

Sequential Integrated and Contingent antenatal screening for Down's syndrome

WEB TABLES

Table

A **Comparison of Sequential Integrated screening and Integrated test on all women**

B-F **Comparison of contingent screening and Integrated test for all women**

Table A: Sequential Integrated screening performance compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)								
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		85			90			95		
				Unaffected	Down's	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
Integrated Test														
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29
Sequential Integrated screening (Combined test in 1 st trimester)	0.01	25	1 in 2	99.99	75	0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29
	0.05	44	1 in 6	99.95	56	0.88	1 in 70	1:5	2.11	1 in 192	1:10	6.15	1 in 760	1:29
	0.1	51	1 in 9	99.9	49	0.89	1 in 69	1:5	2.12	1 in 191	1:10	6.15	1 in 759	1:29
	0.5	66	1 in 30	99.5	34	1.09	1 in 61	1:6	2.25	1 in 184	1:11	6.23	1 in 751	1:29
	1.0	72	1 in 58	99.0	28	1.40	1 in 51	1:7	2.46	1 in 169	1:12	6.38	1 in 742	1:30
	2.0	79	1 in 114	98.0	21	2.15	1 in 32	1:11	2.97	1 in 144	1:15	6.74	1 in 719	1:31
	3.0	82	1 in 175	97.0	18	3.05	1 in 16	1:16	3.65	1 in 119	1:18	7.16	1 in 696	1:33
	4.0	84	1 in 237	96.0	16	4.00	1 in 4	1:21	4.42	1 in 96	1:22	7.60	1 in 664	1:35
	5.0	86	1 in 307	95.0	14	^c	^c	^c	5.23	1 in 72	1:26	8.13	1 in 632	1:38
Sequential Integrated screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	99.99	82	0.89	1 in 72	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30
	0.05	31	1 in 6	99.95	69	0.91	1 in 71	1:5	2.16	1 in 197	1:11	6.36	1 in 786	1:30
	0.1	38	1 in 9	99.9	62	0.93	1 in 71	1:5	2.18	1 in 196	1:11	6.37	1 in 784	1:30
	0.5	56	1 in 28	99.5	44	1.15	1 in 62	1:6	2.33	1 in 186	1:11	6.45	1 in 773	1:30
	1.0	65	1 in 54	99.0	35	1.49	1 in 53	1:8	2.57	1 in 172	1:13	6.62	1 in 763	1:31
	2.0	72	1 in 100	98.0	28	2.28	1 in 39	1:12	3.16	1 in 147	1:16	7.00	1 in 734	1:33
	3.0	76	1 in 147	97.0	24	3.15	1 in 27	1:16	3.89	1 in 128	1:19	7.47	1 in 700	1:35
	4.0	79	1 in 192	96.0	21	4.07	1 in 19	1:21	4.67	1 in 112	1:23	8.02	1 in 677	1:37
	5.0	81	1 in 244	95.0	19	5.03	1 in 12	1:26	5.47	1 in 93	1:27	8.54	1 in 639	1:40

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester, ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone

Table B: Contingent screening performance with a lower risk cut-off of 1 in 1000 for the 1st trimester test compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)								
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
				Unaffected	Down's									
Integrated Test														
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29
Contingent screening (Combined test in 1 st trimester)	0.01	25	1 in 2	13	68	0.95	1 in 85	1:5	2.67	1 in 340	1:13	-	-	-
	0.05	44	1 in 6	13	49	0.96	1 in 84	1:5	2.68	1 in 339	1:13	-	-	-
	0.1	51	1 in 9	13	42	0.97	1 in 83	1:5	2.68	1 in 337	1:13	-	-	-
	0.5	66	1 in 30	13	27	1.16	1 in 74	1:6	2.79	1 in 324	1:14	-	-	-
	1.0	72	1 in 58	12	21	1.44	1 in 61	1:8	2.99	1 in 309	1:15	-	-	-
	2.0	79	1 in 114	11	14	2.17	1 in 39	1:11	3.45	1 in 273	1:17	-	-	-
	3.0	82	1 in 175	10.3	11	3.05	1 in 19	1:16	4.02	1 in 231	1:20	-	-	-
	4.0	84	1 in 237	9.3	9	4.00	1 in 4	1:21	4.66	1 in 186	1:23	-	-	-
	5.0	86	1 in 307	8.3	7	^c	^c	^c	5.37	1 in 139	1:26	-	-	-
Contingent screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	17	73	1.19	1 in 118	1:6	4.21	1 in 798	1:21	-	-	-
	0.05	31	1 in 6	17	60	1.20	1 in 117	1:6	4.21	1 in 796	1:21	-	-	-
	0.1	38	1 in 9	17	53	1.22	1 in 115	1:6	4.23	1 in 795	1:21	-	-	-
	0.5	56	1 in 28	16	36	1.40	1 in 104	1:7	4.29	1 in 769	1:21	-	-	-
	1.0	65	1 in 54	16	27	1.71	1 in 90	1:9	4.44	1 in 744	1:22	-	-	-
	2.0	72	1 in 100	15	19	2.41	1 in 65	1:13	4.85	1 in 686	1:24	-	-	-
	3.0	76	1 in 147	14	15	3.23	1 in 46	1:17	5.29	1 in 603	1:26	-	-	-
	4.0	79	1 in 192	13	13	4.11	1 in 31	1:21	5.87	1 in 547	1:29	-	-	-
	5.0	81	1 in 244	12	10	5.05	1 in 18	1:26	6.43	1 in 469	1:32	-	-	-

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone, ^d Triage screening cannot detect 95% of Down's syndrome pregnancies with a first trimester lower risk cut-off as high as 1 in 1000

Table C: Contingent screening performance with a lower risk cut-off of 1 in 2000 for the 1st trimester test compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)								
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
				Unaffected	Down's									
Integrated Test														
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29
Contingent screening (Combined test in 1 st trimester)	0.01	25	1 in 2	22	71	0.89	1 in 75	1:5	2.27	1 in 228	1:11	9.41	1 in 2436	1:44
	0.05	44	1 in 6	22	52	0.91	1 in 74	1:5	2.29	1 in 227	1:11	9.41	1 in 2436	1:44
	0.1	51	1 in 9	22	45	0.91	1 in 73	1:5	2.29	1 in 226	1:11	9.42	1 in 2436	1:44
	0.5	66	1 in 30	21	30	1.10	1 in 64	1:6	2.42	1 in 217	1:12	9.49	1 in 2426	1:44
	1.0	72	1 in 58	21	23	1.41	1 in 53	1:7	2.62	1 in 203	1:13	9.60	1 in 2411	1:45
	2.0	79	1 in 114	20	17	2.16	1 in 34	1:11	3.11	1 in 173	1:15	9.84	1 in 2369	1:46
	3.0	82	1 in 175	19	14	3.06	1 in 17	1:16	3.74	1 in 143	1:18	10.01	1 in 2261	1:47
	4.0	84	1 in 237	18	11	4.00	1 in 4	1:21	4.47	1 in 113	1:22	10.31	1 in 2175	1:48
	5.0	86	1 in 307	17	10	^c	^c	^c	5.27	1 in 85	1:26	10.58	1 in 2078	1:49
Contingent screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	28	77	0.97	1 in 85	1:5	2.61	1 in 291	1:13	20.09	1 in 20856	1:94
	0.05	31	1 in 6	28	64	0.99	1 in 84	1:5	2.63	1 in 290	1:13	20.09	1 in 20856	1:94
	0.1	38	1 in 9	28	57	1.00	1 in 83	1:5	2.64	1 in 289	1:13	20.09	1 in 20856	1:94
	0.5	56	1 in 28	27	39	1.22	1 in 73	1:6	2.77	1 in 277	1:14	20.11	1 in 20856	1:94
	1.0	65	1 in 54	27	30	1.54	1 in 62	1:8	2.99	1 in 258	1:15	20.14	1 in 20847	1:94
	2.0	72	1 in 100	26	23	2.31	1 in 46	1:12	3.53	1 in 223	1:17	20.24	1 in 20794	1:94
	3.0	76	1 in 147	25	19	3.16	1 in 32	1:16	4.17	1 in 195	1:20	20.23	1 in 20159	1:94
	4.0	79	1 in 192	24	16	4.09	1 in 22	1:21	4.88	1 in 169	1:24	20.31	1 in 19784	1:95
	5.0	81	1 in 244	23	14	5.03	1 in 13	1:26	5.64	1 in 141	1:28	20.41	1 in 19511	1:95

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester, ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone

Table D: Contingent screening performance with a lower risk cut-off of 1 in 3000 for the 1st trimester test compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)											
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	85			90			95		
				Unaffected	Down's				Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
Integrated Test																	
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30			
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29			
Contingent screening (Combined test in 1 st trimester)	0.01	25	1 in 2	29	72	0.88	1 in 73	1:5	2.19	1 in 208	1:11	7.34	1 in 1193	1:34			
	0.05	44	1 in 6	28	53	0.89	1 in 72	1:5	2.20	1 in 208	1:11	7.35	1 in 1193	1:34			
	0.1	51	1 in 9	28	46	0.90	1 in 71	1:5	2.21	1 in 207	1:11	7.35	1 in 1192	1:34			
	0.5	66	1 in 30	28	31	1.10	1 in 63	1:6	2.32	1 in 199	1:11	7.43	1 in 1182	1:35			
	1.0	72	1 in 58	28	25	1.40	1 in 52	1:7	2.53	1 in 186	1:12	7.57	1 in 1172	1:35			
	2.0	79	1 in 114	27	18	2.16	1 in 33	1:11	3.03	1 in 157	1:15	7.83	1 in 1133	1:36			
	3.0	82	1 in 175	26	15	3.05	1 in 16	1:16	3.66	1 in 129	1:18	8.08	1 in 1077	1:38			
	4.0	84	1 in 237	25	12	4.00	1 in 4	1:21	4.45	1 in 104	1:22	8.42	1 in 1020	1:39			
5.0	86	1 in 307	24	11	^c	^c	^c	5.25	1 in 77	1:26	8.85	1 in 974	1:41				
Contingent screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	36	78	0.93	1 in 78	1:5	2.39	1 in 241	1:12	9.18	1 in 1792	1:43			
	0.05	31	1 in 6	36	65	0.94	1 in 77	1:5	2.40	1 in 240	1:12	9.19	1 in 1792	1:43			
	0.1	38	1 in 9	36	58	0.96	1 in 76	1:5	2.41	1 in 238	1:12	9.20	1 in 1790	1:43			
	0.5	56	1 in 28	36	41	1.19	1 in 67	1:6	2.56	1 in 226	1:13	9.22	1 in 1764	1:43			
	1.0	65	1 in 54	35	32	1.51	1 in 57	1:8	2.77	1 in 210	1:14	9.33	1 in 1741	1:43			
	2.0	72	1 in 100	34	24	2.29	1 in 42	1:12	3.33	1 in 183	1:16	9.56	1 in 1678	1:45			
	3.0	76	1 in 147	33	20	3.16	1 in 29	1:16	4.02	1 in 157	1:20	9.82	1 in 1605	1:46			
	4.0	79	1 in 192	32	18	4.08	1 in 20	1:21	4.76	1 in 136	1:23	10.26	1 in 1566	1:48			
5.0	81	1 in 244	31	15	5.03	1 in 12	1:26	5.55	1 in 114	1:27	10.71	1 in 1511	1:50				

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester, ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone

Table E: Contingent screening performance with a lower risk cut-off of 1 in 5000 for the 1st trimester test compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)								
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
				Unaffected	Down's									
Integrated Test														
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	1:11	6.35	1 in 786	1:30
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	1:10	6.14	1 in 760	1:29
Contingent screening (Combined test in 1 st trimester)	0.01	25	1 in 2	39	73	0.87	1 in 72	1:5	2.13	1 in 199	1:10	6.46	1 in 880	1:30
	0.05	44	1 in 6	39	54	0.88	1 in 71	1:5	2.14	1 in 198	1:11	6.47	1 in 880	1:30
	0.1	51	1 in 9	39	47	0.89	1 in 69	1:5	2.14	1 in 197	1:11	6.47	1 in 879	1:30
	0.5	66	1 in 30	38	32	1.10	1 in 61	1:6	2.28	1 in 189	1:11	6.57	1 in 872	1:31
	1.0	72	1 in 58	38	26	1.40	1 in 51	1:7	2.50	1 in 175	1:12	6.72	1 in 863	1:31
	2.0	79	1 in 114	37	19	2.15	1 in 33	1:11	2.99	1 in 149	1:15	7.04	1 in 836	1:33
	3.0	82	1 in 175	36	16	3.05	1 in 16	1:16	3.65	1 in 122	1:18	7.41	1 in 802	1:35
	4.0	84	1 in 237	35	14	4.00	1 in 4	1:21	4.42	1 in 98	1:22	7.85	1 in 768	1:37
	5.0	86	1 in 307	34	12	^c	^c	^c	5.24	1 in 74	1:26	8.32	1 in 729	1:39
Contingent screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	49	80	0.90	1 in 74	1:5	2.24	1 in 212	1:11	7.09	1 in 1024	1:33
	0.05	31	1 in 6	49	67	0.92	1 in 74	1:5	2.25	1 in 211	1:11	7.09	1 in 1024	1:33
	0.1	38	1 in 9	49	60	0.94	1 in 72	1:5	2.26	1 in 210	1:11	7.10	1 in 1023	1:33
	0.5	56	1 in 28	48	42	1.17	1 in 64	1:6	2.41	1 in 200	1:12	7.18	1 in 1011	1:33
	1.0	65	1 in 54	48	33	1.50	1 in 54	1:8	2.64	1 in 186	1:13	7.27	1 in 989	1:34
	2.0	72	1 in 100	47	26	2.28	1 in 40	1:12	3.23	1 in 160	1:16	7.60	1 in 951	1:35
	3.0	76	1 in 147	46	22	3.16	1 in 28	1:16	3.93	1 in 137	1:19	8.01	1 in 901	1:37
	4.0	79	1 in 192	45	19	4.08	1 in 19	1:21	4.69	1 in 119	1:23	8.56	1 in 878	1:40
	5.0	81	1 in 244	44	17	5.03	1 in 12	1:26	5.50	1 in 100	1:27	9.05	1 in 833	1:42

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester, ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone

Table F: Contingent screening performance with a lower risk cut-off of 1 in 10000 for the 1st trimester test compared with routine use of the Integrated test (first trimester markers measured at 11 completed weeks)

	1 st Trimester Test					Overall Detection Rate (%)								
	FPR (%)	DR (%)	Risk cut-off	% that proceed to Integrated test		Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR	Overall FPR (%)	Integrated test risk cut-off	Overall OAPR
				Unaffected	Down's									
Integrated Test														
6 markers ^a						0.89	1 in 73	1:5	2.15	1 in 198	11	6.35	1 in 786	1:30
7 markers ^b						0.86	1 in 71	1:4	2.10	1 in 193	10	6.14	1 in 760	1:29
Contingent screening (Combined test in 1 st trimester)	0.01	25	1 in 2	55	74	0.86	1 in 71	1:4	2.10	1 in 194	10	6.20	1 in 788	1:29
	0.05	44	1 in 6	55	55	0.88	1 in 70	1:5	2.12	1 in 194	10	6.21	1 in 787	1:29
	0.1	51	1 in 9	55	48	0.89	1 in 69	1:5	2.12	1 in 193	10	6.21	1 in 786	1:29
	0.5	66	1 in 30	55	33	1.10	1 in 61	1:6	2.26	1 in 185	11	6.28	1 in 777	1:29
	1.0	72	1 in 58	54	27	1.40	1 in 51	1:7	2.46	1 in 171	12	6.45	1 in 770	1:30
	2.0	79	1 in 114	53	20	2.15	1 in 32	1:11	2.98	1 in 146	15	6.77	1 in 744	1:32
	3.0	82	1 in 175	52	17	3.05	1 in 16	1:16	3.65	1 in 120	18	7.20	1 in 719	1:34
	4.0	84	1 in 237	51	15	4.00	1 in 4	1:21	4.42	1 in 96	22	7.65	1 in 687	1:36
	5.0	86	1 in 307	50	13	^c	^c	^c	5.23	1 in 72	26	8.16	1 in 658	1:38
Contingent screening (NT and PAPP-A in 1 st trimester)	0.01	18	1 in 3	67	81	0.89	1 in 73	1:5	2.16	1 in 200	11	6.47	1 in 830	1:30
	0.05	31	1 in 6	67	68	0.91	1 in 72	1:5	2.17	1 in 199	11	6.48	1 in 830	1:30
	0.1	38	1 in 9	67	61	0.93	1 in 71	1:5	2.19	1 in 199	11	6.48	1 in 828	1:30
	0.5	56	1 in 28	67	43	1.15	1 in 63	1:6	2.35	1 in 188	12	6.58	1 in 817	1:31
	1.0	65	1 in 54	66	35	1.49	1 in 53	1:8	2.57	1 in 174	13	6.72	1 in 801	1:31
	2.0	72	1 in 100	65	27	2.28	1 in 39	1:12	3.17	1 in 149	16	7.09	1 in 772	1:33
	3.0	76	1 in 147	64	23	3.16	1 in 27	1:16	3.90	1 in 129	19	7.55	1 in 739	1:35
	4.0	79	1 in 192	63	20	4.08	1 in 19	1:21	4.67	1 in 113	23	8.11	1 in 713	1:38
	5.0	81	1 in 244	62	18	5.03	1 in 12	1:26	5.48	1 in 94	27	8.65	1 in 682	1:40

DR=Detection rate; FPR=false-positive rate; OAPR=odds of being affected given a positive result

^a with free - β - hCG in 2nd trimester only, ^b with free - β - hCG in 1st and 2nd trimester, ^c More than 85% of Down's syndrome pregnancies detected using first trimester test alone

Sequential Integrated and Contingent antenatal screening for Down's syndrome

WEB APPENDIX

Estimation of excess maternal mortality due to terminations of pregnancy at 17 weeks compared with 13 weeks

Table G shows data on maternal mortality attributable to terminations of pregnancy between 1972 and 1987.¹² Lawson et al¹² reported data on maternal mortality from a termination of pregnancy at different gestational ages from 1972 to 1987. Using this data the predicted maternal mortality at 13 weeks is 1.97 per 100,000 pregnancies and 5.13 at 17 weeks (see table G). The difference in maternal mortality between 17 and 13 weeks was 0.43 per 10 million women screened. Over the 15 years between 1972 and 1987 the rate of maternal mortality (at all gestations) declined by about 80% - 90% associated with the introduction of techniques for performing abortion that have become safer such as the use of misoprotol to prime the cervix for surgical abortion and of the combination of mifepristone and mosoprotol for medical abortion. So the current absolute difference between 17 and 13 weeks is likely to be about one-fifth of 0.43, or 0.09 per 10 million women screened – about 1 per 100 million women screened. UK data corroborates this approximate estimate.^{13,16} The confidential enquiry into maternal deaths in the UK identified two deaths associated with terminations of pregnancy out of 550,398 terminations between 1997-99. One of these was not judged to be due to the abortion; the other may have been. Depending on whether one or both are included the estimate is 0.18 or 0.36 per 100 million women screened (see table G). The US estimate extrapolated to the present and the recent UK estimates are therefore similar. Allowing for the larger

number of terminations at 13 weeks yields an excess maternal mortality between 17 and 13 weeks of 0.16 to 0.33 per 10 million women screened. Even this low risk may be an overestimate because data collected from abortions for unwanted pregnancies may not be representative of those done following prenatal diagnosis, which are more likely to be performed in a safer environment such as a labour ward or gynaecological operating list.

Table G. Comparison of maternal mortality due to termination of pregnancy at 13 and 17 weeks' gestation

		In 10 million pregnancies		
		Based on number of DS pregnancies surviving to each of the specified gestations (13 and 17 weeks) (this includes marker related fetal losses)		
Week of pregnancy	Maternal mortality per 100,000 pregnancies (i)	Number of terminations of DS pregnancies††† (ii)	Expected no. of maternal deaths (i) x (ii)	Excess 17 vs 13
13*	1.97†	23300	0.46	} 0.89 – 0.46 = 0.43
17*	5.13†	17300	0.89	
13**	0.76 – 1.51††	23300	0.18 to 0.35	} 0.16 – 0.33
17**	1.97 – 3.94††	17300	0.34 to 0.68	

* US data 1972 to 1987

** UK data 1997-99

† Predicted risk using data from Lawson et al¹²

†† In the UK between 1997-99¹³ there were 550,398 women having termination of pregnancy most of which were probably at ≤8 weeks. In these women two deaths occurred one of which was probably linked to the abortion, equivalent to a rate of about 0.18 per 100,000, if both cases are attributed to abortion the rate would be 0.36 per 100,000. Using data from Lawson et al¹² to estimate the relative risk of maternal death according to gestation yielded rates between 0.76-1.51 per 100,000 at 13 weeks and 1.97-3.94 per 100,000 at 17 weeks.

††† Based on an expected birth prevalence of 1.74 per1000 for England and Wales 1996-98,^{7,8,10} and 26% fetal loss rate from second trimester to term and 43% fetal loss rate from the first trimester to term. The estimate is based on detection rate of 90% and 90% uptake rate of amniocentesis or CVS.³

However, the adverse medical consequences of a diagnosis some four weeks earlier are significant compared to the use of Integrated screening for all. In the illustration given in this paper, it would lead to: (i) 16% more false positives, Invasive procedures and consequent fetal losses, (ii) a 4-5% failure rate from the earlier diagnostic test (CVS instead of amniocentesis), (iii) 1 in 5 unnecessary terminations of pregnancy, and (iv) two risk estimates being produced in each pregnancy with the associated confusion and anxiety. We conclude, on these grounds alone, that it is not justifiable to offer sequential Integrated or contingent screening when general Integrated screening would avoid the associated adverse consequences.