Curriculum Vitae

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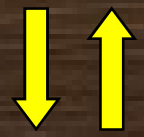
Pekerjaan :
* Guru Besar Tetap Departemen Farmakologi dan Terapeutik, Fakultas Kedokteran, USU, Medan
* Staf Pengajar Program S2 Biomedik & Program Administrasi Kebijakan Kesehatan; Program S3 Kedokteran, Sekolah Pascasarjana, USU, Medan
* Wakil Ketua Komisi Nasional Etika Penelitian Kesehatan (KNEPK), Indonesia

Riwayat Pendidikan:
* Dokter (dr), dari Fakultas Kedokteran, USU. Medan
* Magister Sains (MS), Ilmu Kedokteran Dasar ('Basic Medical Sciences'), dari Fakultas Pascasarjana, Universitas Indonesia, Jakarta
* Doktor (Ph.D), Farmakologi Klinik ('Clinical Pharmacology'), dari Institute of Post-graduated Studies, Universiti Sains Malaysia, Malaysia
* Spesialis Farmakologi Klinik (Sp.FK), dari Dewan Penilai Kepakaran Persatuan Dokter Ahli Farmakologi Klinik Indonesia (PERDAFKI) Pusat, Jakarta.

“Evidence-Based Medicine” Therapy

Rozaimah Zain-Hamid

Community Research Program (‘KBK’)
Faculty of Medicine
Universitas Sumatera Utara



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"Evidence-Based Medicine"
(Papers in Journal of Medicine / Health Sciences)

'VIA'

- 'Valid' ➔ Methodology of study
- 'Important' ➔ Result of study
- 'Applicability' ➔ Discussion

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Treatment / Therapeutic intervention

EBM : Valid, important and applicable to particular patients

High rank of hierarchy of evidence

(Systematic reviews /meta-analyses; Randomized Controlled clinical trial / RCT)

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Treatment / Therapeutic intervention

Answerable Clinical Question (ACQ)

P : Patient, Problem, Population
I : Intervention
C : Comparison
O : Outcome

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Hypertensive patient – should I start ACE inhibitors?

- Patient : middle aged man with diastolic 100 mm Hg
- Intervention : ACE inhibitors
- Comparison : Diuretics
- Outcome : prevent heart disease; stroke; end-organ damage?

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“EBM” for therapy

1. Reports of individual studies
2. Reports of systematic reviews (‘RCT’)
3. Reports of Clinical Decision Analyses (CDA)
4. Reports of economic analyses
5. Reports of qualitative study

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Integrative literature

Review article :
* unsystematic

Systematic review :
* in gathering, evaluating, presenting evidence
* no formal statistical method

Meta-analysis :
* systematic review + formal statistical analysis

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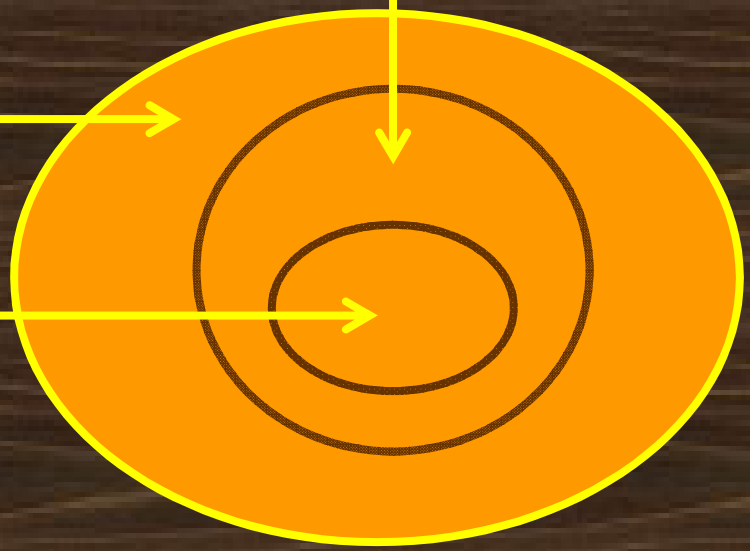
Integrative literature

Review article

Systematic review



Meta-analysis

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Reports of individual studies

High rank of hierarchy of evidence
(Randomized Controlled clinical trial / RCT)

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Key elements of RCT

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Reports of individual studies

1. Are the results of individual studies valid?

2. Are the valid results of individual studies, important?

3. Are the valid, important results of individual studies; applicable to our patient?

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‘Validity’ of individual studies

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1. Are the results of individual studies, valid?

Primary guides:

1. 1. Was the assignment of patients to treatments randomized?

1. 2. Was follow-up of patients sufficiently long and complete?

1. 3. Were patients analyzed in the groups to which they were randomized?

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1.1. Was the assignment of patients to treatments randomized?

- Simple randomization (

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1. 2. Was follow-up of patients sufficiently long and complete?

Lost to follow up no more than 20%

Journals like Evidence-Based Medicine and ACP Journal Club won't publish trials with > 80% follow-up.

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1. 3. Were patients analyzed in the groups to which they were randomized?

"ntention to treat analysis"

All patients are analyzed in the groups to which they were initially assigned

A strategy for analyzing data in which all participants are included in the group to which they were assigned, whether or not they completed the intervention given to the group.

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1. Are the results of the study valid?

Secondary guides:

. . Were patients, health workers, and study personnel "blind" to treatment?

. . Aside from the experimental intervention, were the groups treated equally?

1. 6. Were the groups similar at the start of the trial?

1. 7. Was the randomization concealed?

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1. 4. Patients, health workers, and study personnel "blind" to treatment?

-
- Double blind
- Triple blind

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‘lind’

Similar:

- Form
-
-
-

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CLINICAL TRIAL DESIGNS

1.❖ PARALLEL DESIGN TWO GROUPS :

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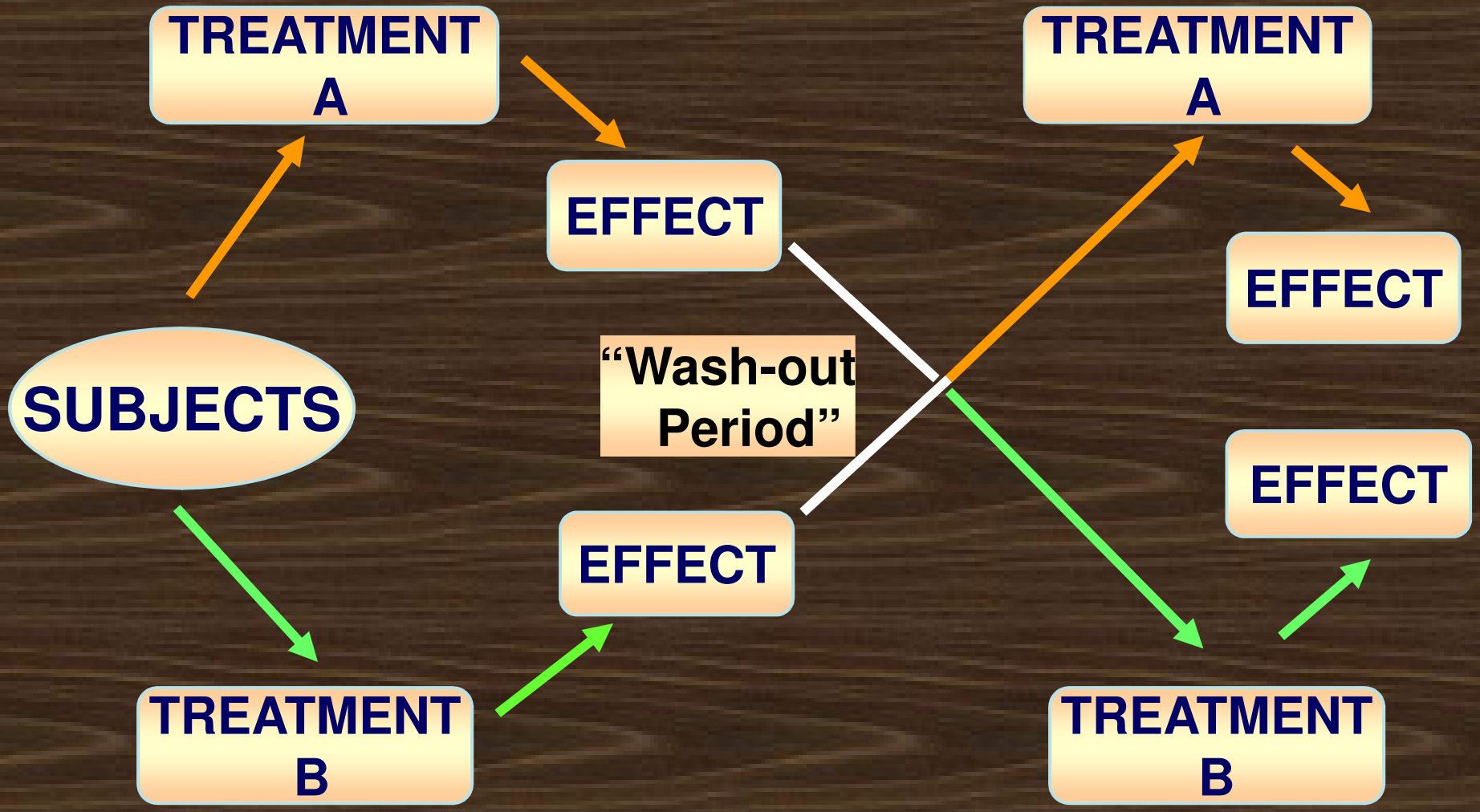
2. ❖ CROSS-OVER DESIGN :



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‘Important’ of individual studies

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2. Elements of important of the treatment effect

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1.2. 1. Elements of magnitude of the treatment effect

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- RRR = {(CER – EER) / CER}

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2. 1. Elements of magnitude of the treatment effect

- RRR = {(CER – EER) / CER}
  RRR = (5.7% – 4.3%) / 5.7% = 25%

↓

Statin therapy decreased the risk of stroke by 25% relative to those who receive placebo

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2. 1. Elements of magnitude of the treatment effect

The situation in which the experimental treatment increase the risk of a good event as the 'Relative Benefit Increase (RBI)' or the risk of bad event as 'Relative Risk Increase(RRI)

also can use the same formula →(RRR):

RRR = RBI = RRI = {(CER – EER) / CER}

RRR = RBI = RRI =(5.7% – 4.3%) / 5.7% = 25%

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2. 1. Elements of magnitude of the treatment effect

- **Relative Risk Reduction (RRR) :**
  is the percent reduction in risk in treated group compared to the control group

- **The RRR is measure of how the treatment studied has reduced the frequency of an adverse event**

- **Absolute Risk reduction (ARR):**
  is the difference in risk between the control group and the treatment group

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2. 1. Elements of magnitude of the treatment effect

The situation in which the experimental treatment increase the risk of a good event as the 'Absolute Benefit Increase (ABI)' or the risk of bad event as 'Absolute Risk Increase(ARI)

also can use the same formula →(ARR):

ARR = ABI = ARI = (CER – EER)

ARR = ABI = ARI =(5.7% – 4.3%) = 1.4%

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Significance of Relative Risk Reduction

- **Negative RRR (- 38%): treatment may do harm: patients given the new treatment might be 38% more likely to die than the control patients**
- **RRR of 0%: no treatment effect or benefit**
- **Positive RRR (50%): patients receiving the new treatment might have less than 1/2 risk of dying compared to not treated**

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2.1. Element of magnitude of the treatment effect

The greater the relative risk reduction the more effective the therapy (>>> RRR→↑↑↑ efficacy of therapy)

$$RRR = \{(CER - EER) / CER\}$$

CER : Control Event Rate (without treatment/placebo)

EER : Experimental Event Rate (with treatment)

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2. 1. Elements of magnitude of the treatment effect

- **Number Needed to Treat (NNT) :**

- **Number Needed to Harm (NNH) :**

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2. 1. Elements of magnitude of the treatment effect

- **Number Needed to Treat (NNT) = 1 / ARR**
  - *** NNT = 1 / 1.4% = 72**

↓

we need to treat 72 people with a statin (rather than placebo) for 5 years to prevent one additional person from suffering a stroke

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Therapy / treatment - case study

A randomized double blind control clinical trial on 3 month – 5 year old children with mild to moderate croup (laryngotracheobronchitis).

The experimental group : 2 mg (4 ml) nebulized budesonide.

The control group : 4 ml nebulized normal saline.

Event being prevented : hospital admission due to upper-airway obstruction.

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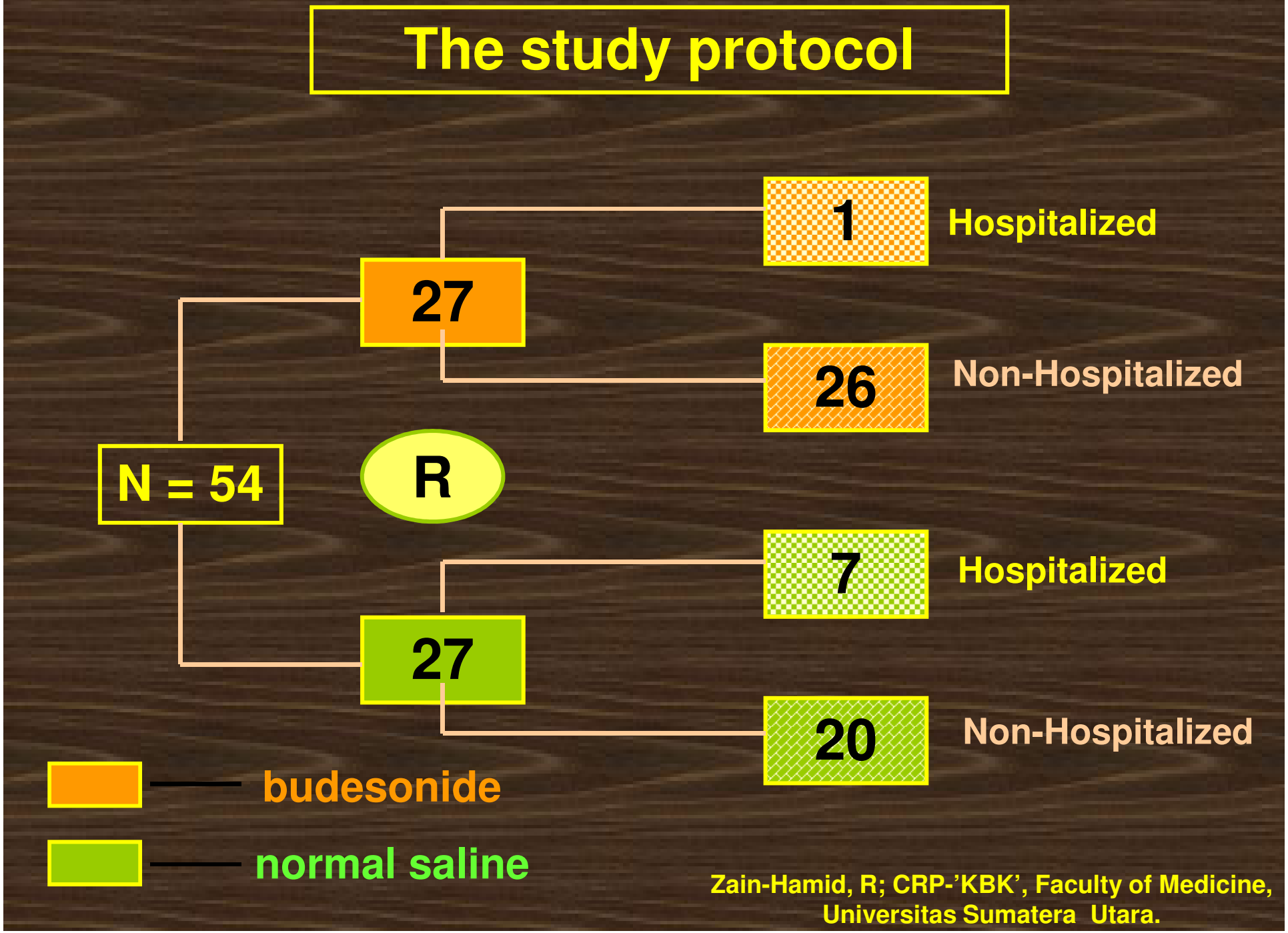
The study protocol



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Important

Upper-airway obstruction

	No	Yes	
Budesonide (E)	26	1	27
NaCl (C)	20	7	27

X^2 df =1 p = 0.04

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Important
Upper-airway obstruction

	No	Yes	
Budesonide (E)	26	1	27
NaCl (C)	20	7	27

CER = 7 / 27 = 0.26 ; EER = 1 / 27 = 0.04

RRR = (CER – EER) / CER
RRR = (0.26 – 0.04) / 0.26 = 85%

ARR = (CER – EER) = (0.26 – 0.04) = 0.22

NNT = 1 / ARR = 1 / 0.22 = 5

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Important

Budesonide vs normal saline; Upper-airway obstruction

	CER	EER	ARR	NNT
In the actual trial	26%	4%	22%	5
In the hypothetical trivial case	0.00026	0.00004	0.00022	5000

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2. 2. Elements for deciding precision of the treatment effect

♦ (<< CI → ↑↑ precission of the treatment effect)

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‘Applicability’ of individual studies

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Are the valid, important results of this individual studies applicable to our patient?

- Is our patient so different from those in the study that its results cannot apply?
- Is the treatment feasible in our setting?
- What are our patient's potential benefits and harms from the therapy?
- What are our patient's values and expectations for both the outcome we are trying to prevent and the treatment we are offering?

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Conclusions

- Application of good therapy must be supported by EBM

- Ability to appraise the results of many kind of studies, reviews, analyses etc

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Therapy Worksheet

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THERAPY WORKSHEET

Citation:

Are the results of this single preventive or therapeutic trial valid?

Was the assignment of patients to treatments randomized?	
Was the randomization list concealed?	
Was follow-up of patients sufficiently long and complete?	
Were all patients analyzed in the groups to which they were randomized?	

THERAPY WORKSHEET

Citation:	

Are the results of this single preventive or therapeutic trial valid?

Were patients, clinicians, and study personnel kept "blind" to treatment?	
Were the groups treated equally, apart from the experimental treatment?	
Were the groups similar at the start of the trial apart from the experimental therapy?	

THERAPY WORKSHEET

Are the valid results of this randomized trial important?

What is the magnitude of the treatment effect?	
How precise is the estimate of the treatment effect?	

SAMPLE CALCULATIONS

Occurrence of diabetic neuropathy at 5 years among insulin-dependent diabetics in the DCCT trial		Relative risk reduction (RRR)	Absolute risk reduction (ARR)	Number needed to treat (NNT)
Usual insulin Regimen control event rate (CER)	Intensive insulin regimen experimental event rate (EER)	$\frac{\text{CER} - \text{EER}}{\text{CER}}$ $\frac{9.6\% - 2.8\%}{9.6\%}$	CER – EER 9.6% – 2.8%	1/ARR 1/6.8% =15 patients
9.6 %	2.8 %	71 %	6.8 %	
		95% CI a	4.4% to 9.2%	11 - 23

a 95% confidence interval (CI) on an NNT =1/(limits on the CI of its ARR)

YOUR CALCULATIONS

		Relative risk reduction (RRR)	Absolute risk reduction (ARR)	Number needed to treat (NNT)
CER	EER	$\frac{\text{CER} - \text{EER}}{\text{CER}}$	CER – EER	1/ARR
		95% CI a		

THERAPY WORKSHEET

Can you apply this valid, important evidence about therapy in caring for your patient?

Do these results apply to our patient?	
Is our patient so different from those in the study that its results cannot apply?	
Is the treatment feasible in our setting?	

What are our patient's potential benefits and harms from the therapy?

Method I **: f**	**Risk of the outcome in our patient, relative to patients in the trial. Expressed as a decimal:_____** **NNT/ f =_____/_____=_____** **(NNT for patients like ours)**
Method II **:** **1/(PEER × RRR)**	**Our patient's expected event rate if they received the control treatment (PEER) =_____** **1/(PEER × RRR) = 1/_____=_____** **(NNT for patients like ours)**

THERAPY WORKSHEET

Are our patient's values and preferences satisfied by the regimen and its consequences?

Do we and our patient have a clear assessment of their values and preferences?	
Are they met by this regimen and its consequences?	

Additional notes: