Multiple Surrogates Validation

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Joint Modelling Results

S	UN_Assoc	ADJ_ASSOC	Lower_CI	Upper_CI	S_Trt	pval	pvaladj
18	0.90	0.83	0.56	0.94	0.52	0.00	0.04
29	0.82	0.57	0.11	0.83	0.40	0.00	0.01
6	0.29	0.56	0.10	0.83	-0.11	0.77	0.92
15	0.12	0.46	-0.05	0.78	-0.35	0.44	0.80
5	0.14	0.41	-0.11	0.75	-0.45	0.60	0.88
14	0.29	0.32	-0.21	0.70	0.19	0.65	0.88
24	-0.18	0.25	-0.28	0.67	-0.36	0.10	0.52
22	0.29	0.23	-0.30	0.65	0.24	0.48	0.80
17	0.27	0.19	-0.34	0.63	0.56	0.45	0.80
26	0.31	0.19	-0.34	0.62	0.35	0.34	0.78
9	0.33	0.15	-0.37	0.60	0.67	0.24	0.65
23	0.17	0.12	-0.40	0.58	0.23	0.66	0.88
2	-0.34	0.10	-0.42	0.57	-0.86	0.03	0.26
19	-0.22	0.10	-0.42	0.56	-0.93	0.17	0.58
13	0.44	-0.04	-0.52	0.47	0.61	0.01	0.11
28	0.31	-0.05	-0.53	0.46	0.66	0.08	0.51
30	-0.18	-0.06	-0.54	0.45	-0.52	0.51	0.80
25	-0.01	-0.08	-0.55	0.43	0.09	0.85	0.92
1	-0.23	-0.09	-0.56	0.42	-0.37	0.40	0.80
8	0.22	-0.10	-0.56	0.42	0.60	0.16	0.58
21	-0.03	-0.11	-0.58	0.41	0.10	0.86	0.92
16	-0.13	-0.12	-0.58	0.40	-0.08	0.77	0.92
3	-0.23	-0.12	-0.58	0.40	-0.35	0.43	0.80
7	-0.29	-0.13	-0.59	0.39	-0.34	0.31	0.77
12	-0.10	-0.14	-0.59	0.38	-0.01	0.96	0.96
20	-0.14	-0.19	-0.63	0.34	-0.06	0.93	0.96
11	-0.05	-0.22	-0.64	0.31	0.10	0.67	0.88
10	-0.20	-0.24	-0.66	0.29	-0.09	0.80	0.92
27	0.10	-0.31	-0.70	0.22	0.62	0.16	0.58
4	-0.52	-0.44	-0.77	0.07	-0.58	0.19	0.58

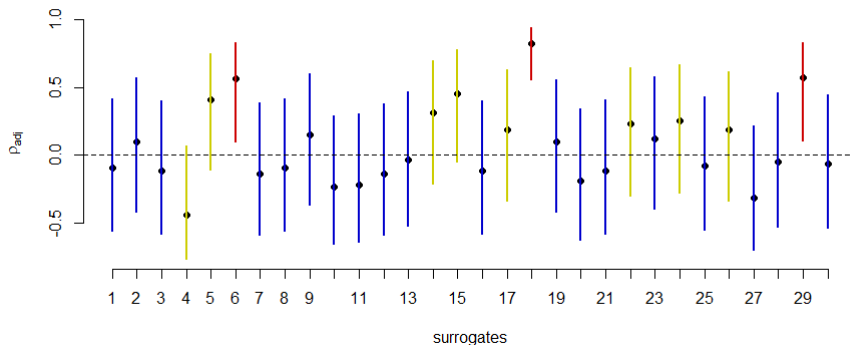# Joint Modelling Results Cont.

Figure 1: Adjusted Association Plot. Top 3 surrogates in red, next 7 including 4 in yellow and others in blue.

- Surrogates 6, 18 and 29 have the highest adjusted association, implying they are good surrogates by this approach.
- surrogate 4 appears to contain information not present in other surrogaes since its adjusted association and confidence interval goes entirely in the opposite direction.

Causal Inference Results

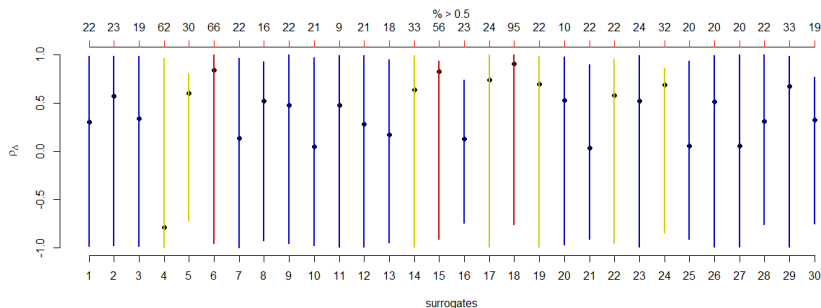| S	ρ_0	LCI0	UCI0	ρ_1	LCI1	UCI1	ICA	lR	UR
18	0.84	0.60	0.94	0.81	0.52	0.93	0.91	-0.76	1.00
6	0.57	0.11	0.83	0.56	0.10	0.83	0.84	-0.96	1.00
15	0.20	-0.33	0.63	0.79	0.49	0.93	0.83	-0.91	0.93
17	0.21	-0.32	0.64	0.14	-0.39	0.59	0.74	-1.00	1.00
19	0.00	-0.49	0.50	0.21	-0.32	0.64	0.70	-0.99	0.99
24	-0.10	-0.57	0.41	0.81	0.52	0.93	0.69	-0.85	0.86
29	0.85	0.60	0.95	-0.11	-0.57	0.41	0.67	-0.81	0.84
14	0.32	-0.21	0.70	0.32	-0.21	0.70	0.63	-0.99	1.00
5	-0.16	-0.60	0.37	0.88	0.67	0.96	0.60	-0.73	0.80
22	0.43	-0.09	0.76	-0.10	-0.57	0.42	0.58	-0.96	0.95
2	0.32	-0.21	0.70	-0.01	-0.50	0.49	0.57	-0.98	0.98
20	-0.51	-0.80	-0.02	0.73	0.37	0.90	0.53	-0.75	0.77
23	0.06	-0.45	0.54	0.30	-0.23	0.69	0.52	-0.99	0.98
8	-0.52	-0.81	-0.03	0.37	-0.15	0.73	0.52	-0.87	0.87
26	0.39	-0.14	0.74	-0.19	-0.63	0.34	0.51	-0.95	0.95
11	-0.57	-0.83	-0.10	0.70	0.32	0.89	0.48	-0.75	0.74
9	0.19	-0.34	0.63	0.01	-0.49	0.50	0.48	-0.99	0.99
3	0.20	-0.33	0.63	-0.38	-0.74	0.14	0.34	-0.94	0.94
30	0.28	-0.25	0.68	-0.28	-0.68	0.25	0.33	-0.95	0.95
28	0.02	-0.48	0.51	-0.23	-0.65	0.30	0.31	-0.99	0.99
1	0.01	-0.49	0.50	-0.24	-0.66	0.29	0.30	-0.99	0.98
12	-0.27	-0.67	0.26	0.09	-0.43	0.56	0.28	-0.97	0.98
13	0.29	-0.24	0.69	-0.50	-0.80	-0.00	0.17	-0.91	0.90
7	0.06	-0.45	0.54	-0.32	-0.70	0.21	0.14	-0.98	0.97
16	-0.10	-0.57	0.42	-0.15	-0.60	0.37	0.13	-0.99	0.99
25	0.18	-0.34	0.62	-0.47	-0.78	0.04	0.05	-0.93	0.93
27	-0.44	-0.77	0.07	0.16	-0.37	0.61	0.05	-0.95	0.95
10	-0.48	-0.79	0.02	0.18	-0.35	0.62	0.05	-0.93	0.94
21	0.12	-0.40	0.58	-0.47	-0.78	0.03	0.03	-0.95	0.94
4	-0.49	-0.79	0.01	-0.59	-0.84	-0.13	-0.79	-1.00	0.97

Causal Inference Results Cont:

Figure 2: ICA and Range plus percentage of ICA > 0.5

- Surrogates 6, 15 and 18 have the highest ICA values but 18 has the least range amongst these 3 surrogates.
- surrogate 4 appears to contain information not present in other surrogaes since its ICA values goes entirely in the opposite direction.

Multivariate Joint Modelling

Since surrogates 18 was promising, only a combination of surrogate 18 and other surrogates will be considered.

S	MAA	MAA_CLI	MAA_CLU	AMAA	AMAA_CLI	AMAA_CLU
18,22	0.77	0.55	0.99	0.73	0.49	0.98
18,4	0.75	0.52	0.99	0.71	0.45	0.98
18,6	0.75	0.52	0.99	0.71	0.45	0.98
18,26	0.72	0.47	0.98	0.68	0.39	0.97
18,5	0.71	0.45	0.98	0.67	0.37	0.96
18,19	0.71	0.44	0.98	0.66	0.37	0.96
18,14	0.70	0.43	0.97	0.66	0.36	0.96
18,29	0.70	0.43	0.97	0.66	0.36	0.96
18,17	0.70	0.43	0.97	0.66	0.36	0.96
18,15	0.69	0.40	0.97	0.64	0.32	0.95
18,24	0.69	0.40	0.97	0.64	0.32	0.95

Table 1: Adjusted and Multivariate Adjusted Association ranked by MAA values

- surrogates (18,6), (18,4) and (18,22) are the top 3 bivariate surrogates
- surrogates 6, 4 and 22 added some more information to surrogate 18, since the ρ^2_{adj} increased from 0.689 in the univariate case(i.e. 18 alone) to 0.77, 0.75 and 0.75 respectively.
- the uncertainty about these three bivariate surogates appears to be within the same range(see plot on the next slide).

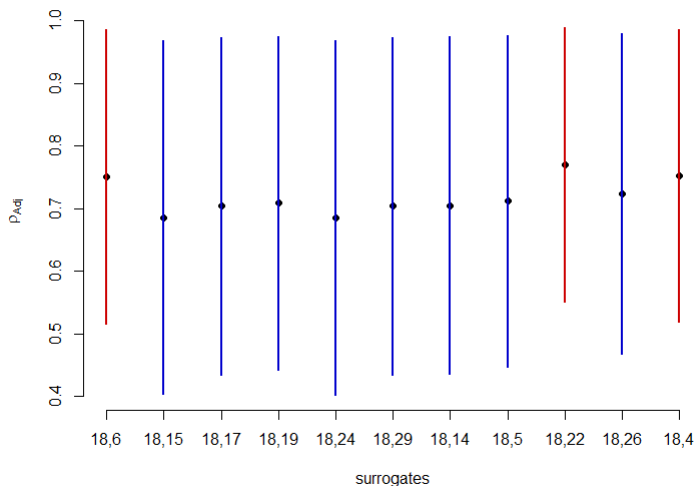# Multivariate Adjusted Association(Cont:)

Figure 3: Multivariate Adjusted Association, top 3 in red.

Multivariate Causal Inference

S	MMICA	lower_MMICA	upper_MMICA	MAMICA	lower_MAMICA	upper_MAMICA
S18,S22	0.83	0.17	0.96	0.80	0.04	0.95
S18,S6	0.81	0.22	0.98	0.78	0.09	0.98
S18,S5	0.80	0.32	0.97	0.77	0.22	0.97
S18,S4	0.79	0.42	0.97	0.76	0.33	0.97
S18,S29	0.78	0.30	0.97	0.74	0.19	0.97
S18,S19	0.76	0.23	0.99	0.73	0.12	0.98
S18,S14	0.76	0.14	0.97	0.73	0.00	0.97
S18,S17	0.76	0.13	0.96	0.72	-0.01	0.95
S18,S26	0.75	0.29	0.98	0.71	0.19	0.97
S18,S15	0.75	0.21	0.97	0.71	0.09	0.97
S18,S24	0.72	0.24	0.97	0.67	0.13	0.96

Table 2: MMICA and Range

- addition of other surrogate 22 improved ICA value for surrogate 18 but the range of the bivariate surrogates 18 and 22 is more than the other top bivariate surrogates
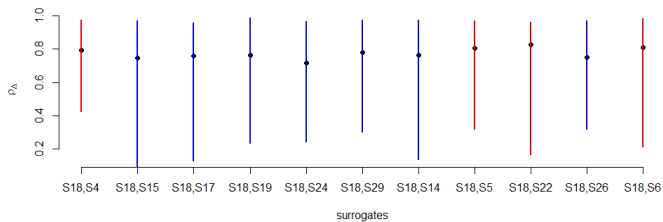- again surrogate 4 improves surrogates 18 by narrowing down the range of ICA values compared to addition of other surrogates to surrogate 18.

MICA Plots

Figure 4: ICA and Range plus