Universitätsspital Basel

Treatment Duration and Associated Outcomes for Skin and Soft Tissue Infections in Patients With Obesity or Heart Failure

Claudia Ihm, Jesse D. Sutton, Tristan T. Timbrook, and Emily S. Spivak

Open Forum Infectious Diseases, Volume 6, Issue 6, June 2019, ofz217

Background

Although existing literature supports **durations of 5–7 days** for skin and soft tissue infections (SSTIs), longer durations are commonly used. **Obesity** and **heart failure** (HF) have been associated with increased risk for treatment failure of SSTIs; however, **whether prolonged antibiotic durations reduce the risk of treatment failure is unknown**. We evaluated practice patterns for SSTIs in patients with obesity and/or HF and whether short antibiotic durations (**≤8 days**) were associated with treatment failure.

Methods

- single-center, retrospective cohort study
- inpatients between January 1, 2006, and December 30, 2016
- SSTIs based on ICD coding, and obesity and/or HF
- propensity score-weighted logistic regression for the full cohort
  - heart failure, obesity, and treatment duration as predictors of treatment failure
- propensity score matching was used to estimate the risk of treatment failure between short duration of antibiotic therapy (<=8 days) as compared with a long duration (>8 days)
  - multivariable regression model. dependent: antibiotic duration. covariates: age, history of SSTI, obesity, lower extremity edema, and Charlson comorbidity index

Primary Outcome

- treatment failure for SSTI within 30 days
  - extending therapy beyond the originally planned treatment course as determined at the time of hospital discharge
  - changing or adding antimicrobials after hospital discharge
  - reinitiating antimicrobials after completion of the originally planned treatment course
  - incision and drainage after the end of the original planned antibiotic course

Seconday outcome

- length of hospital stay
- 30-day readmission
- 30-day SSTI-related readmission
- Clostridium difficile infection within 60 days of admission

Exclusion criteria

- SSTI complicated by deep underlying tissue infection (eg, osteomyelitis, septic arthritis, fasciitis), infected wounds, and/or bacteremia
- previous treatment for an SSTI in the 30 days before admission
- infection localized to the head and neck area, rectum, perineum, or genitals
- immunosuppression
- transfer to or from another facility where hospitalization occurred
- received antibiotics for a non-SSTI indication
- death within 5 days of admission

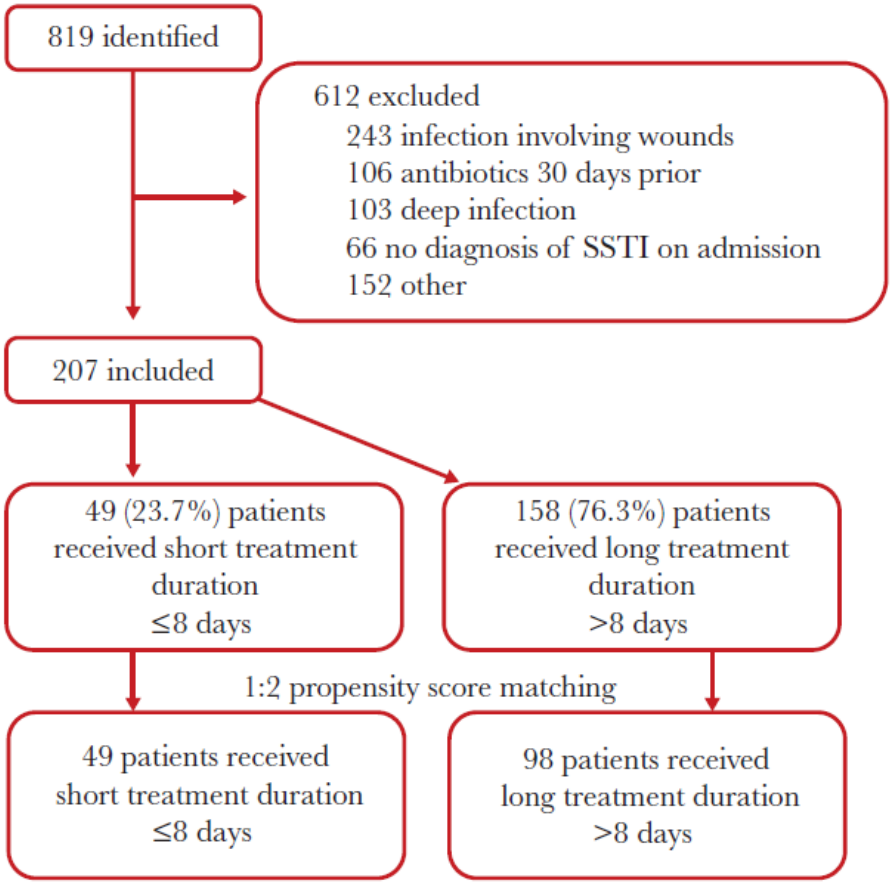


Figure 1. Study flowchart. Abbreviation: SSTI, skin and soft tissue infection.

Table 1. Demographic and Clinical Characteristics of Hospitalized Adults With Skin and Soft Tissue Infections Receiving Short (≤8 Days) or Long (>8 Days) Durations of Antibiotic Therapy

	Overall Cohort			Propensity Score–Matched Cohort		
Characteristic	Short Duration (n = 49)	Long Duration (n = 158)	*P* Value	Short Duration (n = 49)	Long Duration (n = 98)	*P* Value
Age, median (IQR), y	68 (57–75)	64 (59–73)	.38	68 (57–75)	67 (76–59.3)	.90
Gender (male)	49 (100.0)	154 (97.5)	.60	49 (100)	96 (98.0)	.80
BMI, median (IQR), kg/m^2	34 (30–40)	34.4 (31–40)	.90	34 (30–40)	33.5 (30–39.5)	.53
Comorbidities						
Heart failure only	10 (20.4)	19 (12.0)	.14	10 (20.4)	16 (16.3)	.54
Obesity only	33 (67.6)	112 (70.9)	.64	33 (67.3)	67 (68.4)	.90
Heart failure & obesity	6 (12.2)	27 (17.1)	.42	6 (12.2)	15 (15.3)	.62
Diabetes with complications	9 (18.4)	25 (15.8)	.84	9 (18.4)	15 (15.3)	.81
Lower extremity edema	19 (38.8)	78 (49.4)	.26	19 (38.8)	41 (42.9)	.77
Lymphedema	0 (0)	2 (1.3)	1.00	0 (0)	2 (2.0)	.80
History of SSTI	5 (10.2)	36 (22.8)	.08	5 (10.2)	9 (9.2)	1.00
Injection drug use	4 (8.2)	7 (4.4)	.51	4 (8.2)	4 (4.1)	.52
Charlson comorbidity index, median (IQR)	2 (1–3)	2 (1–3)	.75	2 (1–3)	2 (1–3)	.59
Type of infection						
Nonpurulent cellulitis	36 (73.5)	121 (76.6)	.80	36 (73.5)	74 (75.5)	.95
Purulent cellulitis	13 (26.5)	37 (23.4)	.80	13 (26.5)	24 (24.5)	.95
Cutaneous abscess	7 (14.3)	21 (13.3)	1.0	7 (14.3)	13 (13.3)	1.00
Location of infection						
Torso	1 (8.2)	11 (7.0)	1.0	4 (8.2)	4 (4.1)	.52
Upper extremity	12 (24.5)	37 (23.4)	1.0	12 (24.5)	24 (24.5)	1.00
Lower extremity	31 (63.3)	108 (68.4)	.63	31 (63.3)	70 (71.4)	.41
Head and neck	2 (4.1)	1 (0.6)	.28	2 (4.1)	0 (0)	.21
Buttock	1 (2.0)	2 (1.3)	1.0	1 (2.0)	1 (1.0)	1.00
Bilateral lower extremity	2 (4.1)	5 (3.2)	1.0	2 (4.1)	4 (4.1)	1.00
Clinical characteristics						
ICU on admission	1 (2.0)	4 (2.5)	1.00	1 (2.0)	2 (2.0)	1.00
Fever on admission	13 (26.5)	47 (29.7)	.80	13 (26.5)	29 (29.6)	.85
WBC ≥12 000 cells/mm^3 on admission	17 (34.7)	73 (46.2)	.21	17 (34.7)	45 (45.9)	.26
ICU on day 5	0 (0)	1 (0.6)	1.0	0 (0)	0 (0)	1.00
Fever on day 5	0 (0)	1 (0.6)	1.0	0 (0)	0 (0)	1.00
WBC ≥12 000 cells/mm^3 on day 5	3 (6.1)	15 (9.5)	.66	3 (6.1)	10 (10.2)	.61
Antibiotic therapy						
Anti-MRSA active agent for ≥48 h	18 (36.7)	108 (68.4)	<.001	18 (36.7)	65 (66.3)	.001
Days of intravenous antibiotics, median (IQR)	2 (1–3)	4 (3–6)	<.001	2 (1–3)	4 (3–6.8)	<.001
Total antibiotic days, median (IQR)	7 (7–8)	14 (10–15)	<.001	7 (7–8)	13 (10–15)	<.001

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: BMI, body mass index; ICU, intensive care unit; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*; SSTI, skin and soft tissue infection; WBC, white blood cell.

Table 2. Microbiologic Characteristics of Hospitalized Adults With Skin and Soft Tissue Infections Receiving Short (≤8 Days) and Long (>8 Days) Durations of Antibiotic Therapy

	Overall Cohort			Propensity Score–Matched Cohort		
Characteristic	Short Duration (n = 49)	Long Duration (n = 158)	*P* Value	Short Duration (n = 49)	Long Duration (n = 98)	*P* Value
MRSA colonized	6 (12.2)	26 (16.5)	.65	6 (12.2)	13 (13.3)	.71
Any cutaneous culture obtained	7 (14.3)	35 (22.2)	.23	7 (14.3)	22 (22.5)	.24
Wound or tissue culture	3 (6.1)	18 (11.4)	.68	3 (6.1)	13 (13.3)	.45
Abscess culture	4 (8.2)	17 (10.8)		4 (8.2)	9 (9.2)	
Any microorganism identified	7 (14.3)	29 (18.4)	.51	7 (14.3)	18 (18.4)	.54
Polymicrobial	0 (0)	11 (7.0)	.06	0 (0)	9 (9.2)	.03
Staphylococcus aureus	3 (6.1)	17 (10.8)	.34	3 (6.1)	10 (10.2)	.41
MSSA	1 (2.0)	7 (4.4)	.45	1 (2.0)	5 (5.1)	.38
MRSA	2 (4.1)	10 (6.3)	.56	2 (4.1)	5 (5.1)	.78
Streptococcal species	3 (6.1)	8 (5.1)	.77	3 (6.1)	5 (5.1)	.80
Other gram-positive	1 (2.0)	9 (5.7)	.30	1 (2.0)	7 (7.1)	.20
Aerobic gram-negative	0 (0)	4 (2.5)	.26	0 (0)	3 (3.1)	.22

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

Table 3. Primary Secondary Outcomes in Hospitalized Adults With Skin and Soft Tissue Infections Receiving Short (≤8 Days) and Long (>8 Days) Durations of Antibiotic Therapy

	Overall Cohort			Propensity Score–Matched Cohort		
Characteristic	Short Duration (n = 49)	Long Duration (n = 158)	*P* Value	Short Duration (n = 49)	Long Duration (n = 98)	*P* Value
Treatment failure	5 (10.2)	40 (25.3)	.04	5 (10.2)	28 (28.6)	.02
Length of stay, median (IQR), d	2 (2–3)	3 (2–5)	.001	2 (2–3)	3 (3–5)	<.001
30-d readmission	4 (8.2)	27 (17.1)	.19	4 (8.2)	16 (16.3)	.27
30-d SSTI-related readmission	1 (2.0)	8 (5.1)	.61	1 (2.0)	5 (5.1)	.66
Clostridium difficile infection	2 (4.1)	1 (0.6)	.28	2 (4.1)	0 (0)	.21

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: BMI, body mass index; IQR, interquartile range; SSTI, skin and soft tissue infection.

Conclusion

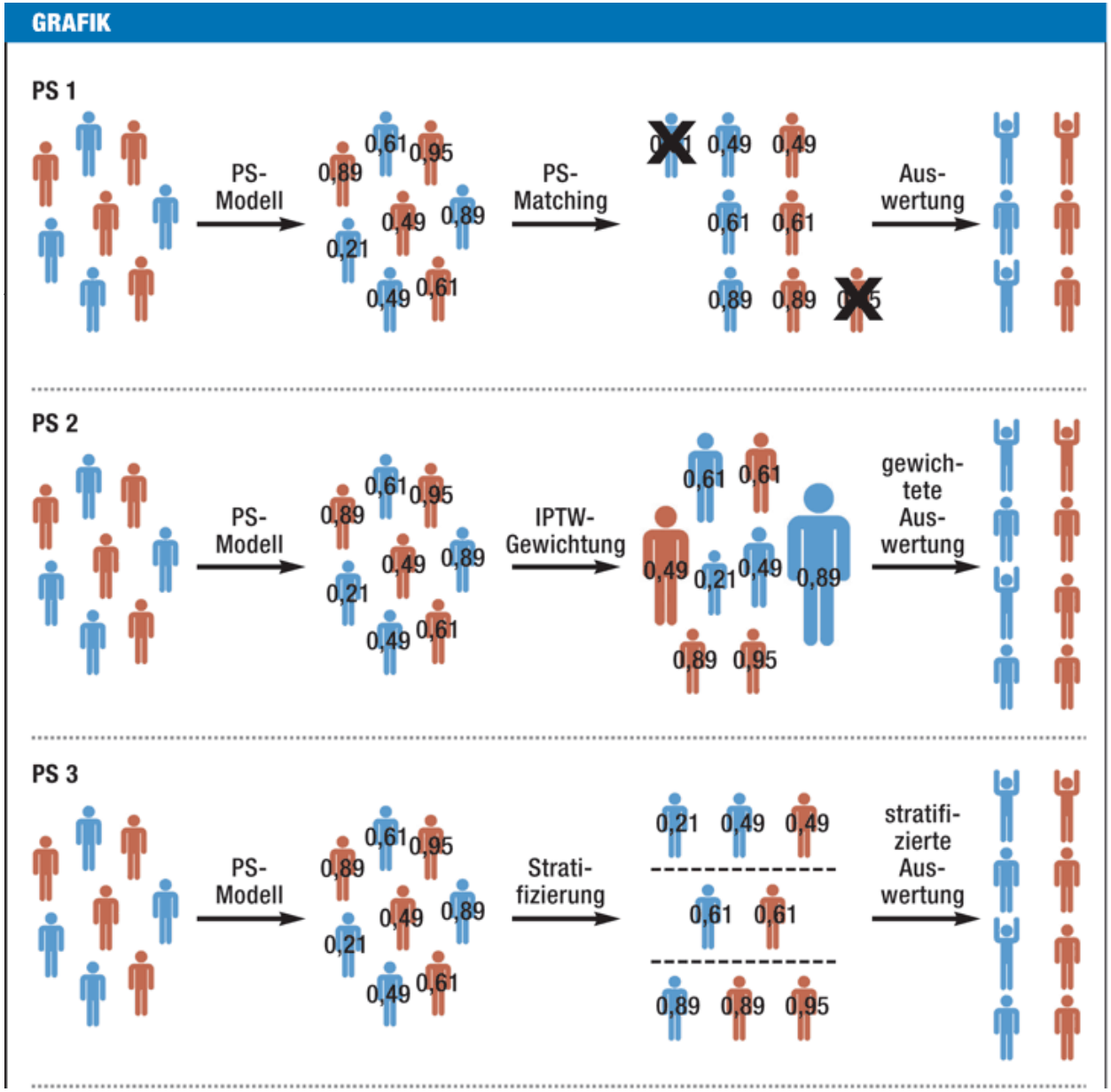
- short treatment duration remained significantly associated with reduced treatment failure (10.2 vs. 28.6%)
- heart failure and obesity were not associated with treatment failure
- why do we treat SSTI longer? (non-significant)
  - history of SSTI, obesity, lower extremity edema, WBC
  - more MRSA active antibiotics but same proportion of MRSA colonization

Discussion

- data quality?
  - no difference in CDI rates (4.1% [2/49] vs 0%, short vs long, respectively; P = .21)
  - nonsignificantly higher readmission rate in the long-duration group as compared with the short-duration group (16.3% vs. 8.2%, respectively; P = .27)
- male cohort
- risk factors history of cancer and lymphedema not analyzed
- confounding factors?
- clinical entity SSTI

Treatment Duration and Associated Outcomes for SSTI in Patients With Obesity or Heart Failure,
Claudia Ihm et al., Open Forum Infectious Diseases, Volume 6, Issue 6, June 2019, ofz217

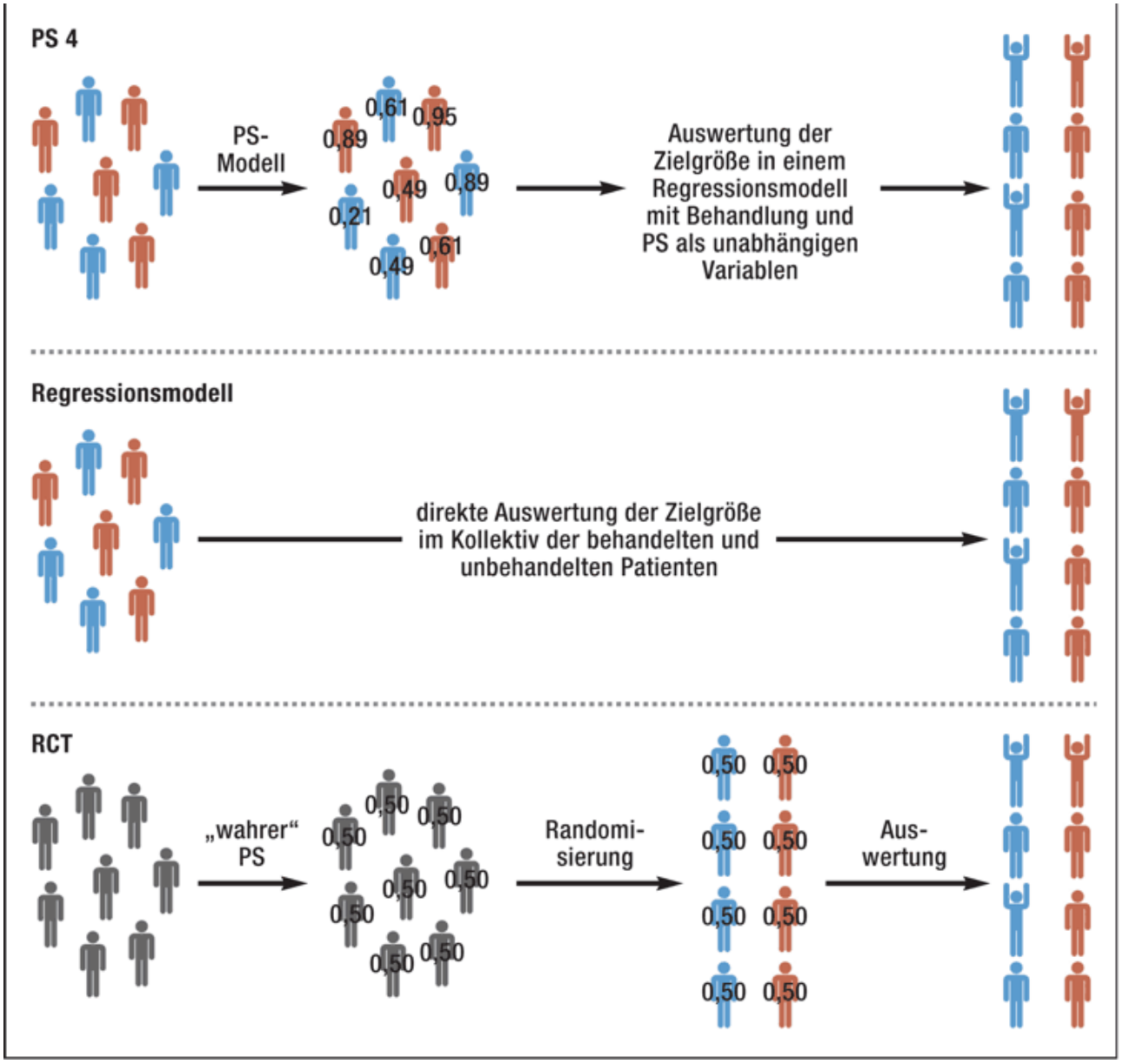
Universitätsspital Basel



Durchführung einer PS-Analyse im Vergleich zu einer herkömmlichen Regressionsanalyse und einer randomisierten kontrollierten Studie
Die Abkürzungen PS 1–PS 4 stehen für die vier Methoden zur Berücksichtigung des Propensity Scores (PS):
PS 1 = PS-Matching,
PS 2 = „inverse probability of treatment weighting"(IPTW)-Schätzung,
PS 3 = Stratifizierung und
PS 4 = Regressionsadjustierung für den PS.

Am Beginn jeder PS-Analyse steht eine Gruppe von Patienten, die mit der interessierenden Intervention behandelt (rot) oder nicht behandelt (blau) wurden. Mit Hilfe der vorliegenden Patientenmerkmale wird ein PS-Modell geschätzt und für jeden Patienten der Propensity Score berechnet (in der Grafik als Zahlenwerte bei den Piktogrammen). Entsprechend der jeweiligen PS-Methode werden Patienten dann gematcht (PS 1, in der Regel werden Patienten ausgeschlossen, für die kein Matching-Partner gefunden worden ist; sie sind mit einem X gekennzeichnet), in Abhängigkeit von ihrem PS gewichtet (PS 2, Patienten mit höherem IPTW-Gewicht sind in der Grafik größer dargestellt), stratifiziert (PS 3, hier in Terzilen), oder es wird (PS 4) eine Regressionsanalyse unter Berücksichtigung des PS durchgeführt. Entsprechend der PS-Methode werden die klinischen Zielgrößen ausgewertet.
(In der Grafik sind geheilte Patienten der

https://www.aerzteblatt.de/archiv/181706/Propensity-Score-eine-alternative-Methode-zur-Analyse-von-Therapieeffekten



Einfachheit halber in einer Jubelpose dargestellt.)

In einem herkömmlichen Regressionsmodell wird dagegen ein einziges statistisches Modell berechnet, in das die klinische Zielgröße als abhängige Variable, die Therapie und die anderen Patientenmerkmale als unabhängige Variablen eingehen.

Die Ähnlichkeit zwischen einer randomisierten kontrollierten Studie (RCT, „randomised controlled trial“) und einer PS-Analyse wird im unteren Teil der Grafik verdeutlicht: Zu Beginn sind die Patienten in einer RCT noch unbehandelt (grau) und ihr PS (also die Wahrscheinlichkeit, die Intervention zu erhalten) ist bekannt und gleich 0,5. Bei der Randomisierung wird jedem Patienten eine Therapie zugeteilt, so dass wie beim PS je eine Gruppe von behandelten und unbehandelten Patienten gebildet wird. Schließlich folgt als letzter Schritt die Auswertung der klinischen Zielgröße.

https://www.aerzteblatt.de/archiv/181706/Propensity-Score-eine-alternative-Methode-zur-Analyse-von-Therapieeffekten

Universitätsspital Basel