How to Asses Dose-Response Study Outcome: a Statistical Approach

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Statement of the Problem & Research Aim

Confidence interval are defines as an estimated range of values that is likely to include an unknown population parameter, this range being calculates from a given set of sample data. The confidence intervals are uses in experimental research as criterion of assessment of the trustworthiness or robustness of the finding.[1] It is well known that for low proportions, the lower confidence boundaries are frequently less than zero while for the proportions closer to the upper boundaries exceed one.[2,3] The main problem of the existent methods is represented by the inadequate coverage and inappropriate intervals.[3] The aim of the research was to develop an algorithm for calculation of exact confidence intervals based on the probability matrix.

Method

The binomial distribution has its origins and applications in the natural phenomena studies.[4] Carlton and Stansfield [5] defined very well the frame and limits of binomial distribution model relative to its application to the natural phenomena. A series of methods were proposed and are use for calculation of confidence interval limits.[6,7] Twelve methods were proposed and are used for assessment of confidence intervals.[8] The formula for probability calculation: $P_B(n,X,Y)=\frac{n!}{Y!(n-Y)!}\frac{X^Y(n-X)^{(n-Y)}}{n^n}$ was used in order to obtain the probability matrix. Starting from this matrix an algorithm for confidence intervals calculation has been developed and was applied. Five confidence intervals methods were assessed and compared with proposed one (NewAlg). Twelve evaluation methods are proposed (starting from five proposed in [7], extended to 12 in [8], one of them being corrected from [8] and another two being modified) for confidence intervals assessment.

Table 1. Assessment methods for confidence interval calculation methods (A take values of 0 and 1)

AvgOEA	StDOEA	SiDOEA	AvADAA	AvADSA	S8DOEA
$\left\lvert 100\alpha-\sum_{X=A}^{n-A}\frac{\varepsilon^{M}_{X,n}}{n+1-2A}\right\rvert$	$\sqrt{\sum_{X=A}^{n-A}\frac{(\varepsilon^{M}_{X,n}-AvgOEA)^2}{n-2A}}$	$\sqrt{\sum_{X=A}^{n-A}\frac{(\varepsilon^{M}_{X,n}-100\alpha)^2}{n+1-2A}}$	$\sum_{X=A}^{n-A}\frac{\lvert\varepsilon^{M}_{X,n}-AvgOEA\rvert}{n-2A}$	$\sum_{X=A}^{n-A}\frac{\lvert\varepsilon^{M}_{X,n}-100\alpha\rvert}{n+1-2A}$	$\sqrt[8]{\sum_{X=A}^{n-A}\frac{(\varepsilon^{M}_{X,n}-100\alpha)^8}{n+1-2A}}$

Results

The proposed probability matrix, exemplified for a sample size of 30 is presented in Table 2. The upper and the lower limits as well as the cumulated experimental errors for six methods (one being new proposed - NewAlg), five being selected from the literature for comparison: Wilson_N (normal Wilson's formula), Logit_C (continuity corrected Logit formula), BetaCJ0 (Jeffrey's formula), Blyth-Still-Cassella (B-S-C), and OptiBin (an optimized one, see [8]).

Table 2. Proposed method: probability matrix (n = 30)

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	Err
0	100	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	36.17	37.41	18.71	6.02	1.40	0.25	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.69
2	12.62	27.05	28.01	18.67	9.00	3.34	1.00	0.24	0.05	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.64
3	4.24	14.13	22.77	23.61	17.71	10.23	4.74	1.80	0.58	0.16	0.04	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.58
4	1.37	6.31	14.07	20.20	20.98	16.78	10.76	5.67	2.51	0.94	0.30	0.09	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.87
5	0.42	2.53	7.33	13.68	18.47	19.21	16.01	10.98	6.31	3.09	1.30	0.47	0.15	0.04	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.92
6	0.12	0.93	3.37	7.85	13.25	17.23	17.95	15.38	11.06	6.76	3.55	1.61	0.64	0.22	0.07	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.61
7	0.03	0.32	1.39	3.95	8.12	12.85	16.29	17.00	14.88	11.07	7.07	3.91	1.89	0.79	0.29	0.10	0.03	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.85
8	0.01	0.10	0.52	1.78	4.36	8.25	12.49	15.58	16.28	14.47	11.05	7.31	4.21	2.12	0.94	0.36	0.12	0.04	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.22
9	0.00	0.03	0.18	0.72	2.08	4.64	8.29	12.19	15.01	15.73	14.16	11.03	7.49	4.44	2.31	1.06	0.42	0.15	0.05	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.94
10	0.00	0.01	0.06	0.26	0.89	2.32	4.84	8.29	11.92	14.57	15.30	13.91	11.01	7.62	4.63	2.47	1.16	0.48	0.17	0.05	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.27
11	0.00	0.00	0.02	0.09	0.34	1.04	2.50	4.97	8.27	11.70	14.23	14.98	13.73	11.00	7.74	4.78	2.59	1.24	0.52	0.19	0.06	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.78
12	0.00	0.00	0.00	0.03	0.12	0.41	1.15	2.63	5.05	8.23	11.52	13.96	14.74	13.60	11.01	7.83	4.89	2.69	1.29	0.54	0.20	0.06	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.84
13	0.00	0.00	0.00	0.01	0.04	0.15	0.47	1.24	2.72	5.09	8.18	11.37	13.76	14.57	13.53	11.04	7.91	4.98	2.75	1.33	0.56	0.20	0.06	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.08
14	0.00	0.00	0.00	0.00	0.01	0.05	0.17	0.52	1.30	2.78	5.10	8.12	11.25	13.63	14.48	13.51	11.08	7.99	5.05	2.79	1.34	0.56	0.20	0.06	0.02	0.00	0.00	0.00	0.00	0.00	0.00	4.23
15	0.00	0.00	0.00	0.00	0.00	0.01	0.06	0.19	0.55	1.33	2.80	5.09	8.06	11.15	13.54	14.45	13.54	11.15	8.06	5.09	2.80	1.33	0.55	0.19	0.06	0.01	0.00	0.00	0.00	0.00	0.00	4.28
16	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.06	0.20	0.56	1.34	2.79	5.05	7.99	11.08	13.51	14.48	13.63	11.25	8.12	5.10	2.78	1.30	0.52	0.17	0.05	0.01	0.00	0.00	0.00	0.00	4.23
17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.06	0.20	0.56	1.33	2.75	4.98	7.91	11.04	13.53	14.57	13.76	11.37	8.18	5.09	2.72	1.24	0.47	0.15	0.04	0.01	0.00	0.00	0.00	4.08
18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.06	0.20	0.54	1.29	2.69	4.89	7.83	11.01	13.60	14.74	13.96	11.52	8.23	5.05	2.63	1.15	0.41	0.12	0.03	0.00	0.00	0.00	3.84
19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.06	0.19	0.52	1.24	2.59	4.78	7.74	11.00	13.73	14.98	14.23	11.70	8.27	4.97	2.50	1.04	0.34	0.09	0.02	0.00	0.00	4.78
20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.05	0.17	0.48	1.16	2.47	4.63	7.62	11.01	13.91	15.30	14.57	11.92	8.29	4.84	2.32	0.89	0.26	0.06	0.01	0.00	4.27
21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.05	0.15	0.42	1.06	2.31	4.44	7.49	11.03	14.16	15.73	15.01	12.19	8.29	4.64	2.08	0.72	0.18	0.03	0.00	4.94
22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.04	0.12	0.36	0.94	2.12	4.21	7.31	11.05	14.47	16.28	15.58	12.49	8.25	4.36	1.78	0.52	0.10	0.01	4.22
23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.03	0.10	0.29	0.79	1.89	3.91	7.07	11.07	14.88	17.00	16.29	12.85	8.12	3.95	1.39	0.32	0.03	4.85
24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.07	0.22	0.64	1.61	3.55	6.76	11.06	15.38	17.95	17.23	13.25	7.85	3.37	0.93	0.12	3.61
25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.04	0.15	0.47	1.30	3.09	6.31	10.98	16.01	19.21	18.47	13.68	7.33	2.53	0.42	4.92
26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.09	0.30	0.94	2.51	5.67	10.76	16.78	20.98	20.20	14.07	6.31	1.37	3.87
27	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.04	0.16	0.58	1.80	4.74	10.23	17.71	23.61	22.77	14.13	4.24	2.58
28	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.05	0.24	1.00	3.34	9.00	18.67	28.01	27.05	12.62	4.64
29	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.25	1.40	6.02	18.71	37.41	36.17	1.69
30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	100	0.00

Table 3. Confidence intervals (Low, Upp) and errors (Err) for other five methods selected for comparison

		Wilson_N			Logit_C			BetaCJ0			Blyth-Still-Castella			OptiBin			NewAlg		
n	X	Low	Upp	Err	Low	Upp	Err	Low	Upp	Err	Low	Upp	Err	Low	Upp	Err	Low	Upp	Err
30	0	0.00	3.42	0.00	0.00	3.30	0.00	0.00	2.85	0.00	0	3.3	0.00	0.00	2.97	0.00	0	0	0.00
30	1	0.18	5.01	7.71	0.36	5.37	7.71	0.12	4.35	1.69	0	4.8	1.69	0.03	4.98	7.71	0	3	1.69
30	2	0.54	6.39	4.64	0.78	6.81	4.64	0.42	5.91	1.30	0.3	6.3	4.64	0.03	6.96	4.64	0	4	4.64
30	3	1.05	7.68	2.59	1.26	8.10	7.33	0.87	7.29	6.83	0.9	7.8	2.58	1.02	7.98	6.83	0	6	2.58
30	4	1.59	8.91	5.23	1.80	9.27	5.23	1.41	8.61	5.23	1.5	9	2.73	1.02	8.97	5.23	0	7	3.87
30	5	2.19	10.08	2.39	2.40	10.41	5.48	2.01	9.81	4.92	2.1	10.5	4.92	2.04	9.96	4.92	2	9	4.92
30	6	2.85	11.19	3.61	3.06	11.49	3.61	2.64	11.01	6.98	2.7	11.4	3.61	2.04	11.97	3.61	2	10	3.61
30	7	3.54	12.27	4.85	3.72	12.57	4.85	3.33	12.12	4.85	3.3	12.3	4.85	3.03	12.96	4.85	3	11	4.85
30	8	4.26	13.32	6.00	4.41	13.59	4.22	4.05	13.23	6.00	3.9	13.5	3.88	4.02	13.98	6.00	3	12	4.22
30	9	5.01	14.37	7.01	5.13	14.58	4.93	4.80	14.31	4.70	4.8	14.4	4.94	4.02	14.97	4.70	4	13	4.94
30	10	5.76	15.36	3.09	5.88	15.54	3.09	5.58	15.33	5.41	5.4	15.6	3.10	5.04	15.96	5.41	6	16	4.27
30	11	6.57	16.35	3.52	6.66	16.50	3.52	6.39	16.35	6.02	6.3	16.5	3.51	6.03	16.98	3.52	7	17	4.78
30	12	7.38	17.31	3.82	7.44	17.43	3.82	7.20	17.34	3.82	7.2	17.7	3.84	7.02	17.97	3.82	7	17	3.84
30	13	8.22	18.24	4.08	8.25	18.33	4.08	8.07	18.30	4.08	7.8	18.6	4.08	8.04	18.96	4.08	8	18	4.08
30	14	9.06	19.17	4.23	9.09	19.20	4.23	8.94	19.23	4.23	9	19.5	4.23	8.04	19.98	4.23	9	19	4.23
30	15	9.96	20.04	4.28	9.93	20.07	4.28	9.84	20.16	4.28	9.6	20.4	4.28	9.03	20.97	4.28	10	20	4.28
30	16	10.83	20.94	4.23	10.80	20.91	4.23	10.77	21.06	4.23	10.5	21	4.23	10.02	21.96	4.23	11	21	4.23
30	17	11.76	21.78	4.08	11.67	21.75	4.08	11.70	21.93	4.08	11.4	22.2	4.08	11.04	21.96	4.08	12	22	4.08
30	18	12.69	22.62	3.82	12.57	22.56	3.82	12.66	22.80	3.82	12.3	22.8	3.84	12.03	22.98	3.82	13	23	3.84
30	19	13.65	23.43	3.52	13.50	23.34	3.52	13.65	23.61	6.02	13.5	23.7	3.51	13.02	23.97	3.52	13	23	4.78
30	20	14.64	24.24	3.09	14.46	24.12	3.09	14.67	24.42	5.41	14.4	24.6	3.10	14.04	24.96	5.41	14	24	4.27
30	21	15.63	24.99	7.01	15.42	24.87	4.93	15.69	25.20	4.70	15.6	25.2	4.94	15.03	25.98	4.70	17	26	4.94
30	22	16.68	25.74	6.00	16.41	25.59	4.22	16.77	25.95	6.00	16.5	26.1	3.88	16.02	25.98	6.00	18	27	4.22
30	23	17.73	26.46	4.85	17.43	26.28	4.85	17.88	26.67	4.85	17.7	26.7	4.85	17.04	26.97	4.85	19	27	4.85
30	24	18.81	27.15	3.61	18.51	26.94	3.61	18.99	27.36	6.98	18.6	27.3	3.61	18.03	27.96	3.61	20	28	3.61
30	25	19.92	27.81	2.39	19.59	27.60	5.48	20.19	27.99	4.92	19.5	27.9	4.92	20.04	27.96	4.92	21	28	4.92
30	26	21.09	28.41	5.23	20.73	28.20	5.23	21.39	28.59	5.23	21	28.5	2.73	21.03	28.98	5.23	23	30	3.87
30	27	22.32	28.95	2.59	21.90	28.74	7.33	22.71	29.13	6.83	22.2	29.1	2.58	22.02	28.98	6.83	24	30	2.58
30	28	23.61	29.46	4.64	23.19	29.22	4.64	24.09	29.58	1.30	23.7	29.7	4.64	23.04	29.97	4.64	26	30	4.64
30	29	24.99	29.82	7.71	24.63	29.64	7.71	25.65	29.88	1.69	25.2	30	1.69	25.02	29.97	7.71	27	30	1.69
30	30	26.58	30.00	0.00	26.70	30.00	0.00	27.15	30.00	0.00	26.7	30	0.00	27.03	30.00	0.00	30	30	0.00

Table 4. Twelve assessment methods for CI's

AssMeth	Wilson_N	Logit_C	BetaCJ0	B-S-C	OptiBin	NewAlg
AvgOE0	0.52	0.25	0.30	1.47	0.06	1.21
AvgOE1	0.81	0.56	0.60	1.22	0.37	0.95
StDOE0	1.51	1.30	1.61	1.31	1.17	1.33
StDOE1	1.84	1.73	1.95	0.94	1.68	0.89
SiDOE0	1.58	1.30	1.61	1.95	1.16	1.78
SiDOE1	1.98	1.79	2.01	1.53	1.69	1.30
AvADA0	1.23	1.00	1.23	1.47	0.92	1.21
AvADA1	1.39	1.21	1.51	1.22	1.16	0.95
AvADS0	1.34	1.04	1.19	1.01	0.91	0.97
AvADS1	1.58	1.30	1.43	0.77	1.17	0.66
S8DOE0	2.15	2.02	2.77	3.57	1.95	3.57
S8DOE1	3.56	3.55	3.60	2.41	3.55	2.39

Conclusion

The new proposed method shows to be a promising method for confidence intervals calculation for binomial distributed variables.

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Annex: Our Proposed New Algorithm Program Source

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  gname='cie';
type
  arr_data=array[0..lmax] of integer;
  row_data=array[0..lmax] of extended;
  prowdata=^row_data;
  mat_data=array[0..lmax] of prowdata;
var
  p_m:mat_data;
  err:row_data;
  cil:arr_data;
  ciu:arr_data;

procedure cie_init(var cil,ciu:arr_data;var err:row_data;m:integer);
var
  i:integer;
begin
  for i:=0 to m do
begin
    cil[i]:=0;
    ciu[i]:=m;
    err[i]:=0.0;
  end;
end;
procedure mat_init(var pm:mat_data);
var
  i:integer;
begin
  for i:=0 to lmax do
getmem(pm[i],sizeof(row_data));
end;
procedure mat_done(var pm:mat_data);
var
  i:integer;
begin
  for i:=0 to lmax do
freemem(pm[i],sizeof(row_data));
end;
procedure cie_afi(var cil,ciu:arr_data;var err:row_data;m:integer);
var
  i:integer;
  f:text;
  s:string[4];
begin
  str(m,s);
  assign(f,gname+s+'.txt');
  rewrite(f);
  for i:=0 to m do
begin

  writeln(f,cil[i],chr(9),i,chr(9),ciu[i],chr(9),err[i]);
  end;
  close(f);
end;
procedure mat_afi(var pm:mat_data;m:integer);
var
  i,j:integer;
  f:text;
  s:string[4];
begin
  str(m,s);
  assign(f,fname+s+'.txt');
  rewrite(f);
  for i:=0 to m do
begin
    for j:=0 to m do
begin

  write(f,pm[i]^[j],chr(9));
    end;
    writeln(f);
  end;
  close(f);
end;
function dbino(m,x,xx:integer):extended;
var
  i:integer;
  rm,rx,rmx:extended;
begin
  rx:=exp(xx*ln(x/m));
  rmx:=exp((m-xx)*ln(1.0-x/m));
  rm:=1;
  if(2*xx<m)then
begin//xx mic
    for i:=1 to xx do
rm:=rm*i/(m+1.0-i);
  end else begin//xx mare
    for i:=1 to m-xx
do rm:=rm*i/(m+1.0-i);
  end;
  dbino:=100.0*(rx*rmx/rm);
end;
procedure mat_pro(var pm:mat_data;m:integer);
var
  i,j,m2:integer;
begin

pm[0]^[0]:=100.0;pm[m]^[m]:=100.0;
  for j:=1 to m do
begin

  pm[0]^[j]:=0.0;pm[m]^[m-j]:=0.0;
  end;
  for i:=1 to m-1 do
begin
  pm[i]^[0]:=100.0*exp(m*ln(1.0-i/m));
  pm[m-i]^[m]:=pm[i]^[0];
  end;
  m2:=m div 2 + 1;
  for i:=1 to m2 do
begin
  for j:=1 to m do
begin

  pm[i]^[j]:=dbino(m,i,j);
    pm[m-i]^[m-j]:=pm[i]^[j];
  end;
 end;

end;
procedure ci_comp(var pm:mat_data;var cil,ciu:arr_data;var err:row_data;m:integer);
var
  i,j,k,mm:integer;
  l,u:extended;
begin
  mm:=m div 2 + m mod 2;//pair m -> has middle point
  for i:=0 to mm do
begin
    l:=0.0;u:=0.0;
    j:=0;k:=m;
    while(l+u<alpha)do
begin

  if(pm[i]^[j]<pm[i]^[k])then begin

  if(l+u+pm[i]^[j]<alpha)then begin

  l:=l+pm[i]^[j];
          j:=j+1;
      end else
break;
    end else
if(pm[i]^[j]>pm[i]^[k])then begin

  if(l+u+pm[i]^[k]<alpha)then begin

  u:=u+pm[i]^[k];
          k:=k-1;
      end else
break;
    end else begin

  if(l+u+pm[i]^[j]+pm[i]^[k]<alpha)then begin

  l:=l+pm[i]^[j];

  u:=u+pm[i]^[k];
          k:=k-1;
          j:=j+1;
      end else
break;
    end;
   end;
   if(k<m)then

  if(l+pm[i]^[j]+u-pm[i]^[k+1]<alpha)then
begin
      write('aa ');

  write(pm[i]^[k+1],chr(9),pm[i]^[j]);
      readln;

  if(pm[i]^[k+1]<pm[i]^[j]) then begin

  l:=l+pm[i]^[j];
        u:=u-pm[i]^[k+1];
        j:=j+1;
        k:=k+1;
      end;
    end;
   if(j>0)then
    if(l-pm[i]^[j-1]+u+pm[i]^[k]<alpha)then begin
      write('bb ');

  write(pm[i]^[k],chr(9),pm[i]^[j-1]);
      readln;

  if(pm[i]^[k]>pm[i]^[j-1]) then begin
        l:=l-pm[i]^[j-1];

  u:=u+pm[i]^[k];
        j:=j-1;
        k:=k-1;
      end;
    end;
   err[i]:=l+u;
    cil[i]:=j;
    ciu[i]:=k;
  end;
  for i:=m downto mm+1
do begin
    cil[i]:=m-ciu[m-i];
    ciu[i]:=m-cil[m-i];
    err[i]:=err[m-i];
  end;
  exit;

end;
var
  m:integer;
  i,j:integer;
begin
  mat_init(p_m);
  write('m=');readln(m);
  mat_pro(p_m,m);
  cie_init(cil,ciu,err,m);
  ci_comp(p_m,cil,ciu,err,m);
  cie_afi(cil,ciu,err,m);
  mat_afi(p_m,m);
  mat_done(p_m);
end.
```

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HOW TO ASSES DOSE-RESPONSE STUDY OUTCOME: A STATISTICAL APPROACH

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Confidence interval defines as an estimated range of values that is likely to include an unknown population parameter, the estimated range being calculates from a given set of sample data. Are uses in experimental research as a criterion of assessment of the trustworthiness or robustness of the finding. [1] It is well known that for low proportions, the lower confidence boundaries is frequently less than zero while for the proportions closer to the upper boundaries exceed one. [2,3] The main problem of the existent methods is represented by the inadequate coverage and inappropriate intervals. [3]

The binomial distribution has its origins and applications in the natural phenomena studies: heterometric bands of tetrameric enzyme, the stoichiometry of the donor and acceptor chromophores implied in enzymatic ligand/receptor interactions, translocation and exfoliation of type I restriction endonucleases, biotinidase activity on neonatal thyroid hormone stimulator, the parasite induced mortality at fish, the occupancy/activity for proteins at multiple nonspecific sites containing replication. [4] Carlton and Stansfield [5] defined very well the frame and limits of binomial distribution model applied to the natural phenomena.

A series of confidence intervals assessment methods were proposed. [6] The formula for probability calculation:

$$P_B(n, X, Y) = \frac{n!}{Y!(n-Y)!}\frac{X^Y(n-X)^{(n-Y)}}{n^n}$$

has been used in order to obtain the probability matrix. An algorithm for confidence intervals calculation has been developed and applied.

This project focuses on the application and usefulness of the proposed confidence intervals calculation algorithm and on its evaluation for a sample size of 30. The evaluation of the algorithm has been done by comparison with Logit, Jeffreys and Blyth-Still-Casella methods and the results are presented here.

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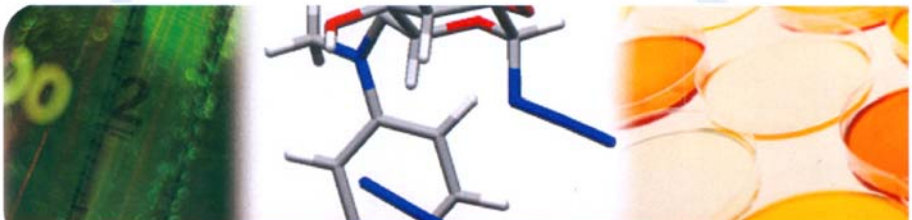

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