Understanding the Studies

A Brief Refresher on Statistics

Austin Smith, MD DiMM
Chair, Department of Emergency Medicine
Medical Director, North Summit Fire Department
Medical Staff President
Park City Hospital

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Disclosures

- No relevant financial disclosures

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Outline

- History of Research
- Current Research
- Designing a Study
- Future of Research

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First Studies

- Book of Daniel
  - King Nebuchadnezzar (PI), 500BC
  - Double arm study of
    - General Population: meat and wine
    - Royals: vegetables

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First Studies

- Book of Daniel[1]
  - Vegetable group appeared better nourished

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First Studies

- First Controlled Trial[1]
  - James Lind 1747
  - Noticed “putrid gums” in sailors
  - Selected 12 sailors, different diets
  - Those with “oranges and lemons” had “sudden and visible good effects”

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First Studies

- First Controlled Trial[1]
  - "Treatise on Scurvy" published in 1753 in Edniburgh

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First Studies

- Placebo[2]
  - Term appeared in medical literature in 1800s
  - Began appearing in literature in late 1800s

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First Studies

- 1943: First Double-Blind Controlled Trial[2]
  - Patulin (Penicillin extract) treatment for common cold
  - Had a PI and statisticians
  - Disappointing outcome- no protective effect found
- 1946: First Randomized Curative Trial[2]
  - Streptomycin vs bed rest for tuberculosis patients
  - Very complex and well designed
  - One of the most influential designs for clinical trials

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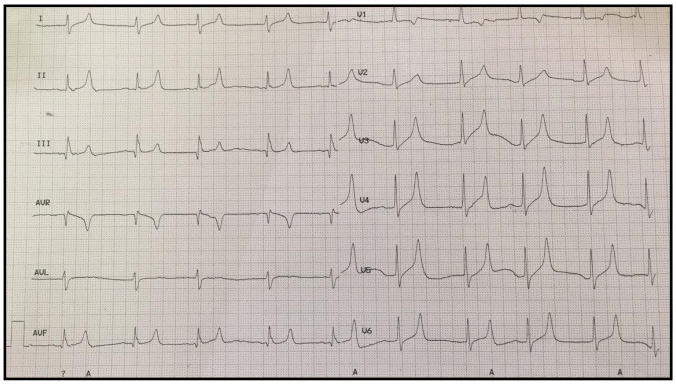

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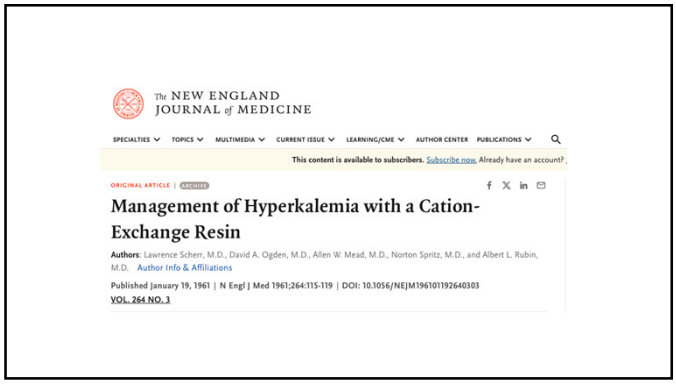
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ORIGINAL ARTICLE | ARCHIVE
Management of Hyperkalemia with a Cation-Exchange Resin
Authors: Lawrence Scherr, M.D., David A. Ogden, M.D., Allen W. Mead, M.D., Norton Spritz, M.D., and Albert L. Rubin, M.D. Author Info & Affiliations
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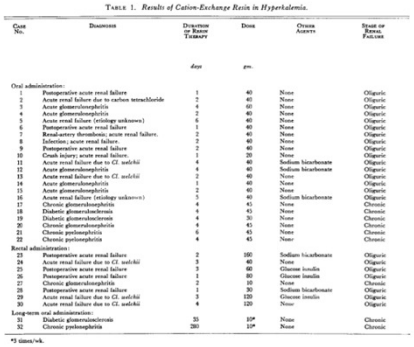

TABLE 1. *Results of Cation-Exchange Resin in Hyperkalemia.*

Case No.	Diagnosis	Duration of Resin Therapy	Dose	Other Agents	Stage of Renal Failure
		days	*gm.*		
Oral administration:					
1	Postoperative acute renal failure	1	40	None	Oliguric
2	Acute renal failure due to carbon tetrachloride	7	40	None	Oliguric
3	Acute glomerulonephritis	4	60	None	Oliguric
4	Acute glomerulonephritis	2	40	None	Oliguric
5	Acute renal failure (etiology unknown)	6	40	None	Oliguric
6	Postoperative acute renal failure	1	40	None	Oliguric
7	Renal-artery thrombosis; acute renal failure.	2	40	None	Oliguric
8	Infection; acute renal failure	2	40	None	Oliguric
9	Postoperative acute renal failure	2	40	None	Oliguric
10	Crush injury; acute renal failure.	1	20	None	Oliguric
11	Acute renal failure due to Cl. welchii	4	40	Sodium bicarbonate	Oliguric
12	Acute glomerulonephritis	4	40	Sodium bicarbonate	Oliguric
13	Acute renal failure due to Cl. welchii	2	40	None	Oliguric
14	Acute glomerulonephritis	1	40	None	Oliguric
15	Acute glomerulonephritis	2	40	None	Oliguric
16	Acute renal failure (etiology unknown)	3	40	Sodium bicarbonate	Oliguric
17	Chronic glomerulonephritis	4	45	None	Chronic
18	Diabetic glomerulosclerosis	4	45	None	Chronic
19	Diabetic glomerulosclerosis	4	30	None	Chronic
20	Chronic glomerulonephritis	4	45	None	Chronic
21	Chronic pyelonephritis	6	45	None	Chronic
22	Chronic pyelonephritis	4	45	None	Chronic
Rectal administration:					
23	Postoperative acute renal failure	2	160	Sodium bicarbonate	Oliguric
24	Acute renal failure due to Cl. welchii	3	40	None	Oliguric
25	Postoperative acute renal failure	3	60	Glucose insulin	Oliguric
26	Postoperative acute renal failure	1	80	Glucose insulin	Oliguric
27	Chronic glomerulonephritis	2	10	None	Chronic
28	Postoperative acute renal failure	1	30	Sodium bicarbonate	Oliguric
29	Acute renal failure due to Cl. welchii	3	120	Glucose insulin	Oliguric
30	Acute renal failure due to Cl. welchii	4	120	None	Oliguric
Long-term oral administration:					
31	Diabetic glomerulosclerosis	35	15*	None	Chronic
32	Chronic pyelonephritis	280	15*	None	Chronic

*3 times/wk.

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Kayexalate© Study

- 32 patients
- No description of patient selection
- Not blinded or randomized
- No discussion of limitations
- Table 1 was the entire study

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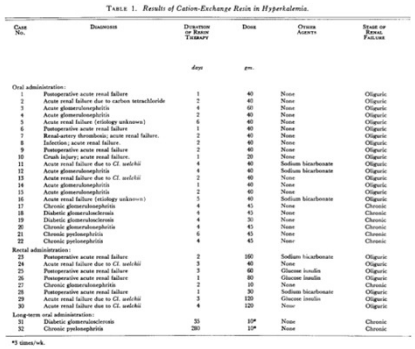

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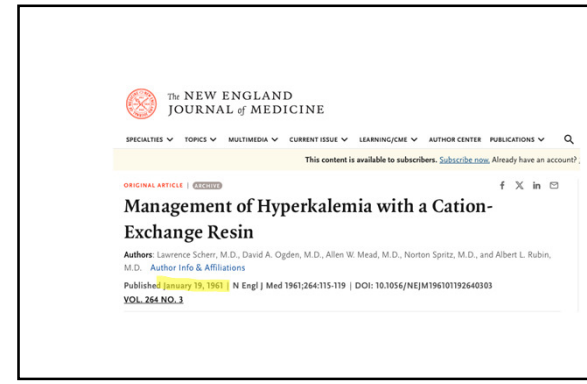

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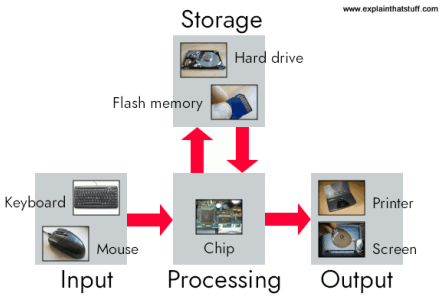

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Today

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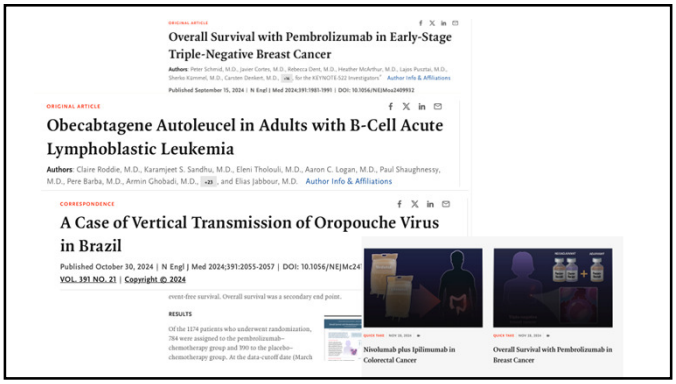

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Basic Study Design

- Randomized Controlled Trial
- Case-Control Studies
- Cross-Sectional Studies
- Cohort Studies

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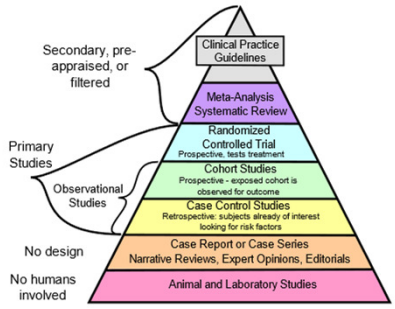

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Randomized Control Trial

- Considered the “gold standard”

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Randomized Control Trial

- Randomization: creating groups that are the same in every way
- Controlled: includes a comparison group

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Randomized Control Trial

- Best for answering a question in which there is true equipoise

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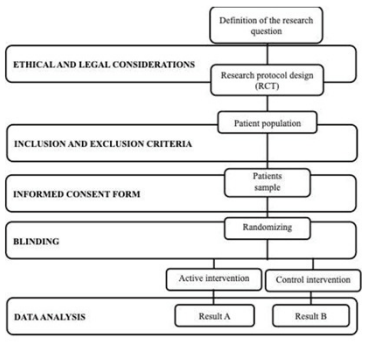

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Parachute use to prevent death and major trauma when jumping from aircraft: randomized controlled trial

Robert W Yeh,[1] Linda R Valsdottir,[1] Michael W Yeh,[2] Changyu Shen,[1] Daniel B Kramer,[1] Jordan B Strom,[1] Eric A Secemsky,[1] Joanne L Healy,[1] Robert M Domeier,[3] Dhruv S Kazi,[1] Brahmajee K Nallamothu[4] On behalf of the PARACHUTE Investigators

ABSTRACT

OBJECTIVE
To determine if using a parachute prevents death or major traumatic injury when jumping from an aircraft.

DESIGN
Randomized controlled trial.

SETTING
Private or commercial aircraft between September 2017 and August 2018.

PARTICIPANTS
92 aircraft passengers aged 18 and over were screened for participation. 23 agreed to be enrolled and were randomized.

INTERVENTION
Jumping from an aircraft (airplane or helicopter) with a parachute versus an empty backpack (unblinded).

regarding the effectiveness of an intervention exist in the community, randomized trials might selectively enroll individuals with a lower perceived likelihood of benefit, thus diminishing the applicability of the results to clinical practice.

Introduction

Parachutes are routinely used to prevent death or major traumatic injury among individuals jumping from aircraft. However, evidence supporting the efficacy of parachutes is weak and guideline recommendations for their use are principally based on biological plausibility and expert opinion.[1,2] Despite this widely held yet unsubstantiated belief of efficacy, many studies of parachutes have suggested injuries related to their use in both military and recreational settings,[3-6] and parachutist injuries are formally recognized in

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Fig 2 | Representative study participant jumping from aircraft with an empty backpack. This individual did not incur death or major injury upon impact with the ground

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Case-Control Studies

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Case-Control Studies

- Comparing cases of interest (outcomes) to control groups to figure something out

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Case-Control Studies

- Start with cases of interest (an outcome)
- Then pick a similar population that doesn't have illness

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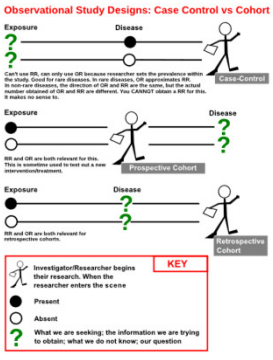

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Case-Control Studies

- Best for rare outcomes or disease
- Good design for conditions in which there is a long time from exposure to disease development
- Great for when quick results are desired (sudden outbreak of disease)

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Case-Control Studies

- Highly at risk of selection bias
- Inefficient for rare exposures

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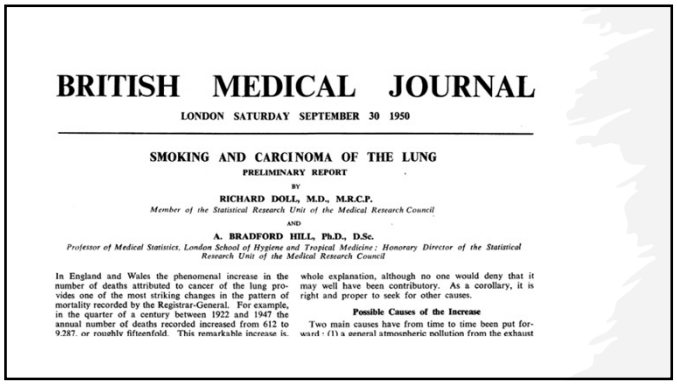

BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 30 1950

SMOKING AND CARCINOMA OF THE LUNG

PRELIMINARY REPORT

BY

RICHARD DOLL, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

AND

A. BRADFORD HILL, Ph.D., D.Sc.

Professor of Medical Statistics, London School of Hygiene and Tropical Medicine: Honorary Director of the Statistical Research Unit of the Medical Research Council

In England and Wales the phenomenal increase in the number of deaths attributed to cancer of the lung provides one of the most striking changes in the pattern of mortality recorded by the Registrar-General. For example, in the quarter of a century between 1922 and 1947 the annual number of deaths recorded increased from 612 to 9,287, or roughly fifteenfold. This remarkable increase is, whole explanation, although no one would deny that it may well have been contributory. As a corollary, it is right and proper to seek for other causes.

Possible Causes of the Increase

Two main causes have from time to time been put forward: (1) a general atmospheric pollution from the exhaust

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Cross-Sectional Studies

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Cross-Sectional Studies

- A snapshot in time

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Cross-Sectional Studies

- Looking at outcomes and exposures at a certain point in time

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Cross-Sectional Studies

- Quick and “easy”
- Great for generating hypotheses

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Cross-Sectional Studies

- Don’t give information about incidence
- Not good for rare diseases with short durations
- Can’t attribute causation

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A Cross-Sectional Study of the Relationship Between Mental Health Problems and Overweight and Obesity in Adolescents

Asborg Aarstad Bjortnaes[1,2*] Ingrid Nesdal Fossum[3] Ingvild Oma[4] Kjersti Sletten Bakken[5] Tor Arne Strand[6] Mads Nikolaj Holten-Andersen[1,3]

[1] Department of Pediatrics, Lillehammer Hospital, Innlandet Hospital Trust, Lillehammer, Norway
[2] Department of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway
[3] Division of Mental Health Care, BUP, Lillehammer, Innlandet Hospital Trust, Lillehammer, Norway
[4] Department of Medical Microbiology, Innlandet Hospital Trust, Lillehammer, Norway
[5] Women's Clinic, Innlandet Hospital Trust, Lillehammer, Norway
[6] Department of Research, Innlandet Hospital Trust, Brumunddal, Norway

Background: There is a suggested coexistence between obesity and mental health discomfort in adolescence. The objective of this study was to explore if mental health indices covaried with body mass index (BMI) in adolescence and if there were gender-related disparities.

Methods: Data were collected in two cross-sectional surveys of 10th-grade students (15 to 16 years old) carried out in 2002 and 2017. The questionnaires included self-reported height and weight, questions covering mental health using the Strengths and Difficulties Questionnaire (SDQ), lifestyle, and sociodemographic variables. We estimated the associations between SDQ subscale scores and BMI and the prevalence of overweight and obesity in linear and logistic multivariable models. We also estimated the extent to which gender modified these associations.

Results: BMI was positively associated with peer problems (beta (β): 0.08, (95% confidence interval 0.01, 0.14)), indicating that for every point increase in peer problems subscore, BMI increased by 0.08 kg/m^2. The association between internalizing (i.e., peer and emotional) problems and BMI and conduct problems and BMI was different for boys and girls ($p < 0.05$ for all effect modifications).

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Cohort Studies

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Cohort Studies

- A group of individuals followed over time

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Cohort Studies

- Measures and compares the occurrence of disease in one or more cohorts
- Can be prospective or retrospective

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Cohort Studies

- Can determine a temporal relationship
- Can examine multiple outcomes

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Cohort Studies

- Inefficient for rare outcomes
- Can take time and lots of funding (prospective)
- Can require lots of data (retrospective)

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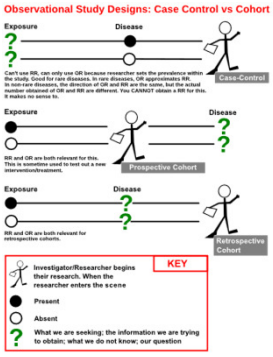

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The Framingham Heart Study and the Epidemiology of Cardiovascular Diseases: A Historical Perspective

Syed S Mahmood [a], Daniel Levy [b,c], Ramachandran S Vasan [b,d], Thomas J Wang [b,e]

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PMCID: PMC4159698 NIHMSID: NIHMS588573 PMID: 24084292

The publisher's version of this article is available at Lancet

Summary

On October 11, 2013, the Framingham Heart Study will celebrate 65 years since the examination of its first participant in 1948. During this period, the study has provided substantial insight into the epidemiology of cardiovascular disease and its risk factors. The origin of the study is closely linked to the cardiovascular health of President Franklin D. Roosevelt and his premature death from hypertensive heart disease and stroke in 1945. The present article describes the events leading to the founding of the Framingham Heart Study, and provides a brief historical overview of selected contributions from the study.

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Efficacy vs Effectiveness

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Efficacy vs Effectiveness

- Efficacy: expected effect of a treatment in an ideal situation
- Effectiveness: expected effect of a treatment in actual practice

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Future of Research

- Pragmatic Trials
- Individual Trials
- Embedded Trials

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Pragmatic Trials

- Focus on real world outcomes
- In Vivo vs in In Vitro
- Relaxed eligibility requirements

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Individual Trials

- N-of-1 Trial

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Embedded Trials

- VASSPR

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References

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