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TECHNICAL REPORT

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TITLE: Statistical analysis of interlaboratory studies. XXVII. Calculation of dPOD and 95% confidence interval for two microbiological methods compared on paired test portions.

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ABSTRACT: Formulas are given for estimating the difference dPOD in detection probabilities for two quantal methods, and an associated approximate 95% confidence interval, when the methods are matched on test portions. Coverage accuracy for the confidence interval was investigated by simulation and found to be excellent when N = 12 replicates or more are used.

KEYWORDS: 1) QUANTAL 2) dPOD 3) PAIRED

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INTRODUCTION

Sometimes it is possible to compare a candidate and reference method using the same test portions ("paired replicates"). This typically requires a common enrichment step so that aliquots of the enrichment broth can be used with both methods. Pairing (or "matching") of test portions removes the stochastic component of the presence of one or more CFU of the analyte, if the concentration averages below 5 CFU/test portion, resulting in a more precise estimate of the difference in proportion detected ("dPOD") of the two methods. For this to happen, the results of the two methods must be positively correlated.

RECOMMENDATIONS

Let a series of N replicate test portions be tested, each by both the candidate and reference methods. Let x_{1k} denote the result for the candidate method on test portion k = 1,2,..., N, and x_{2k} denoted the result for the reference method. The values of x_{1k} and x_{2k} will be either "1", denoting a positive result, or "0" denoting a negative result.

Let

$$d_k = x_{1k} - x_{2k} \qquad (1)$$

denote the numerical difference of the two method results on test portion k. Note that d_k must take on only the values –1, 0 or +1.

The recommended method for estimating dPOD is the mean of differences d_k:

$$\text{dPOD} = \Sigma\, d_k / N \qquad (2)$$

The recommended approximate 95% confidence interval is the usual student-t based interval, with the standard error of dPOD computed in the usual manner from the replicate differences:

$$s_d = \sqrt{\{\Sigma\, [d_k - \text{dPOD}]^2 / (N - 1)\}} \qquad (3a)$$

$$SE_{dPOD} = s_d / \sqrt{N} \qquad (3b)$$

and

$$LCL = \text{dPOD} - t_c\, SE_{dPOD} \qquad (4a)$$

$$UCL = \text{dPOD} + t_c\, SE_{dPOD} \qquad (4b)$$

where t_c is the 97.5% quantile of the student-t distribution for N-1 degrees of freedom, and the 95% confidence interval is (LCL, UCL).

The degree of coverage accuracy for this approximate confidence interval should improve as N increases and the Central Limit Theorem forces the distribution of dPOD to become normal. Given the finite range of the d_k's, this will happen quickly, even for small N.

VALIDATION OF COVERAGE ACCURACY

Validation of coverage accuracy of this confidence interval was performed by simulation using 10,000 realizations for each case.

A case was specified by three parameters:

ρ_1 = True probability of detection by candidate method

ρ_2 = True probability of detection by reference method

r = Bivariate normal correlation (assumed positive)

For each case, each realization consisted of a set of N pairs (x_{1k}, x_{2k}) as the method results.

For each k = 1, 2, ..., N for each realization, a random pair of variates (z_1, z_2) was drawn from a bivariate normal distribution with unit variances and correlation r. The result x_{1k} for the candidate method was 1 if z_1 was less than the ρ_1 quantile of a univariate normal distribution, and 0 otherwise. Similarly for the value of x_{2k}. The correlation r in the bivariate normal distribution induces a correlation in the method results x_{1k} and x_{2k}. Only positive values for r were considered.

Table 1 summarizes the cases run, each of which is based on 10,000 realizations.

The results show:

1. For N = 6 replicates, coverage can drop to 0.73 for some cases.

2. For N = 9 replicates, coverage increases to 0.85+.

3. For N = 12 replicates, coverage generally is 0.93 or higher for all cases considered.

The coverage accuracy is very good with N = 12 replicates, and marginal with N = 9 replicates.

Table 1. Validation cases, each based upon 10,000 realizations.

N	rho1	rho2	r	p1ave	p2ave	r(1,2)	dPOD	sdPOD	LCL95	UCL95	Cover
6	0.1000	0.3000	0.0000	0.0996	0.3039	-0.0046	-0.2042	0.5114	-0.7406	0.3328	0.9107
6	0.1000	0.3000	0.2000	0.1015	0.3018	0.1582	-0.2003	0.4801	-0.7039	0.3038	0.8886
6	0.1000	0.3000	0.6000	0.0983	0.2989	0.4462	-0.2006	0.4113	-0.6319	0.2315	0.8249
6	0.1000	0.3000	0.8000	0.0996	0.2990	0.6180	-0.1994	0.3649	-0.5824	0.1836	0.7684
6	0.1000	0.3000	1.0000	0.1005	0.3043	0.6885	-0.2037	0.3438	-0.5644	0.1573	0.7405
6	0.2000	0.2000	0.0000	0.1999	0.1980	-0.0109	0.0019	0.5209	-0.5447	0.5485	0.9888
6	0.2000	0.2000	0.2000	0.1997	0.2029	0.1424	-0.0031	0.4813	-0.5082	0.5020	0.9930
6	0.2000	0.2000	0.6000	0.2003	0.2002	0.4727	0.0001	0.3678	-0.3859	0.3860	0.9981
6	0.2000	0.2000	0.8000	0.1994	0.1975	0.6540	0.0018	0.2836	-0.2958	0.2995	0.9992
6	0.2000	0.2000	1.0000	0.1989	0.1989	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
6	0.2000	0.4000	0.0000	0.2006	0.3976	-0.0035	-0.1970	0.6034	-0.8294	0.4371	0.9510
6	0.2000	0.4000	0.2000	0.2015	0.4002	0.1357	-0.1987	0.5640	-0.7898	0.3940	0.9369
6	0.2000	0.4000	0.6000	0.1957	0.3982	0.4125	-0.2024	0.4647	-0.6896	0.2857	0.8746
6	0.2000	0.4000	0.8000	0.2012	0.4046	0.5774	-0.2033	0.3993	-0.6223	0.2159	0.8115
6	0.2000	0.4000	1.0000	0.2008	0.4008	0.6937	-0.2000	0.3386	-0.5552	0.1555	0.7309
6	0.4000	0.4000	0.0000	0.3982	0.4001	-0.0007	-0.0019	0.6645	-0.6991	0.6956	0.9678
6	0.4000	0.4000	0.2000	0.3982	0.3998	0.1344	-0.0016	0.6148	-0.6469	0.6436	0.9787
6	0.4000	0.4000	0.6000	0.4036	0.3998	0.4280	0.0038	0.4776	-0.4975	0.5050	0.9933
6	0.4000	0.4000	0.8000	0.4014	0.4037	0.6041	-0.0023	0.3713	-0.3920	0.3873	0.9974
6	0.4000	0.4000	1.0000	0.4009	0.4009	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
6	0.4000	0.6000	0.0000	0.4010	0.6015	0.0034	-0.2004	0.6679	-0.8998	0.5020	0.9596
6	0.4000	0.6000	0.2000	0.3985	0.5985	0.1310	-0.2000	0.6201	-0.8498	0.4516	0.9509
6	0.4000	0.6000	0.6000	0.4034	0.6037	0.4076	-0.2002	0.5006	-0.7252	0.3255	0.8994
6	0.4000	0.6000	0.8000	0.3986	0.5988	0.5565	-0.2002	0.4227	-0.6438	0.2434	0.8338
6	0.4000	0.6000	1.0000	0.4012	0.5997	0.6957	-0.1985	0.3379	-0.5531	0.1561	0.7300
9	0.2000	0.2000	0.0000	0.2005	0.2008	-0.0002	-0.0004	0.5416	-0.4167	0.4159	0.9381
9	0.2000	0.2000	0.2000	0.2026	0.2005	0.1189	0.0021	0.5072	-0.3878	0.3920	0.9270
9	0.2000	0.2000	0.6000	0.1989	0.1984	0.4046	0.0005	0.4040	-0.3101	0.3110	0.8568
9	0.2000	0.2000	0.8000	0.1988	0.1999	0.5984	-0.0011	0.3162	-0.2441	0.2420	0.7434
9	0.2000	0.2000	1.0000	0.2008	0.2008	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
9	0.4000	0.4000	0.0000	0.3977	0.3990	-0.0026	-0.0013	0.6781	-0.5225	0.5199	0.9473
9	0.4000	0.4000	0.2000	0.4013	0.3994	0.1314	0.0019	0.6276	-0.4805	0.4843	0.9449

9	0.4000	0.4000	0.6000	0.3998	0.3997	0.4091	0.0001	0.5033	-0.3868	0.3870	0.9222
9	0.4000	0.4000	0.8000	0.3979	0.3990	0.5861	-0.0010	0.4023	-0.3103	0.3082	0.8596
9	0.4000	0.4000	1.0000	0.3998	0.3998	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
9	0.4000	0.5000	0.0000	0.4019	0.5007	0.0003	-0.0988	0.6868	-0.6267	0.4291	0.9442
9	0.4000	0.5000	0.2000	0.3992	0.5016	0.1253	-0.1024	0.6374	-0.5924	0.3875	0.9452
9	0.4000	0.5000	0.6000	0.4000	0.4992	0.4032	-0.0992	0.5141	-0.4944	0.2960	0.9374
9	0.4000	0.5000	0.8000	0.3992	0.4993	0.5759	-0.1002	0.4179	-0.4214	0.2210	0.8811
9	0.4000	0.5000	1.0000	0.4014	0.5009	0.8169	-0.0995	0.2319	-0.2778	0.0787	0.6137
9	0.5000	0.5000	0.0000	0.4987	0.4998	0.0067	-0.0012	0.6911	-0.5324	0.5301	0.9464
9	0.5000	0.5000	0.2000	0.4995	0.5041	0.1245	-0.0046	0.6446	-0.5001	0.4909	0.9458
9	0.5000	0.5000	0.6000	0.5017	0.4996	0.4093	0.0021	0.5147	-0.3935	0.3977	0.9310
9	0.5000	0.5000	0.8000	0.5011	0.5015	0.5879	-0.0004	0.4121	-0.3171	0.3164	0.8695
9	0.5000	0.5000	1.0000	0.4985	0.4985	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
12	0.1000	0.3000	0.0000	0.1001	0.2980	0.0083	-0.1978	0.5315	-0.5355	0.1398	0.9573
12	0.1000	0.3000	0.2000	0.1002	0.2987	0.1157	-0.1984	0.5080	-0.5212	0.1243	0.9582
12	0.1000	0.3000	0.6000	0.1000	0.3008	0.3640	-0.2008	0.4457	-0.4839	0.0824	0.9493
12	0.1000	0.3000	0.8000	0.1016	0.2994	0.5115	-0.1978	0.4023	-0.4534	0.0578	0.9304
12	0.1000	0.3000	1.0000	0.0983	0.2998	0.5841	-0.2015	0.3806	-0.4433	0.0404	0.9269
12	0.2000	0.2000	0.0000	0.1998	0.1993	0.0030	0.0006	0.5473	-0.3472	0.3483	0.9560
12	0.2000	0.2000	0.2000	0.1989	0.2007	0.1136	-0.0018	0.5147	-0.3289	0.3252	0.9539
12	0.2000	0.2000	0.6000	0.1989	0.1977	0.3846	0.0012	0.4192	-0.2651	0.2676	0.9767
12	0.2000	0.2000	0.8000	0.1981	0.1987	0.5739	-0.0006	0.3343	-0.2130	0.2118	0.9925
12	0.2000	0.2000	1.0000	0.2029	0.2029	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
12	0.2000	0.4000	0.0000	0.2007	0.3981	0.0008	-0.1974	0.6210	-0.5920	0.1972	0.9619
12	0.2000	0.4000	0.2000	0.1995	0.4008	0.1102	-0.2014	0.5858	-0.5735	0.1708	0.9635
12	0.2000	0.4000	0.6000	0.2013	0.4005	0.3703	-0.1992	0.4937	-0.5129	0.1145	0.9570
12	0.2000	0.4000	0.8000	0.2005	0.3996	0.5166	-0.1991	0.4316	-0.4733	0.0751	0.9446
12	0.2000	0.4000	1.0000	0.1973	0.3963	0.6245	-0.1991	0.3789	-0.4398	0.0417	0.9269
12	0.2000	0.6000	0.0000	0.2012	0.6016	-0.0025	-0.4004	0.6234	-0.7964	-0.0042	0.9505
12	0.2000	0.6000	0.2000	0.2002	0.5992	0.1087	-0.3990	0.5896	-0.7736	-0.0244	0.9558
12	0.2000	0.6000	0.6000	0.2004	0.5992	0.3109	-0.3987	0.5235	-0.7313	-0.0660	0.9628
12	0.2000	0.6000	0.8000	0.1996	0.5967	0.3957	-0.3971	0.4948	-0.7115	-0.0827	0.9672
12	0.2000	0.6000	1.0000	0.2021	0.6011	0.4154	-0.3990	0.4874	-0.7086	-0.0893	0.9641
12	0.4000	0.4000	0.0000	0.4015	0.4012	0.0039	0.0003	0.6822	-0.4331	0.4338	0.9520
12	0.4000	0.4000	0.2000	0.4014	0.3996	0.1233	0.0019	0.6366	-0.4026	0.4063	0.9509

12	0.4000	0.4000	0.6000	0.4009	0.4000	0.4029	0.0009	0.5154	-0.3265	0.3284	0.9593
12	0.4000	0.4000	0.8000	0.3970	0.4000	0.5849	-0.0031	0.4164	-0.2677	0.2615	0.9791
12	0.4000	0.4000	1.0000	0.4020	0.4020	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000
12	0.4000	0.6000	0.0000	0.4008	0.6001	-0.0026	-0.1993	0.6843	-0.6341	0.2354	0.9543
12	0.4000	0.6000	0.2000	0.3999	0.5999	0.1227	-0.2001	0.6380	-0.6054	0.2053	0.9585
12	0.4000	0.6000	0.6000	0.3993	0.6015	0.3830	-0.2022	0.5303	-0.5392	0.1347	0.9635
12	0.4000	0.6000	0.8000	0.4002	0.6008	0.5334	-0.2005	0.4552	-0.4897	0.0887	0.9497
12	0.4000	0.6000	1.0000	0.3983	0.5985	0.6626	-0.2003	0.3795	-0.4414	0.0408	0.9272
12	0.5000	0.5000	0.0000	0.5015	0.4996	0.0005	0.0018	0.6974	-0.4412	0.4449	0.9515
12	0.5000	0.5000	0.2000	0.5006	0.4974	0.1321	0.0031	0.6481	-0.4086	0.4149	0.9510
12	0.5000	0.5000	0.6000	0.4989	0.4990	0.4038	-0.0001	0.5270	-0.3350	0.3348	0.9609
12	0.5000	0.5000	0.8000	0.5010	0.5012	0.5890	-0.0002	0.4239	-0.2696	0.2691	0.9805
12	0.5000	0.5000	1.0000	0.4997	0.4997	1.0000	0.0000	0.0000	-0.0001	0.0001	1.0000

NOTES:

N: number of replicate test portions in set
rho1: ρ_1
rho2: ρ_2
r: bivariate normal correlation
p1ave: average of average x_{1k} values observed (POD_1)
p2ave: average of average x_{2k} values observed (POD_2)
dPOD: average of dPOD values for realizations
s_d: average standard deviation of d_k values across realizations
LCL95: average approximate 95% confidence interval lower limit
UCL95: average approximate 95% confidence interval upper limit
Cover: coverage for confidence interval (accurate is 0.950)