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Exploratory Analysis for an Ordered Series of a Dichotomous Attribute: Airborne Radiation and Congenital Hypothyroidism of California Newborns

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Confirmatory hypothesis-testing methodology was recently demonstrated with an example assessing the effect of airborne beta nuclear radiation emanating from the Fukushima nuclear meltdown on the risk of confirmed congenital hypothyroidism (CH) for newborns in California in the years 2011-2012. Eyeball inspection of the data suggests that the *a priori* hypothesis which was evaluated is inconsistent with the actual data, so an exploratory analysis is conducted.

Data are from research investigating the effect of increased airborne radiation originating from the Fukushima nuclear meltdown on risk of congenital hypothyroidism (CH) for California newborns in 2011-2012.[1] Original research used an approximate method to test the hypothesis that newborns in two time periods reflecting exposure to airborne radiation had higher CH rates than newborns in four time periods without exposure, for borderline CH, and for confirmed *plus* borderline CH. Exact analysis revealed that combining borderline and confirmed data would induce paradoxical confounding.[2] The *a priori* hypothesis was supported for the confirmed cases, but effect strength was minutely greater than expected by chance. Eyeball examination of confirmed data (Table 1) suggests a different pattern than was hypothesized underlies CH rate data: 2011 has high, relatively homogeneous rates through June (class 1 and 2); rate is highest in the latter half of 2011 (class 3); the rate in the latter half of 2012 is lowest (class 6); and rates for the first half of 2012 are homogeneous and intermediate (classes 4 and 5).

Table 1: Data for *Confirmed* CH of Newborns in California

Dates	1/1-3/16/2011	3/17-6/30/2011	7/1-12/31/2011	1/1-3/16/2012	3/17-6/30/2012	7/1-12/31/2012
Class Code	1	2	3	4	5	6
n Class=1	69	94	200	63	88	144
Total *n*	99,953	142,592	252,874	99,122	138,529	259,056
% Class=1	0.0690	0.0659	0.0791	0.0636	0.0635	0.0556

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Optimal Range Test

The *post hoc* hypothesis that CD rate differed between the six time-based classes is tested using MegaODA software (the sample is too large for UniODA software).[3-7] Data are ordered over time but they can't be ipsatively standardized because the data in each time period are presented as a scalar, so the entire data sample would be reduced to only six time-ordered data points.[8-14]

An ASCII data set (nuclear.dat) was constructed in which every observation formed a separate row.[15] Data were *datecode* (dummy-coded as 1-6, see Table 1) and *confirm* (dummy-coded as 1 if thyroid stimulating hormone >29 µIL/ml, and as 0 otherwise).[1] The *post hoc* hypothesis was tested by running the following MegaODA[3] analysis (commands are indicated in red). The Monte Carlo simulator is set for one test of a statistical hypothesis with experimentwise $p<0.05$.

```
OPEN nuclear.dat;
OUTPUT nuclear.out;
VARS datecode confirm;
CLASS confirm;
ATTR datecode;
CAT datecode;
MC ITER 25000 TARGET .05 SIDAK 1
    STOP 99.9 STOPUP 99.9;
GO;
```

The resulting model was statistically marginal: estimated $p<0.059$, confidence for $p<0.10$ is >99.99%; ESS=5.3; ESP=0.02. The omnibus *post hoc* ODA model is mapped using symbolic representation:

(1,3) $\underline{\geq}$ (2,4,5,6),

where $\underline{\geq}$ indicates marginal significance, and commas within parentheses are relationships to be disentangled—replaced by (in)equality signs on the basis of an optimal range test.[16,17]

The left-hand parentheses of the symbolic representation is disentangled by excluding classes 2, 4, 5, and 6; parameterizing the MC simulator for 2 tests of statistical hypotheses; and running the MegaODA program.[16,17] The resulting model was not statistically significant (exact $p<0.34$; ESS=2.7; ESP=0.01). The symbolic representation is updated:

(1=3) $\underline{\geq}$ (2,4,5,6).

The right-hand parentheses of the symbolic representation is disentangled by excluding classes 1 and 3, parameterizing the MC simulator for 3 tests of statistical hypotheses, and running the MegaODA program. The resulting model was not statistically significant (estimated $p<0.47$, confidence for $p>0.10$ is >99.99%; ESS=3.5; ESP=0.01). Symbolic representation is completed:

(1=3) $\underline{\geq}$ (2=4=5=6).

For California newborns the confirmed CH rate immediately before the Fukushima catastrophe was comparable to the CH rate in the final six months of 2011. During these times the confirmed CH rate was marginally greater than the CH rate measured in the other time periods (which were statistically comparable).

Forward-Stepping Little Jiffy

The *post hoc* hypothesis that CD rate differed between successive time-based classes is tested using a forward-stepping little jiffy analysis with a bin-width of two periods.[18-20] This analysis is efficiently accomplished using the special-purpose TABLE command in both UniODA and MegaODA software[3] as indicated below for the first comparison between class codes 1 and 2 (control commands are in red).[2]

```
OPEN DATA;
OUTPUT jiffy.out;
CAT ON;
```

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```
TABLE 2;
CLASS ROW;
DATA;
99884 69
142498 94
END DATA;
GO;
```

Monte Carlo (MC) simulation is not used because exact *p* is given for purely binary problems.[2,3] Because a total of five tests of statistical hypotheses will be conducted, the criterion for experimentwise $p<0.05$ is per-comparison $p<0.01021$.[3] Table 2 presents the findings of this analysis (*p* are two-tailed).

Table 2: Comparing Confirmed CH Rates Between Successive Time Periods

Times Compared	Exact *p*<	ESS	ESP
1 *vs*. 2	0.82	0.00	1.12
2 *vs*. 3	0.17	0.01	4.09
3 *vs*. 4	0.14	0.02	4.21
4 *vs*. 5	0.99	0.00	0.01
5 *vs*. 6	0.35	0.01	3.09

The effects summarized in Table 2 have among the weakest ESS and ESP values ever observed in the ODA laboratory for large real-world data. The period-over-period comparison of 4 *vs*. 5 is *the* weakest effect yet observed in the laboratory for a large sample of real-world data. Considered as a whole, exploratory findings are weaker than the meager confirmatory results, and are at best marginally significant.

These findings do *not* suggest that this avenue of investigation is unproductive and should be abandoned, but rather the opposite conclusion seems warranted. One should be mindful that the nuclear disaster in Japan is still unfolding, and recall that the first articles on AIDS consisted of collections of a handful of case reports. For future research to be rid of paradoxical confounding, the CH rate and radiation data must be assessed using a more sensitive time period with a fixed interval: weekly or monthly. Real-time monitoring is optimal, of course.

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