

UNIVERSITY OF PITTSBURGH
GRADUATE SCHOOL OF PUBLIC HEALTH
DEPARTMENT OF BIostatISTICS

Mail Address: 9650 Rockville Pike
Bethesda, Maryland 20014

Telephone: (301) 530-6092

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Dr. Christian R. Klimt
Department of Epidemiology and Biostatistics
University of Maryland
660 West Redwood Street
Baltimore, Maryland 21201

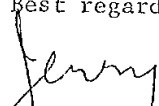
Dear Chris:

Enclosed are tables summarizing the relative betting odds (rbo) calculated for the Williamsburg meeting. The minimum rbo for tolbutamide or phenformin over variation in the value of the alternative is underlined. The basis for the calculations is with one exception the same as that in note 4 of the memorandum of October 2, 1968 to the Safety Monitoring Committee and Data Analysis Committee of the Coronary Drug Project entitled Probabilistic Analysis of CDP Results: Problems and Proposals. The exception relates to the assumption made there that the placebo value was known. That assumption has been relaxed and the rbo's given reflect the full uncertainty of the placebo value as well. For your records a copy of the mathematics underlying this is enclosed as well as a listing of the BASIC program used for the tolbutamide clinics. A corresponding program for 4 rather than 3 drugs is available if you desire a copy.

The basis for my recommendation that tolbutamide be dropped is provided by the increasing excess mortality from cardiovascular disease shown in Table 10 and the corresponding decrease in the rbo values.

I should be happy to answer any questions that arise in connection with this.

Best regards,


Jerome Cornfield
Research Professor in Biostatistics

JC:scr

Enclosures

Tolbutamide clinics

Table 1, all deaths

Alternative ^{/1}	IVAR	ISTD	TOLB	PLCBO
	(7.4) ^{/2}	(9.0)	(14.2)	(9.3)
		RBO		
.15	.79	.94	.52	
.25	.88	1.11	<u>.42</u>	
.35	1.11	1.42	<u>.42</u>	
.50	1.56	2.03	.50	

Table 2, cardiovascular deaths

	(5.4)	(5.7)	(12.2)	(4.4)
.25	.80	.82	.088	
.35	1.00	1.02	.050	
.50	1.37	1.37	.035	
.75	2.05	2.01	.032	
.90	2.49	2.44	.035	

Table 3.1, 6 year survival, all deaths

	(7.63)	(8.22)	(12.59)	(10.26)
.10	.97	1.01	0.90	
.15	.99	1.05	<u>0.88</u>	
.25	1.16	1.28	0.96	
.35	1.47	1.64	1.16	

Table 3.1, 7 year survival, all deaths

	(8.90)	(12.14)	(18.77)	(10.26)
.25	.76	.99	.21	
.50	1.36	1.62	<u>.19</u>	
.75	2.13	2.47	.24	

Table 3.1, 8 year survival, all deaths

	(8.90)	(12.14)	(21.89)	(10.26)
.25	.62	.81	.077	
.50	1.15	1.32	<u>.039</u>	
.75	1.82	1.96	.040	

Table 10, 5 year survival, cardiovascular deaths

	(4.43)	(4.07)	(8.98)	(3.62)
.25	.93	.91	.33	
.50	1.37	1.34	<u>.21</u>	
.75	2.01	1.99	.22	

^{/1}Alternative = $\sqrt{\frac{2}{\pi}}$ x assumed st. dev. of prior

^{/2}Percentage deaths

Tolbutamide clinics (continued)

Table 10, 6 year survival, cardiovascular deaths

Alternative ^{/1}	IVAR	ISTD	TOLB	PLCBO
	(5.19)	(4.85)	(11.27)	(5.26)
.25	.83	.79	.22	
.50	1.32	1.27	<u>.13</u>	
.75	2.03	1.96	.14	

Table 10, 7 year survival, cardiovascular deaths

Alternative	IVAR	ISTD	TOLB	PLCBO
	(6.49)	(7.58)	(16.32)	(5.26)
.25	.75	.80	.052	
.50	1.31	1.29	.015	
.75	1.98	1.85	<u>.013</u>	
1.00	2.70	2.47	.014	

Table 10, 8 year survival, cardiovascular deaths

Alternative	IVAR	ISTD	TOLB	PLCBO
	(6.49)	(7.58)	(19.54)	(5.26)
.25	.66	.72	.017	
.50	1.25	1.26	.0025	
.75	1.90	1.82	.0016	
1.00	2.60	2.44	<u>.0015</u>	
1.25	3.35	3.10	.0016	

Phenformin clinics

Table 1, all deaths

Alternative	PHEN	IVAR	ISTD	TOLB	PLCBO
	(10.3)	(4.1)	(7.8)	(7.9)	(6.9)
.10	.95	.91	1.09	1.09	
.15	<u>.93</u>	.86	1.20	1.19	
.25	.98	.86	1.51	1.51	

Table 2, cardiovascular deaths

Alternative	PHEN	IVAR	ISTD	TOLB	PLCBO
	(8.3)	(2.7)	(6.5)	(6.6)	(2.8)
.25	<u>.82</u>	.89	1.26	1.24	
.35	.84	.98	1.49	1.46	

Table 3.1, 3 year survival, all deaths

Alternative	PHEN	IVAR	ISTD	TOLB	PLCBO
	(7.39)	(4.11)	(2.60)	(2.63)	(1.39)
.25	.64	1.11	1.08	1.08	
.35	.50	1.20	1.16	1.17	
.50	.38	1.39	1.34	1.35	
.75	<u>.32</u>	1.80	1.76	1.77	
.90	.32	2.10	2.09	2.10	
1.00	.33	2.33	2.33	2.34	

Phenformin clinics (continued)

Table 3.1, 4 year survival, all deaths

Alternative	PHEN	IVAR	ISTD	TOLB	PLCBO
	(9.00)	(4.11)	(2.60)	(4.03)	(2.85)
.25	.60	1.09	.98	1.08	
.50	.32	1.33	1.06	1.32	
1.00	.24	2.21	1.66	2.20	
1.10	.25	2.44	1.83	2.43	

Table 3.1, 5 year survival, all deaths

	(9.74)	(4.11)	(4.38)	(5.81)	(6.62)
.25	.70	1.15	1.21	1.41	

Table 3.1, 6 year survival

	(9.74)	(4.11)	(7.67)	(5.81)	(10.15)
.25	1.19	.89	1.46	1.29	

Table 3.1, 7 year survival, all deaths

	(15.85)	(4.11)	(16.47)	(21.83)	(10.15)
.25	1.14	.62	1.12	.77	

Table 10, 5 year survival, cardiovascular deaths

	(7.85)	(2.75)	(4.38)	(4.55)	(1.98)
.25	.69	1.07	1.19	1.18	
.35	.60	1.17	1.35	1.34	
.50	.55	1.40	1.67	1.66	
.75	.59	1.97	2.39	2.36	

Table 10, 6 year survival, cardiovascular deaths

	(7.85)	(2.75)	(7.67)	(4.55)	(5.68)
.25	1.08	.90	1.10	1.24	