

Study Design Workshop



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Retrospective Study

Design

- To study factors associated with development of congenital heart disease (CHD) in fetuses
- 200 women with first trimester spont AB in which CHD is identified on pathology
- Control group: induced 1st trimester AB with no CHD
- 100 Variables assessed by interview in 120/200 with CHD and 80 / 200 Controls

Findings

- CHD fetuses 3x more anti-nauseant exposure ($P < 0.05$)
- No difference in tranquilizer exposure
- CHD maternal age 23 vs. Control 18 yrs
- CHD coffee 3.7 cups/day vs Control 3.5 ($P < 0.05$)
- Of remaining 96 variables blonde hair and height $> 5'6''$ significantly associated with CHD

Conclusions

- Anti-nauseant drugs cause CHD
- Tranquillizers are safe
- Women should be encouraged to have children before age 20
- Coffee drinking should be avoided in pregnancy
- Unsuspected risk factors of height and hair colour were established

Dogs Aren't Often Allowed in Elevators

Design

Assignment

Outcome

Analysis

Interpretation


Extrapolation

Design

What Design?

- Was a Specific hypothesis stated
- Were study groups properly selected

Design

- Case / Control
- Fishing Expedition
- Design
 - 1) Assumes common etiology, CHD Septal Defects / Outflow Anomalies
 - 2) Only detects CHD severe enough to
  SpAB

Assignment

- Were Controls similar to Cases?
- What possible differences?

Assignment

Differences:

- Age
- Attitudes to pregnancy
- Drug /Alcohol exposure

Outcome

- How determined?
- Follow up rates satisfactory?
- Biases?

Outcome

- High “Lost to follow up”
 - Weakens conclusions
 - Fewer controls – supports different attributes
- Recall bias
 - SpAB highly emotional

Analysis

- Relationship CHD and anti-nauseants?
- Safety of Tranquillizers?
- Significance of height and hair colour?

Analysis

- Lack of cause – effect relationship
 - Cause precedes effect
 - Change Cause changes Effects
 - Dose / Response
 - Biological plausibility
- Tranquillizers used by a small “n”
 - Sample size
- Height / Hair colour
 - 100 Variables, Bonferonni Correction

Interpretation / Extrapolation

- Are tranquilizers safe?
- Should teen pregnancy be encouraged?
- Should coffee be avoided?

Interpretation / Extrapolation

- No proof of tranquillizer safety
- Teen pregnancy \Rightarrow benefits vs. risks
 - Common sense
- Coffee - Statistical vs. Clinical significance



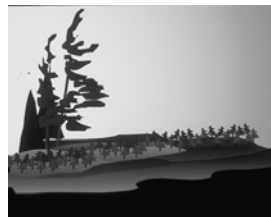
A J Casson's "White Pine"

Observation: Birders report observing most pileated woodpeckers sitting on white pine branches that point to the southeast.



The Question: Can I find the explanation for this?

Hypothesis: Maybe most white pine branches grow towards the SE making more perches for pileated woodpeckers on that side.



Expt: Planted 3000 seedlings, hired a starving medical resident to perform an annual survey

Observation: Branches grow equally on NW and SE sides

Conclusion: White pine branches growing preferentially to the SE is not the explanation

When Not to do a Prospective Study

- Rare conditions
- Long lag times

Observation: Branches on the pines in a nearby valley show random pattern of loss



Conclusion: Lightening strikes or the weight of snow must randomly break branches

Avoid Convenience Samples

Must limit extrapolation

Observation: Forestry reports indicate that most trees fall to the SE (note: Most woodpecker holes on the NW side and more tree branches on the SE side)

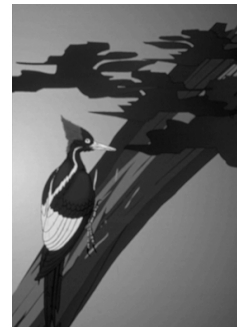


Conclusion: Woodpeckers destroy the branches on the NW side by drilling holes for their nests

Criteria for Cause / Effect

- Plausible
- Cause precedes effect
- Change Cause \implies Changes Effect
- Dose / Response

Observation: Saw a Pileated Woodpecker sitting on the NW side of a white pine tree:



Conclusion: Weight of the bird breaks off branches on the NW side

**When a cause elicits an effect
do not conclude that it is the
only possible cause**

Observation: Saw a NW wind break
a tree branch on the north
side of the pine



Conclusion: Fewer branches on the NW side due
to the prevailing NW wind in Ontario

Experiment: Paid medical resident to observe and document
every branch broken by the wind over an entire
summer

Observation: Rarely did the wind break branches
– certainly not enough to account for
the predominance of branches on
the NW side of the white pine trees

Conclusion: Wind was not the responsible factor

**Don't forget seasonal or period
effects**

Observation: More branches were broken
off the NW side over a cold windy winter

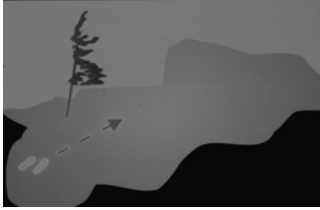


Conclusion: Cold weather – brittle branches
Snow – added stress
NW wind – breaks stressed branches



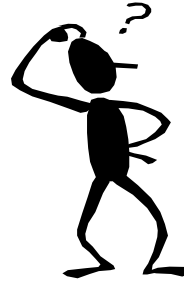
Conclusion: In Ontario white pine branches
point predominantly toward the SE due to
the fact that the prevailing NW winter wind
breaks the brittle snow laden branches
on the NW side!

Epilogue (Tragic)

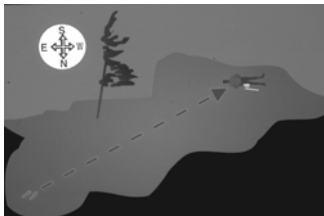


After all his experiments he became lost in the woods

Which way do I go ????



Epilogue (cont'd)



Three days later

Moral of the Story

Sample size too small for definitive conclusion on direction !!!

“In attempting to use pines to determine direction, do not trust a single tree. Pick a large sample and average the direction to pick the south easterly direction.”

