

# 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

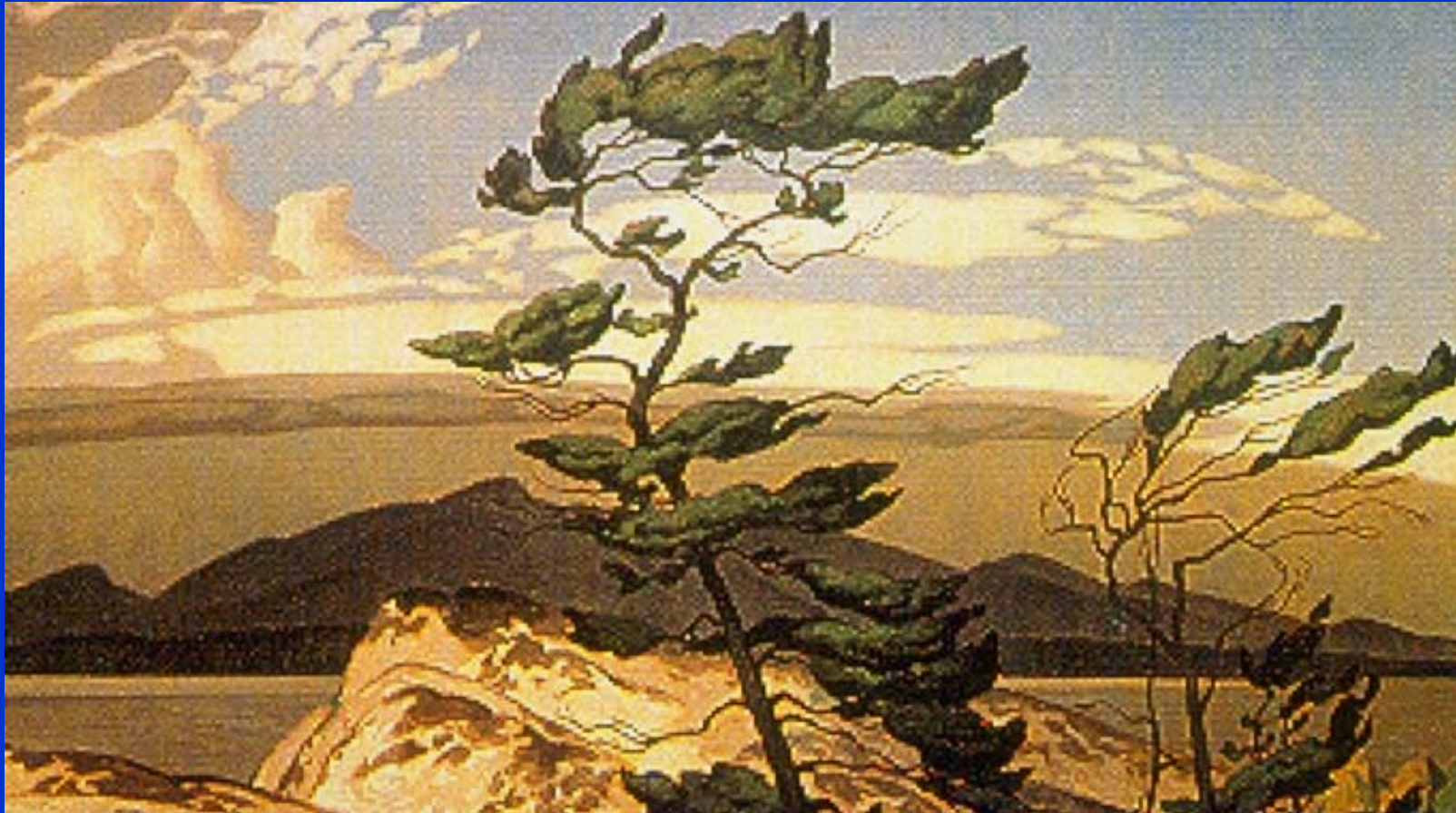
- Lack of **cause – effect** relationship
  - Cause precedes effect
  - Change Cause changes Effects
  - Dose / Response
  - Biological plausibility
- Tranquillizers used by a small “n”
  - **Sample size**
- Height / Hair colour
  - 100 Variables, Bonferonni Correction

# Interpretation / Extrapolation

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

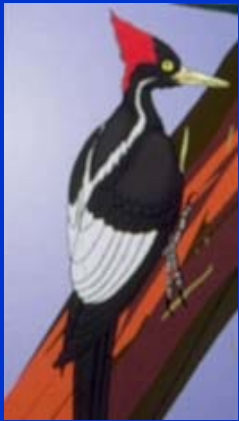
# Interpretation / Extrapolation

- No proof of tranquilizer safety
- Teen pregnancy  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  Changes Effect**
- **Dose / Response**

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

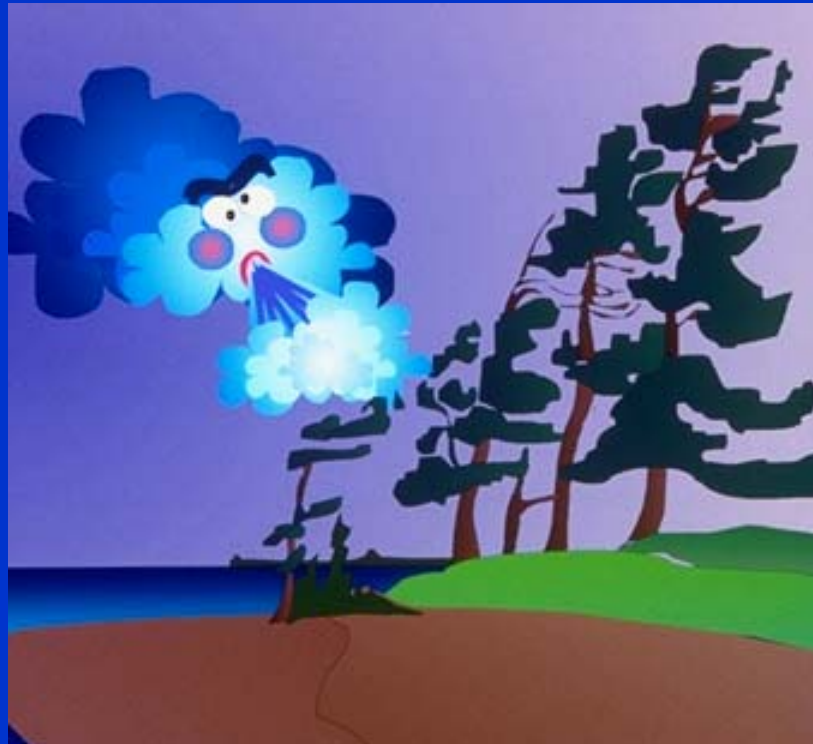


**Conclusion:** Weight of the bird breaks off branches on the NW side



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



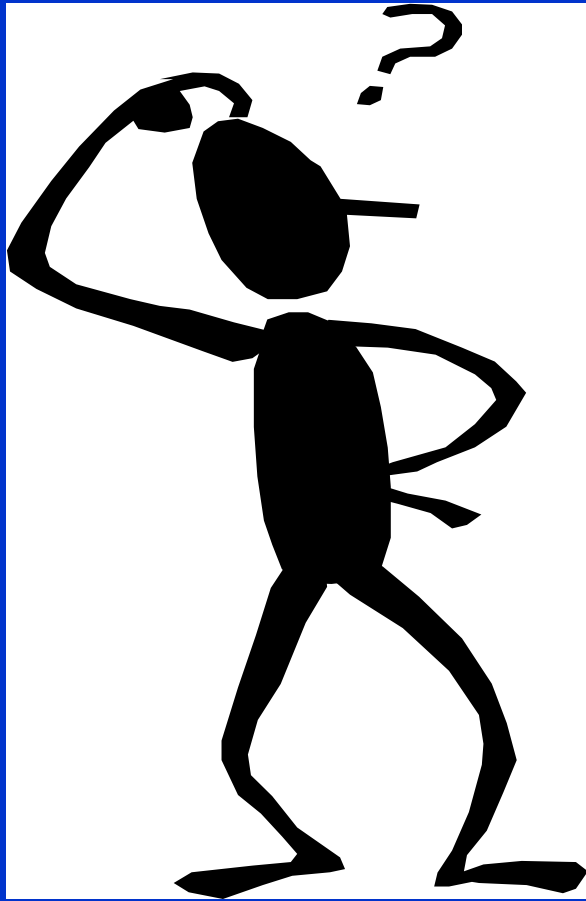
**Conclusion:** In Ontario white pine branches point predominantly toward the SE due to the fact that the prevailing NW winter wind breaks the brittle snow laden branches on the NW side!

# 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.”**

