



Solving the Fragmentation Challenge in RA Trials:

Deriving deeper insights

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Agenda

- The Landscape of Rheumatoid Arthritis & Its Trials
- The Core Problem: Fragmentation & Limited Context
- The High Stakes: Consequences of Fragmentation
- Our Proposed Solution: A Unified Framework
- Transforming Trials: The Strategic Impact
- Case Study & Conclusion

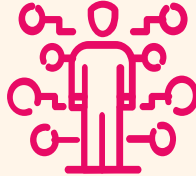
Landscape of Rheumatoid Arthritis



Disease Activity



Physical
Function & QoL



Pain



Safety/
Tolerability

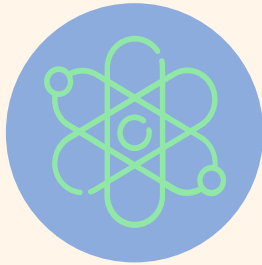


Structural
Damage



Fatigue

Outcome Measures



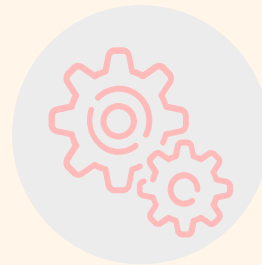
Measure of
Disease
Activity



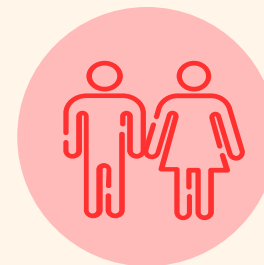
Composite
disease
activity scores
and response
criteria



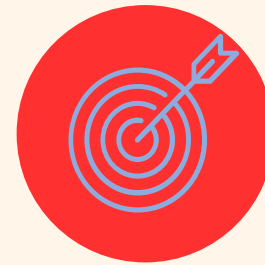
Measures of
physical
function



Measures of
structural
damage



Patient Report
Outcomes



Safety and
Tolerability

Traditional Outputs



Table 1. Baseline Characteristics.*			
Characteristic	Placebo (N=24)	Peresolimbab, 300 mg (N=25)	Peresolimbab, 700 mg (N=49)
Female sex — no. (%)	19 (79)	20 (80)	43 (88)
Age — yr†	55.8±11.1	50.1±15.8	50.5±11.2
Body-mass index‡	28.2±4.8	28.2±3.7	29.3±6.8
Race or ethnic group — no. (%)§			
American Indian or Alaska Native	7 (29)	10 (40)	13 (27)
Black or African American	0	0	2 (4)
White	17 (71)	15 (60)	34 (69)
Seropositivity — no. (%)¶			
For anti-CCP antibody or rheumatoid factor	20 (83)	22 (88)	45 (92)
For anti-CCP antibody	19 (79)	22 (88)	42 (86)
For rheumatoid factor	18 (75)	19 (76)	44 (90)
Use of glucocorticoids — no. (%)	14 (58)	15 (60)	30 (61)
Duration of rheumatoid arthritis — yr	10.9±8.4	9.8±8.9	9.7±7.5
DAS28-CRP¶	5.66±0.59	5.91±0.98	6.00±0.87
Tender joint count among 68 joints — no. of joints	19.0±8.8	22.7±13.7	19.6±8.5
Swollen joint count among 66 joints — no. of joints	13.7±5.2	18.7±13.3	14.6±5.6
Physician's global assessment of disease activity — mm	62.5±16.3	70.2±15.9	67.2±18.4
Patient's global assessment of disease activity — mm	69.0±15.8	69.5±15.5	70.8±17.4
Patient's assessment of arthritis pain — mm	67.3±18.0	70.4±14.3	72.2±18.1
HAQ-DI score**	1.35±0.36	1.63±0.57	1.66±0.54
High-sensitivity C-reactive protein level — mg/liter††	12.0±12.8	13.3±13.8	16.2±15.0
SF-36‡‡			
Mental component score	50.1±13.0	49.0±9.5	47.1±11.0
Physical component score	32.3±7.0	31.6±7.4	32.5±7.9
Clinical Disease Activity Index score§§	38.3±10.5	43.1±12.8	41.7±13.2
Simplified Disease Activity Index score¶¶	39.4±10.2	44.4±13.4	43.8±13.5
RAMRIS for synovitis	8.3±4.8	7.7±4.8	8.3±5.3

* Plus-minus values are mean ± SD. Additional information about the efficacy measures is provided in Table S12.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ Race or ethnic group was reported by the patients.
§ Seropositivity for anti-cyclic citrullinated peptide (anti-CCP) was defined as a level of at least 17 IU per milliliter, and seropositivity for rheumatoid factor was defined as a level of at least 15 IU per milliliter.
¶ The Disease Activity Score for 28 joints based on the C-reactive protein level (DAS28-CRP) ranges from 0 to 9.4, with higher scores indicating more severe disease.
|| This evaluation was based on a visual analogue scale of 0 to 100 mm, with higher values indicating greater disease activity or pain.
** Health Assessment Questionnaire-Disability Index (HAQ-DI) scores range from 0 to 3, with higher scores indicating greater disability.
†† The normal range of the high-sensitivity C-reactive protein level is 0 to 5 mg per liter.
‡‡ The mental and physical component scores on the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) range from 0 to 100, with higher scores indicating greater well-being.
§§ Clinical Disease Activity Index scores range from 0 to 76, with higher scores indicating more severe disease.
¶¶ Simplified Disease Activity Index scores range from 0 to 86, with higher scores indicating more severe disease.
||| The Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) for synovitis ranges from 0 to 24, with higher scores indicating more severe synovitis.

Table 2. Primary and Secondary Efficacy Outcomes at Week 12.*			
Outcome	Placebo (N=24)	Peresolimbab, 300 mg (N=25)	Peresolimbab, 700 mg (N=49)
Primary outcomes			
DAS28-CRP			
Change from baseline	-0.99±0.28	-1.88±0.25	-2.09±0.18
Difference in change vs. placebo (95% CI)	—	-0.88 (-1.60 to -0.14)	-1.09 (-1.71 to -0.44)†
Secondary outcomes			
ACR20-response‡			
No. of patients (%)	10 (42)	11 (44)	35 (71)
Least-squares mean difference vs. placebo (95% CI)	—	2.3 (-2.4 to 7.0)	29.8 (6.3 to 53.2)
ACR50-response‡			
No. of patients (%)	5 (21)	5 (20)	19 (39)
Least-squares mean difference vs. placebo (95% CI)	—	-0.8 (-2.4 to 0.7)	17.9 (-3.3 to 39.2)
ACR70-response‡			
No. of patients (%)	4 (17)	1 (4)	10 (20)
Least-squares mean difference vs. placebo (95% CI)	—	-12.7 (-29.4 to 4.1)	3.7 (-15.0 to 22.4)
Tender joint count for 68 joints			
Change from baseline	-6.8±1.85	-12.0±1.81	-12.33±1.29
Difference in change vs. placebo (95% CI)	—	-5.19 (-10.35 to -0.03)	-5.42 (-9.93 to -0.98)
Swollen joint count for 66 joints — no. of joints			
Change from baseline	-6.18±1.09	-10.22±1.08	-10.49±0.76
Difference in change vs. placebo (95% CI)	—	-4.04 (-7.12 to -0.94)	-4.31 (-6.94 to -1.67)
Physician's global assessment of disease activity			
Change from baseline	-25.35±5.18	-39.07±5.13	-38.55±5.18
Difference in change vs. placebo (95% CI)	—	-13.72 (-28.23 to 0.80)	-13.20 (-25.68 to -0.72)
Patient's global assessment of disease activity			
Change from baseline	-21.66±5.39	-24.75±5.28	-29.67±5.24
Difference in change vs. placebo (95% CI)	—	-3.09 (-17.62 to 12.41)	-8.01 (-21.09 to 5.03)
Patient's assessment of arthritis pain			
Change from baseline	-17.94±5.10	-23.50±5.00	-31.55±5.14
Difference in change vs. placebo (95% CI)	—	-5.56 (-18.76 to 8.65)	-13.61 (-25.95 to -1.26)
HAQ-DI score			
Change from baseline	-0.41±0.11	-0.35±0.11	-0.42±0.08
Difference in change vs. placebo (95% CI)	—	0.06 (-0.24 to 0.36)	-0.01 (-0.27 to 0.26)
SF-36			
Mental component summary score			
Change from baseline	3.48±1.72	0.55±1.63	4.64±1.17
Difference in change vs. placebo (95% CI)	—	-2.93 (-7.63 to 1.77)	1.15 (-3.85 to 5.26)
Physical component summary score			
Change from baseline	5.01±1.71	7.03±1.63	6.43±1.16
Difference in change vs. placebo (95% CI)	—	2.02 (-2.69 to 6.73)	1.42 (-2.67 to 5.50)
High-sensitivity C-reactive protein level			
Change from baseline	1.34±3.72	-5.26±3.63	-6.66±2.57
Difference in change vs. placebo (95% CI)	—	-6.60 (-16.93 to 3.70)	-2.01 (-10.99 to 6.98)
Clinical Disease Activity Index score			
Change from baseline	-13.75±2.71	-24.06±2.63	-25.51±2.85
Difference in change vs. placebo (95% CI)	—	-10.30 (-17.83 to -2.77)	-11.76 (-18.29 to -5.22)
Simplified Disease Activity Index score			
Change from baseline	-13.80±2.68	-25.06±2.57	-26.90±1.88
Difference in change vs. placebo (95% CI)	—	-11.26 (-18.81 to -3.71)	-13.10 (-19.61 to -6.60)

* Plus-minus values are least-squares mean ± SE. The widths of the 95% confidence intervals (CI) have not been adjusted for multiplicity and cannot be used in place of hypothesis tests.
† P<0.001 for the difference in the change from baseline at week 12 in the DAS28-CRP between the 700-mg peresolimbab group and the placebo group.
‡ American College of Rheumatology 20 (ACR20), ACR50, and ACR70 responses are defined as improvements from baseline of 20%, 50%, and 70% or more, respectively, in the numbers of tender and swollen joints and in at least three other important domains.

Table 3. Adverse Events between Baseline and Week 12 (Period 1).*			
Event	Placebo (N=24)	Peresolimbab, 300 mg (N=25)	Peresolimbab, 700 mg (N=49)
no. of patients (%)			
Adverse event during the treatment period			
Overall	9 (38)	8 (32)	14 (29)
According to severity†			
Mild	6 (25)	5 (20)	9 (18)
Moderate	3 (12)	3 (12)	5 (10)
Severe	0	0	0
Serious adverse event	0	0	1 (2)
Discontinuation of placebo or peresolimbab because of adverse event	1 (4)	1 (4)	0
Infections and infestations‡			
Nasopharyngitis	1 (4)	2 (8)	1 (2)
Coronavirus disease 2019	0	1 (4)	1 (2)
Vulvovaginal candidiasis	0	0	1 (2)§
Gastroenteritis	0	1 (4)	0
Helicobacter infections	0	1 (4)	0
Herpes simplex	1 (4)	0	0
Mastitis	0	1 (4)	0
Rhinitis	0	0	1 (2)
Sinusitis	0	1 (4)	0
Skin bacterial infection	0	1 (4)	0
Tooth abscess	1 (4)	0	0
Upper respiratory tract infection¶	0	0	1 (2)
Upper respiratory tract infection bacterial¶	0	0	1 (2)
Urinary tract infections	0	0	1 (2)
Neoplasia benign, malignant, and unspecified, including cysts and polyps, B-cell lymphoma‡	1 (4)	0	0
Skin and subcutaneous tissue disorders§	2 (8)	0	2 (4)
Pruritus	1 (4)	0	1 (2)
Dermatitis atopic	0	0	1 (2)
Onycholysis	1 (4)	0	0

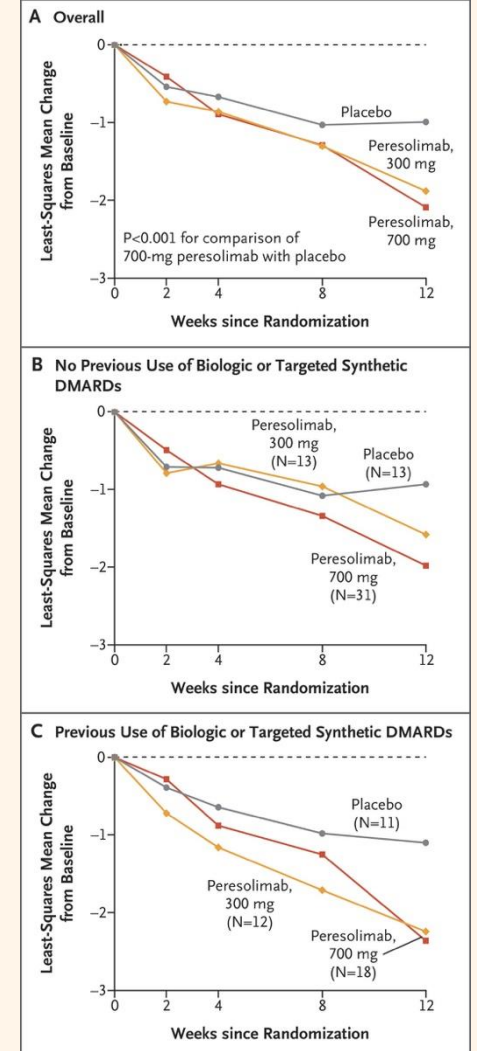
* There were no deaths, cases of herpes zoster, or thromboembolic events.
† For patients with multiple occurrences of the same event, the most severe event is reported.
‡ The headings and subheadings are the system organ classes and preferred terms, respectively, in the Medical Dictionary for Regulatory Activities, version 25.0.
§ The percentage was calculated with 43 female patients as the denominator.
¶ One patient had an adverse event that was coded as "upper respiratory tract infection," and another patient had an adverse event that was coded as "upper respiratory tract infection bacterial."

Parameter	Responders*		Non-responders	
	Subset 1 ^b (n = 6)	Subset 2 (n = 10)	Subset 1 (n = 7)	Subset 2 (n = 10)
Age (years)	54.1 ± 13.8 ^c	55.2 ± 9.2	56.1 ± 11.7	58.9 ± 11.6
Sex (men/women)	1/5	2/8	1/6	4/6
RA duration (years)	11.7 ± 8.0	11.1 ± 7.3	12 ± 10.2	10.5 ± 5.3
Methotrexate (mg/week) ^d	12.5 ± 5.5	13 ± 2.8	15.4 ± 2.7 ^e	11.5 ± 3.2
Prednisone (mg/day)	12.1 ± 5.6	8.5 ± 4.2	10.3 ± 8.7	8.2 ± 5.4
Patients with NSAIDs	3	6	5	4
Patients with rheumatoid factor	4	8	5	6
Patients with anti-CCP abs ^g	3	8	5	8

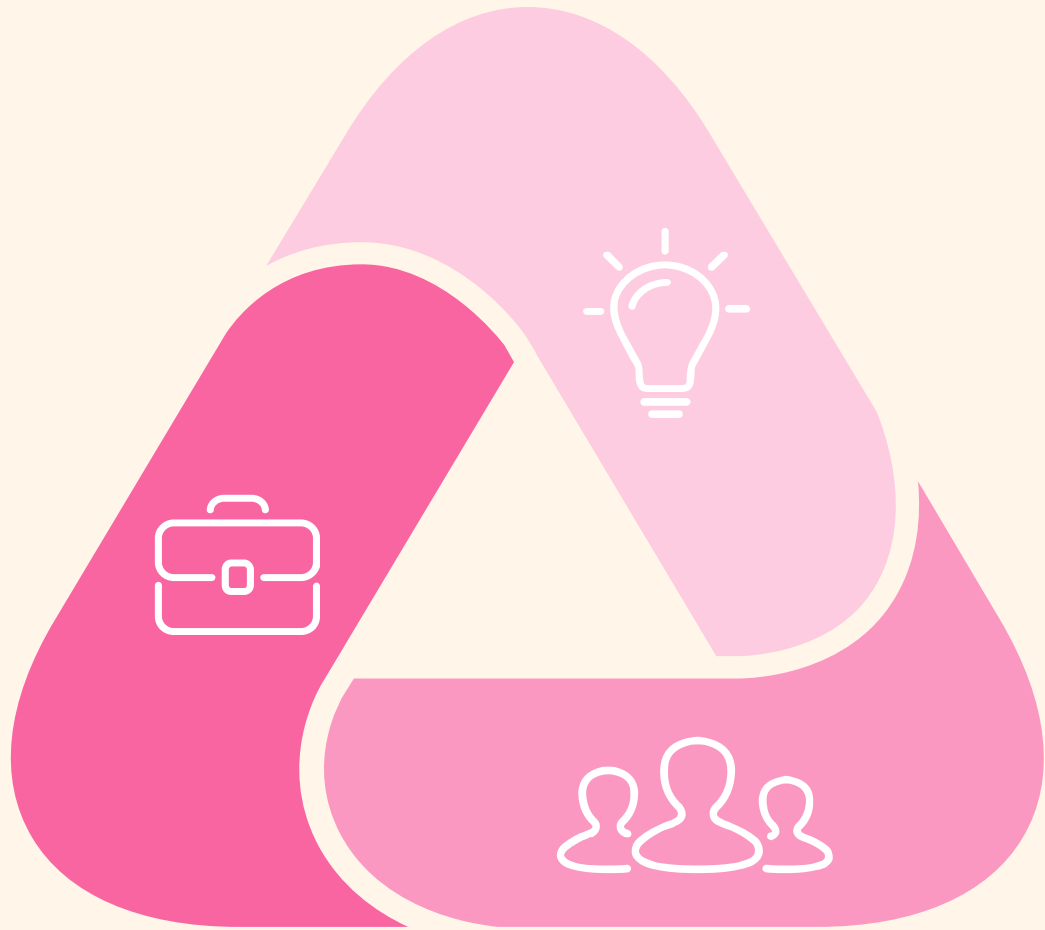
* Categorized as indicated in Materials and methods. ^b Transcript levels were measured by microarray analysis for subset 1 or qRT-PCR for subset 2. ^c Mean ± standard deviation. ^d Maximally tolerated dose in a given patient. ^e Significant difference between subsets 1 and 2 within non-responders (p < 0.05, Mann-Whitney's non-parametric test). In this table, all other comparisons were non-significant. Anti-CCP abs, anti-cyclic citrullinated peptide antibodies; NSAID, non-steroidal anti-inflammatory drugs; RA, rheumatoid arthritis.

Clinical data at baseline and at 3 months

	Responders				Non-responders			
	Subset 1		Subset 2		Subset 1		Subset 2	
	Baseline	3 months ^a	Baseline	3 months ^a	Baseline	3 months ^a	Baseline	3 months ^a
Morning stiffness (minutes) ^b	245 ± 126 ^c	35 ± 24.5 ^c	210 ± 81	58 ± 70.2 ^c	179 ± 159	66.4 ± 86 ^c	133 ± 84	62 ± 67.6 ^c
DAS28 ^b	6.4 ± 1.0	4.2 ± 0.9 ^c	6.2 ± 0.7	3.8 ± 0.6 ^c	5.7 ± 0.8	5.3 ± 1.0	5.5 ± 1.0	4.9 ± 1.0 ^c
Pain (0–100 mm VAS)	59.3 ± 20.3	29.3 ± 9.3 ^c	62.5 ± 15.5	31.3 ± 14.5 ^c	69.3 ± 13.1	54.1 ± 22.1	60.9 ± 11.4	40.6 ± 18.4 ^c
ESR (mm/hour)	44 ± 26.2	27 ± 20.3 ^c	27.2 ± 15.7	11.3 ± 5.2 ^c	35.7 ± 25.7	28.3 ± 15.3	24.1 ± 11.5	27.8 ± 19.2
CRP (mg/l) ^b	42 ± 29.8	20 ± 15.7 ^c	28.6 ± 19.7	6.2 ± 6.1 ^c	18.5 ± 12.7	13 ± 8.2	15.8 ± 15.6	11 ± 7.3



Fragmentation challenge



1 Multiple Endpoints

2 Isolated analysis

3 Disparate sources

High Stakes: Fragmentation



01

Delayed decision-making



02

Data Processing inefficiencies



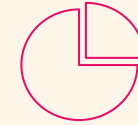
03

Regulatory Ambiguity



04

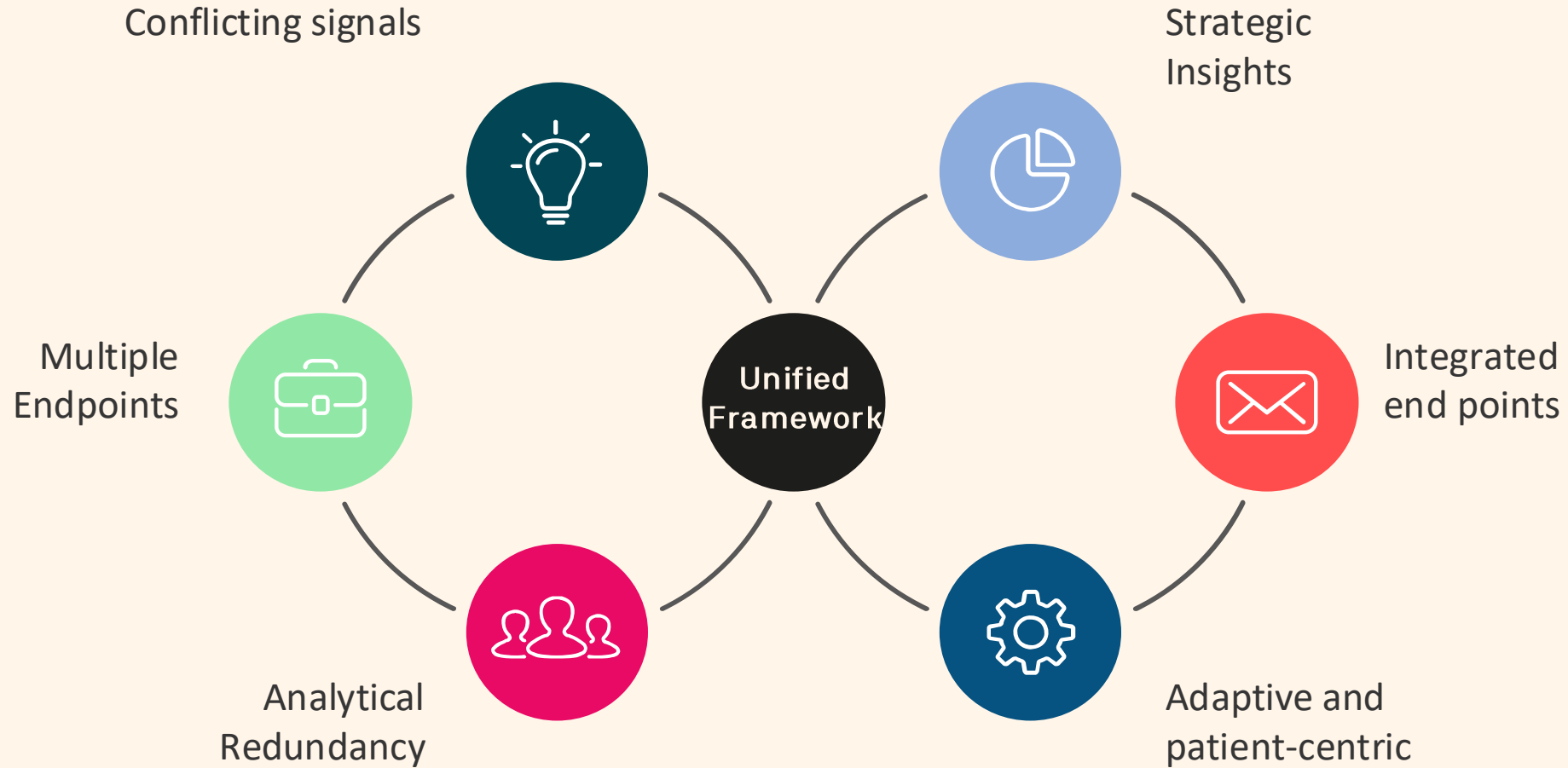
Operation and Scalability



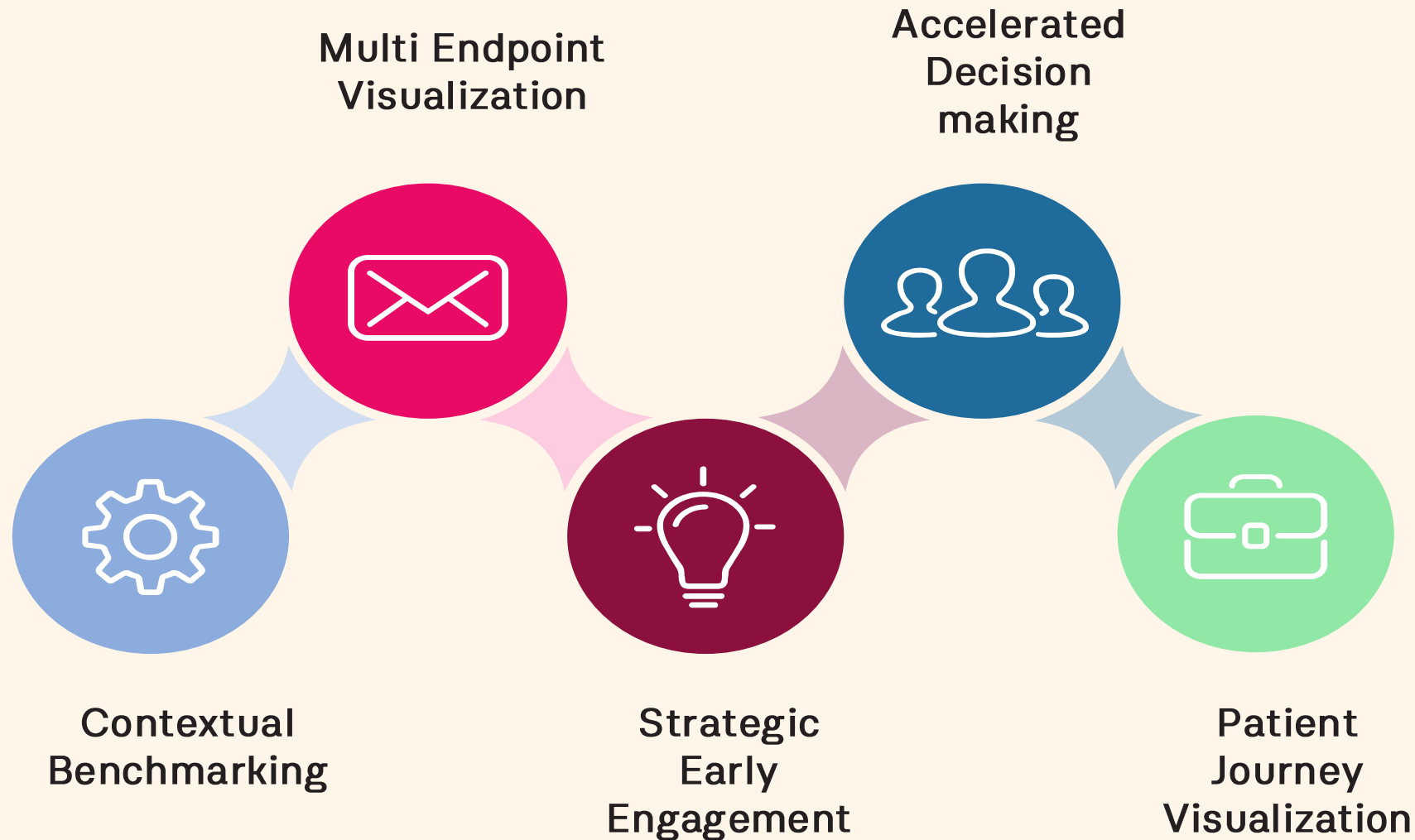
05

Patient Level Insights

Need for a Unified Framework



How Unified approach can solve the Fragmentation problems?

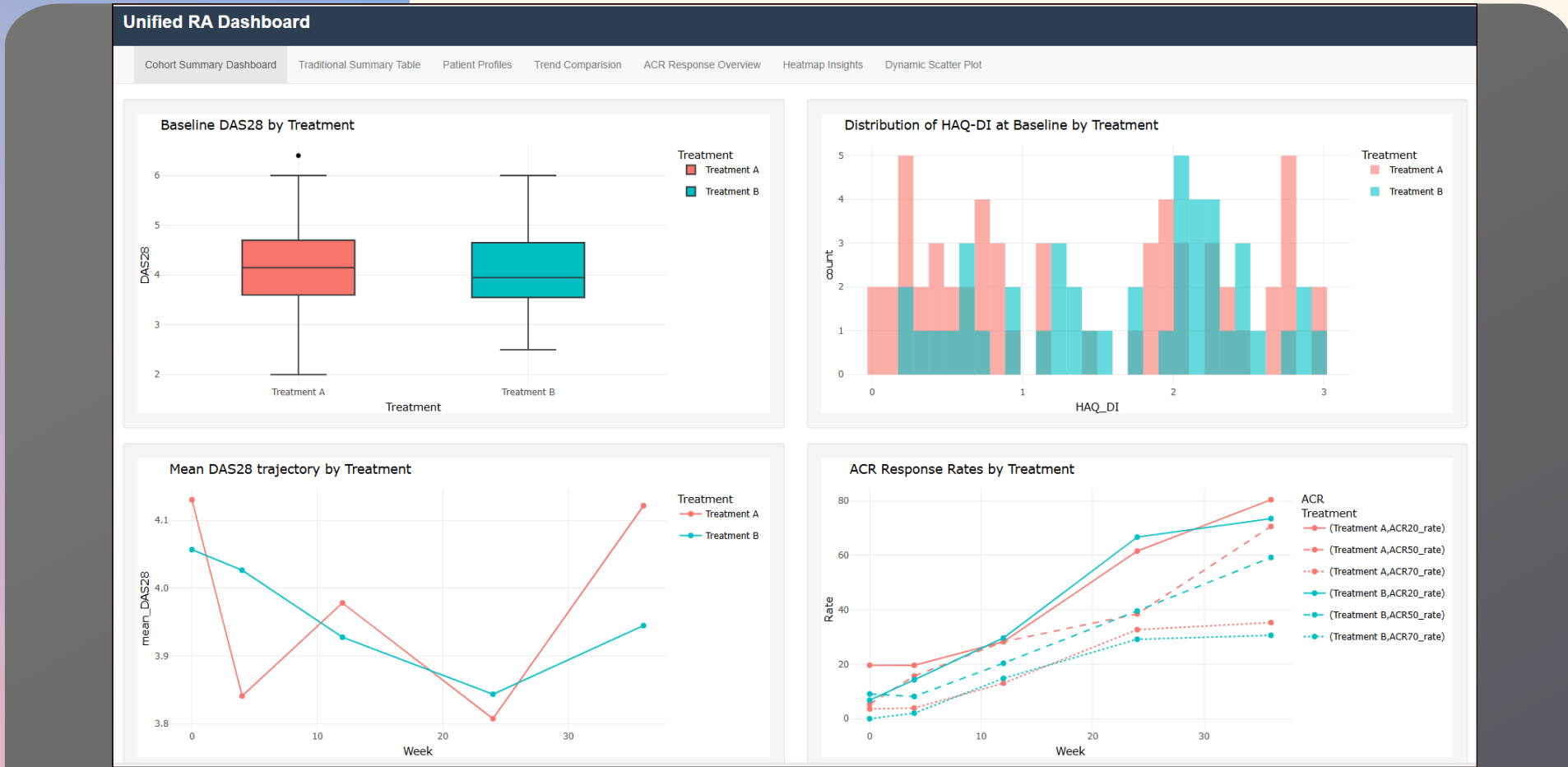




Case Study

Case study

Combines population level insights with individual patient monitoring.



Overall Summary



01

Box Plot

- Shows distribution of DAS28 scores at baseline for both treatment groups.
- Similar medians indicate groups are balanced at baseline.

02

Histogram

- Shows distribution of functional disability at baseline. Overlap suggest comparable patient populations

03

Line plots

- Line plot of mean DAS28 trajectory over weeks for each treatment. Declining curves show improvement. Curve which drops faster shows superior efficacy.
- Line plot of % of patients achieving ACR20/50/70 over time. Higher rates in one treatment arm indicates better efficacy.



Patient Profiles

- 01

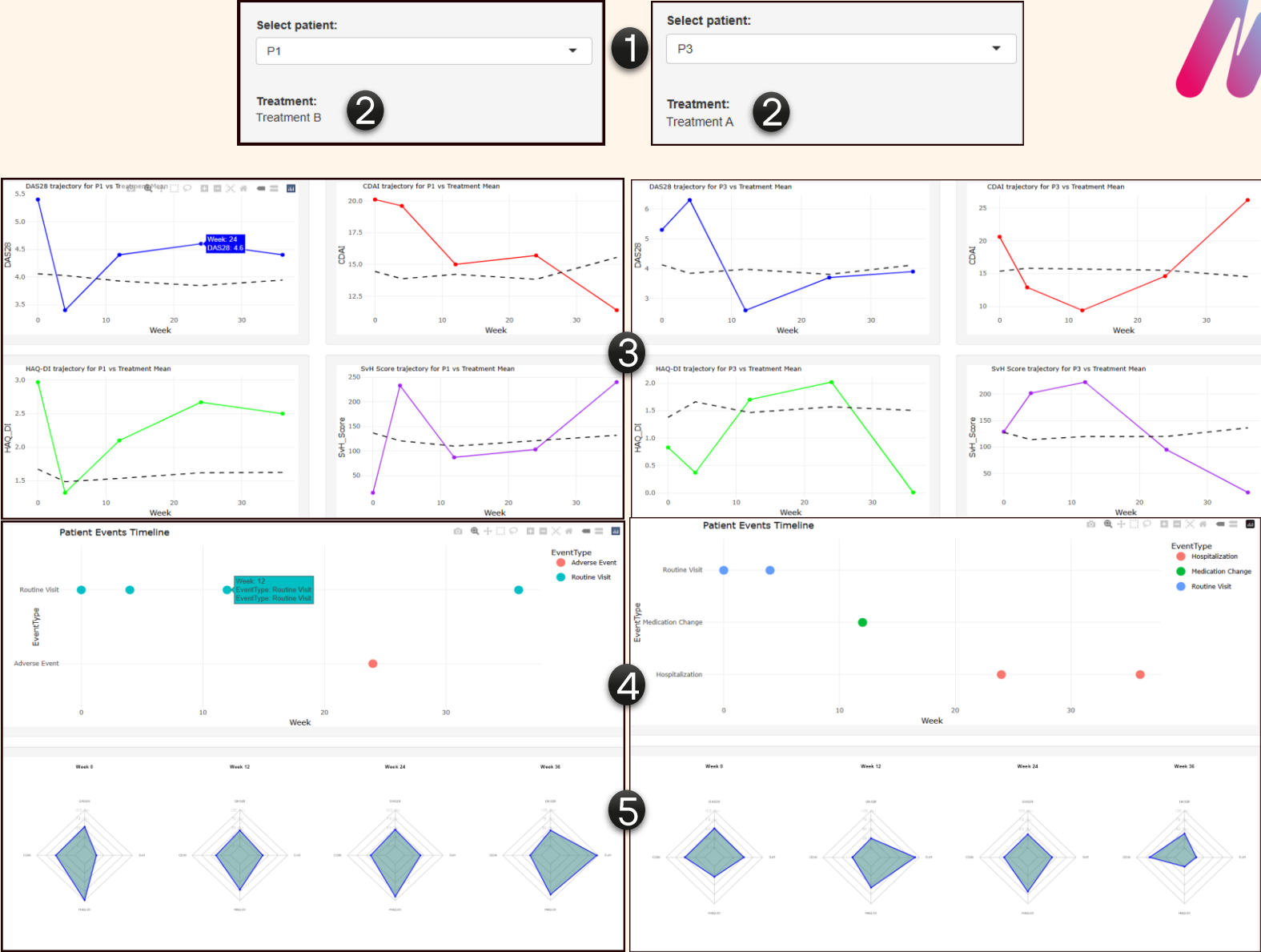
Patient dropdown list
Allows selection patients.
- 02

Treatment
Shows Treatment to which the patient is assigned.
- 03

Longitudinal plots of Individual Metric Trajectories for DAS28, CDAI, HAQ-DI and SvH
Each plot shows patient's score over time vs treatment mean (dashed line). Allows clinicians to see if a patient is responding better/worse than peers.
- 04

Scatter plot of Events (Routine visit, Adverse event, Medication change, Hospitalization, etc.) Timeline
Helps to track clinical course and safety signals for each patient.
- 05

Radar Chart
Spider plot of DAS28, CDAI, HAQ-DI and SvH. Visualizes multi-dimensional disease burden. Larger area = more sever disease.

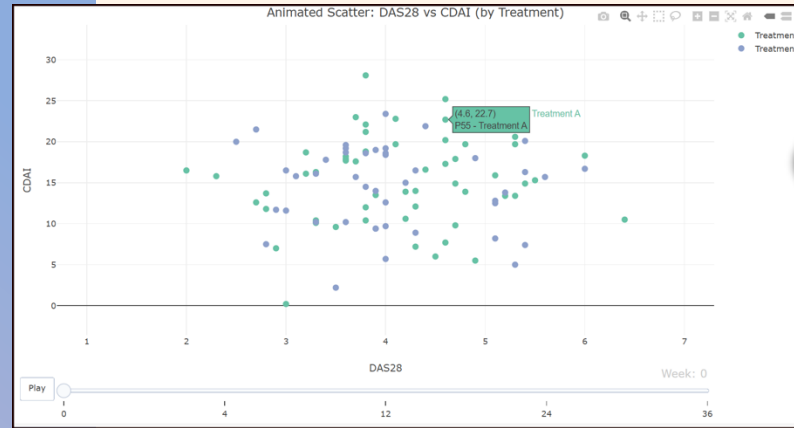


Visual Trends

01

Animated Scatter plot (DAS28 vs CDAI)

- Each dot = patient, colored by treatment, frame = week.
- Movement of dots towards lower DAS28 and CDAI over frames indicate improvement.
- Useful for visualizing correlation between DAS28 and CDAI longitudinally.

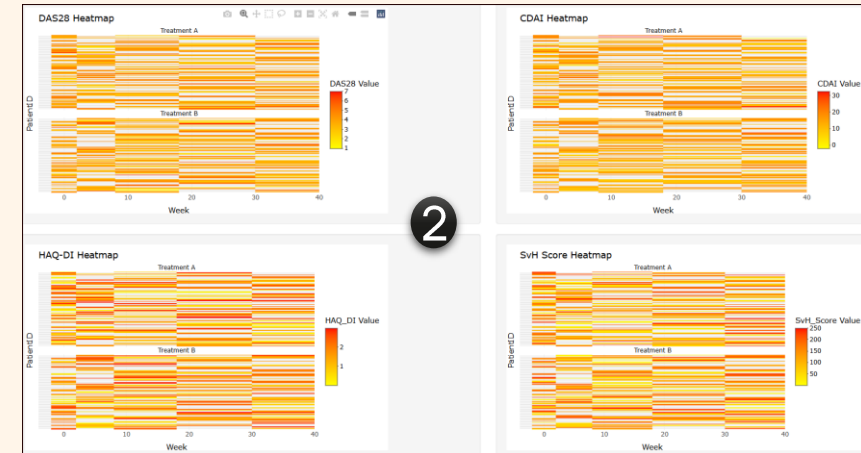


1

02

Heatmaps of (DAS28, CDAI, HAQ-DI, SvH)

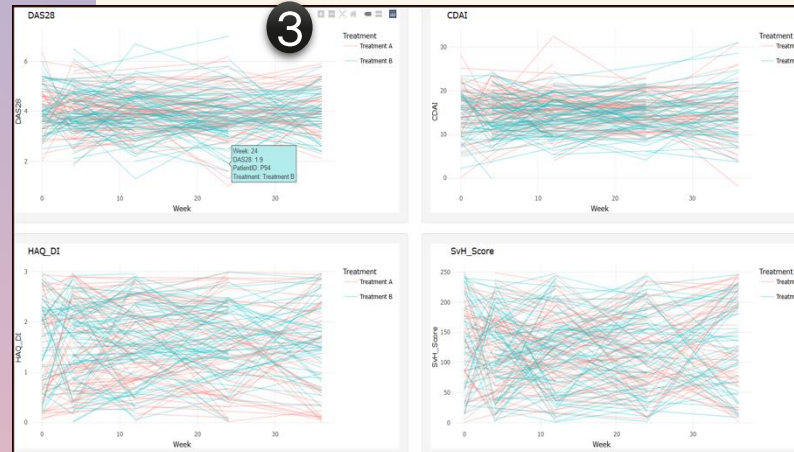
- Rows = patients, columns = weeks, color = severity.
- Lighter color = low values/improvement, darker color = high values/worsening.
- Useful for spotting cluster of responders/non-responders.
- There is minimal visual differences between both treatment groups.



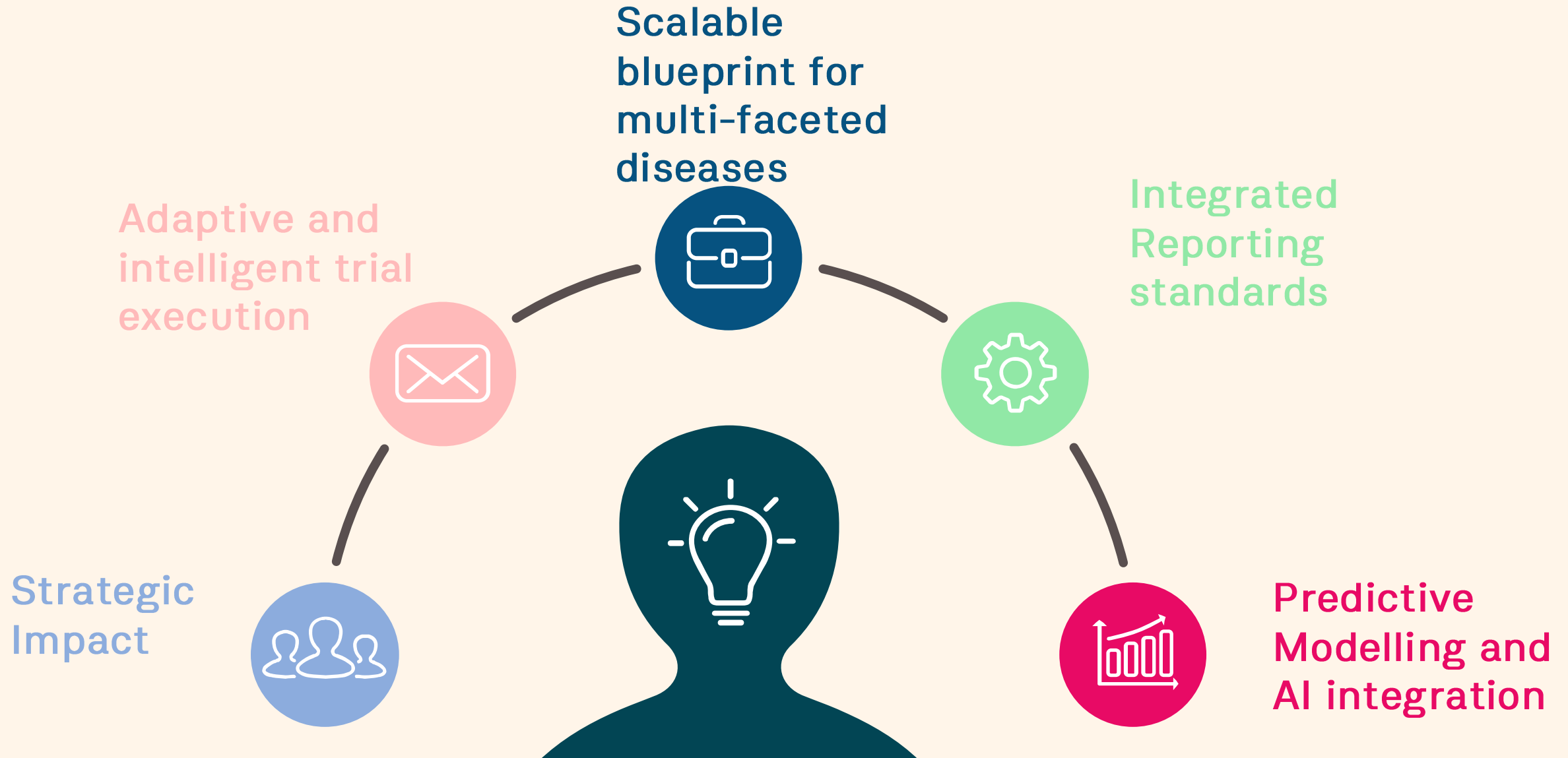
03

Spaghetti Plots (DAS28, CDAI, HAQ-DI, SvH)

- Plots show each patient line colored by treatment. Reveals variability in response.
- Dense downward trend = consistent improvement.
- Outliers highlight non-responders or worsening patients.



Conclusion and Future Directions



Thank you

Reach out to us

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