AN ANALYSIS OF WHY THE FIRST SALK VACCINE TEST GAVE A FALSE CONCLUSION

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ABSTRACT

The reason that the first large-scale test of the Salk vaccine gave a false conclusion is well known. This note suggests an algebraic description of that conclusion.

In the first, 1954, Salk vaccine test, the only children vaccinated were those whose parents had consented to the vaccination program (see Cox, 1958). The incidence of illness (poliomyelitis - "polio") among those vaccinated was less than among other, non-vaccinated children, but nowhere near as much as expected: 25 per 10,000 compared to 44, a reduction in incidence of (1 - 25/44) = 43%.

The reason finally arrived at for this relatively low figure was that children from consenting families (consenters) come, on average, from higher socio-economic homes than those from non-consenting families, and hence have better hygiene and lower natural immunity to illness, and thus a higher incidence of illness. When this fact was taken into account in a second test, by randomly giving vaccine or a placebo to only consenter children, the reduction in incidence rose to (1 - 28/71) = 61%, which was much closer to what had been expected.

This note offers algebraic description of these results: two models (one a modification of the other) for the first test, and one for the second. These descriptions are contained in the four pages that follow.

Reference:

Cox, D.R. (1958). Planning of Experiments, Wiley, N.Y.

Table 1: Incidence of illness among consenters exceeds that among non-consenters. A simple model.

Number of children	N
Rate of consent:	c
Rate of illness:	s_1 (consenters) $>$ s_0 (non-consenters)
Among those who would become ill without vaccine, the fraction who would stay well with vaccine. Call it the "Stay Well" rate.	w

FIRST SALK TEST

	Consenters (vaccinated)	Non-consenters (not vaccinated)
Number in study	cN	$(1-c)N$
Number getting ill		
If no vaccination	$s_1 cN$	$s_0(1-c)N$
If vaccination	$(1-w)s_1 cN$	$s_0(1-c)N$
Observed incidence	$\frac{(1-w)s_1 cN}{cN} = (1-w)s_1$	$\frac{s_0(1-c)N}{(1-c)N} = s_0$
Effectiveness	$1-\frac{(1-w)s_1}{s_0} = w + (1-w)\left(1-\frac{s_1}{s_0}\right) < w \because s_0 < s_1$	

Table 2: Incidence of illness among consenters exceeds that among non-consenters. A more detailed model: differential rates of consent and illness for two socio-economic levels of families, with a fraction h in the higher level.

	Socio-economic level: Upper	Socio-economic level: Lower	
Number in study	hN	$(1-h)N$	
Fraction consenting	c_1	c_0	$c_1 > c_0$
Number of consenters	c_1hN	$c_0(1-h)N$	
Number of non-consenters	$(1-c_1)hN$	$(1-c_0)(1-h)N$	
Rate of illness	s_1	s_0	$s_1 > s_0$
"Stay well" rate	w		

	Consenters	Non-consenters
Number in study	$[c_1h + c_0(1-h)]N$	$[(1-c_1)h + (1-c_0)(1-h)]N$
Number getting ill		
If no vaccination	$[s_1c_1h + s_0c_0(1-h)]N$	$[s_1(1-c_1)h + s_0(1-c_0)(1-h)]N$
If vaccination	$(1-w)[s_1c_1h + s_0c_0(1-h)]N$	$[s_1(1-c_1)h + s_0(1-c_0)(1-h)]N$
Observed incidence	$i_1 = \frac{(1-w)[s_1c_1h + s_0c_0(1-h)]}{c_1h + c_0(1-h)}$	$i_0 = \frac{s_1(1-c_1)h + s_0(1-c_0)(1-h)}{(1-c_1)h + (1-c_0)(1-h)}$
	$= (1-w)n_1/d_1$, say	$= n_0/d_0$, say

Effectiveness

$$1 - \frac{i_1}{i_0} = 1 - (1-w)\,\frac{n_1}{d_1}\,\frac{s_0}{n_0}$$

$$= w + (1-w)\left(1 - \frac{n_1d_0}{n_0d_1}\right)$$

$< w \because n_0d_1 < n_1d_0$, is shown in Table 3

Table 3: Algebra substantiating Table 2:

that $n_0 d_1 < n_1 d_0$; and so $1 - \frac{i_1}{i_0} < w$.

$$n_0 d_1 - n_1 d_0 = [s_1(1-c_1)h + s_0(1-c_0)(1-h)]\,[c_1 h + c_0(1-h)]$$

$$- [s_1 c_1 h + s_0 c_0 (1-h)]\,[(1-c_1)h + (1-c_0)(1-h)]$$

$$= h^2[s_1(1-c_1)c_1 - s_1 c_1(1-c_1)] + (1-h)^2[s_0(1-c_0)c_0 - s_0 c_0(1-c_0)]$$

$$+ h(1-h)[s_1(1-c_1)c_0 + s_0(1-c_0)c_1 - s_1 c_1(1-c_0) - s_0 c_0(1-c_1)]$$

$$= h^2(0) + (1-h)^2 + h(1-h)[s_1(c_0 - c_1) + s_0(c_1 - c_0)]$$

$$= h(1-h)(s_1 - s_0)(c_0 - c_1)$$

$$< 0 \quad \because \quad s_1 > s_0 \quad \text{and} \quad c_1 > c_0 .$$

Therefore

$$n_0 d_1 < n_1 d_0 .$$

Hence

$$1 - \frac{i_1}{i_0} = w + (1-w)\left(1 - \frac{n_1 d_0}{n_0 d_1}\right) < w .$$

Table 4: Estimating effectiveness of the vaccine by administering vaccine or placebo in a double-blind manner to consenters only.

SECOND SALK TEST

	Consenters	
	Vaccinated	Not Vaccinated
Number in study	$\frac{1}{2}cN$	$\frac{1}{2}cN$
Number getting ill		
If no vaccination	$\frac{1}{2}scN$	$\frac{1}{2}scN$
If vaccination	$(1-w)\frac{1}{2}scN$	
Observed incidence	$\frac{(1-w)\frac{1}{2}scN}{\frac{1}{2}cN}$	$\frac{\frac{1}{2}scN}{\frac{1}{2}cN}$
	$=(1-w)s$	$=s$
Effectiveness	$1-\frac{(1-w)s}{s}$	
	$=w\ .$	