**122 patients**
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Sjögren's syndrome trial designed with NTB

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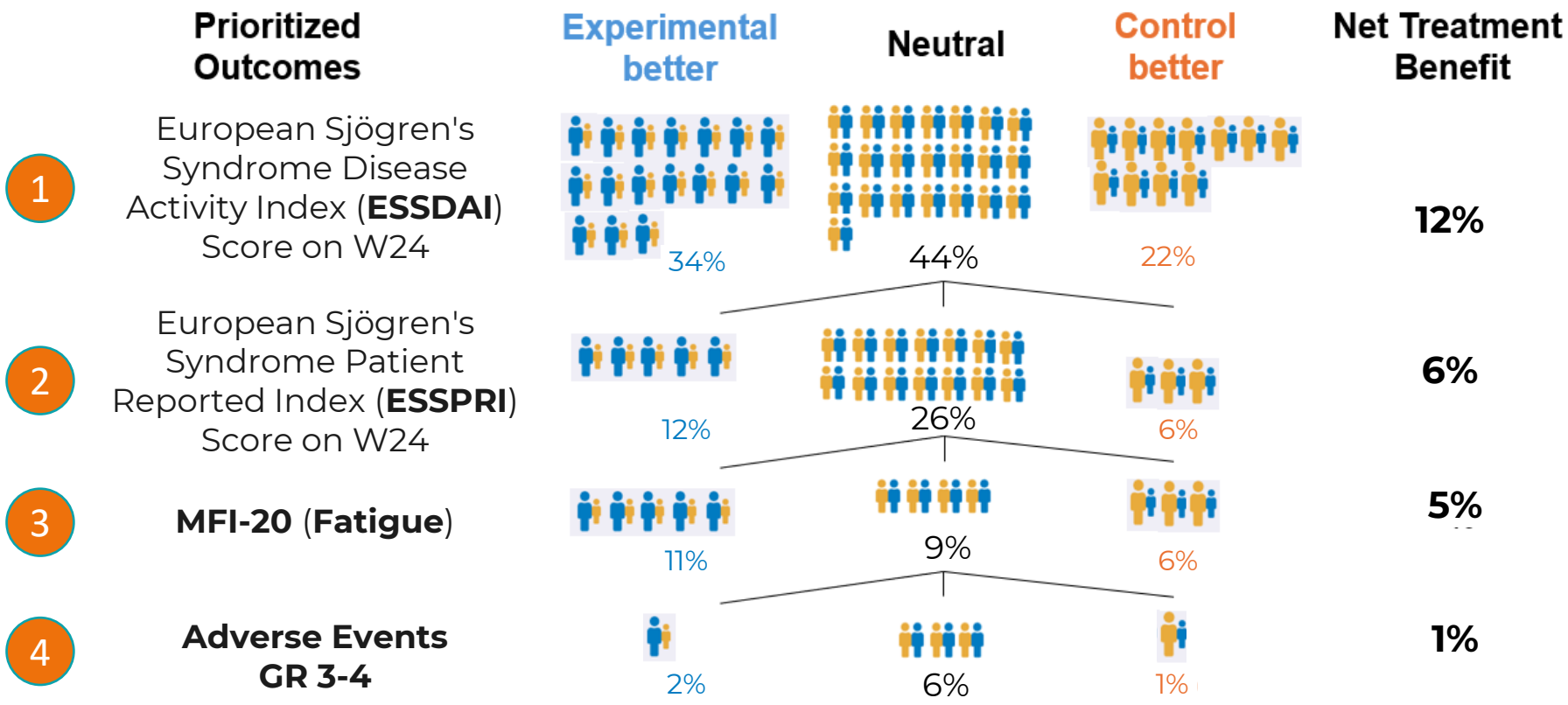

Allows leveraging data collected throughout the study & **derisk** the trial

Allows to reduce sample size

Transparent view on each outcome's contribution to NTB

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Incorporating multiple outcomes in a rare disease clinical trial design (NTB):

- Engage with patient advocates / clinicians
- Increase patient-centricity from trial design
- Increase clinical relevance of trial design
- Decrease sample size
- Decrease clinical timelines / increase speed
- Decrease development risks
- Increase quality of clinician information

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Revolutionizing Treatment Decisions

Thank you!