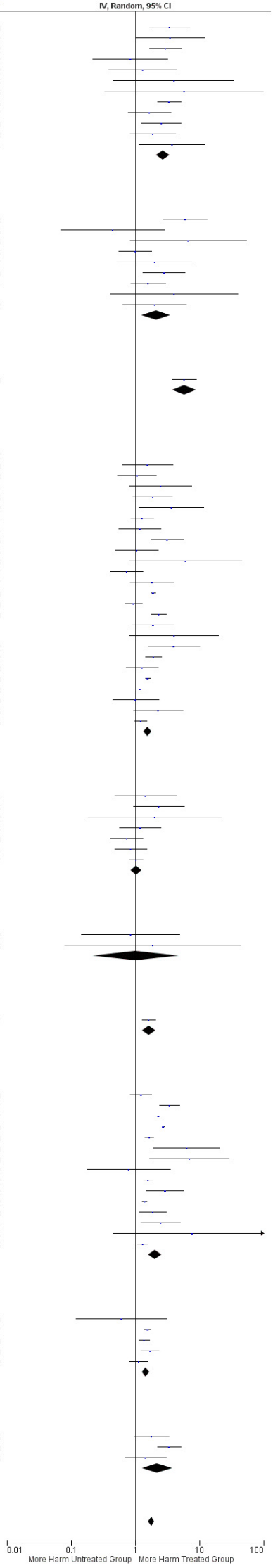Study or Subgroup	Treated Events	Treated Total	Untreated Events	Untreated Total	Weight	Risk Ratio IV, Random, 95% CI	Year
1.2.1 CKC vs No Treatment							
Jones 1979	12	66	14	264	1.2%	3.43 [1.66, 7.06]	1979
Ludviksson 1982	11	83	3	79	0.6%	3.49 [1.01, 12.05]	1982
Larsson 1982	33	197	16	284	1.4%	2.97 [1.68, 5.25]	1982
Buller 1982	3	47	6	79	0.5%	0.84 [0.22, 3.20]	1982
Moinian 1982	3	103	16	720	0.6%	1.31 [0.39, 4.42]	1982
Kuoppala 1986	4	62	1	62	0.2%	4.00 [0.46, 34.78]	1986
Crane 2006	4	21	0	13	0.1%	5.73 [0.33, 98.41]	2006
Klaritsch 2006	17	76	1961	29686	1.8%	3.39 [2.22, 5.16]	2006
Bruinsma 2007	11	71	12	129	1.1%	1.67 [0.77, 3.58]	2007
Ortoft 2010	7	67	283	6889	1.2%	2.54 [1.25, 5.17]	2010
Guo 2013	14	36	6	29	1.0%	1.88 [0.83, 4.28]	2013
Sozen 2014	7	15	3	24	0.6%	3.73 [1.14, 12.26]	2014
Subtotal (95% CI)		**844**		**38258**	**10.3%**	**2.70 [2.14, 3.40]**	
Total events	126		2321				
Heterogeneity: Tau² = 0.00; Chi² = 9.07, df = 11 (P = 0.62); I² = 0%							
Test for overall effect: Z = 8.42 (P < 0.00001)							
1.2.2 LC vs No Treatment							
Hagen 1993	21	56	7	112	1.0%	6.00 [2.71, 13.26]	1993
Spitzer 1995	2	34	2	15	0.3%	0.44 [0.07, 2.84]	1995
Sagot 1995	6	53	1	59	0.2%	6.68 [0.83, 53.69]	1995
Bekassy 1996	20	250	20	250	1.4%	1.00 [0.55, 1.81]	1996
Raio 1997	6	64	3	64	0.5%	2.00 [0.52, 7.65]	1997
Andersen 1999	14	75	10	150	1.1%	2.80 [1.31, 6.00]	1999
Sadler 2004	20	105	14	117	1.3%	1.59 [0.85, 2.99]	2004
Lima 2011	2	11	1	22	0.2%	4.00 [0.41, 39.45]	2011
Simoens 2012	5	24	5	48	0.6%	2.00 [0.64, 6.25]	2012
Subtotal (95% CI)		**672**		**837**	**6.7%**	**2.11 [1.26, 3.54]**	
Total events	96		63				
Heterogeneity: Tau² = 0.30; Chi² = 17.99, df = 8 (P = 0.02); I² = 56%							
Test for overall effect: Z = 2.84 (P = 0.004)							
1.2.3 NETZ vs No Treatment							
Ortoft 2010	17	71	301	7328	1.8%	5.83 [3.80, 8.95]	2010
Subtotal (95% CI)		**71**		**7328**	**1.8%**	**5.83 [3.80, 8.95]**	
Total events	17		301				
Heterogeneity: Not applicable							
Test for overall effect: Z = 8.05 (P < 0.00001)							
1.2.4 LLETZ vs No Treatment							
Gunasekera 1992	0	22	0	22		Not estimable	1992
Blomfield 1993	7	40	9	80	0.9%	1.56 [0.62, 3.87]	1993
Haffenden 1993	15	152	14	152	1.2%	1.07 [0.54, 2.14]	1993
Braet 1994	10	78	4	78	0.7%	2.50 [0.82, 7.63]	1994
Cruickshank 1995	14	147	15	295	1.2%	1.87 [0.93, 3.78]	1995
Paraskevaidis 2002	11	28	3	28	0.6%	3.67 [1.14, 11.75]	2002
Sadler 2004	44	278	38	309	1.8%	1.29 [0.86, 1.93]	2004
Tan 2004	13	119	11	119	1.1%	1.18 [0.55, 2.53]	2004
Samson 2005	44	558	14	558	1.4%	3.14 [1.74, 5.67]	2005
Acharya 2005	9	79	17	158	1.1%	1.06 [0.49, 2.27]	2005
Crane 2006	10	75	1	46	0.2%	6.13 [0.81, 46.36]	2006
Himes 2007	11	114	127	962	1.4%	0.73 [0.41, 1.31]	2007
Bruinsma 2007	11	69	11	125	1.1%	1.81 [0.83, 3.96]	2007
Noehr 2009 (singletons & cone depth)	530	8180	14758	434520	2.4%	1.91 [1.75, 2.07]	2009
Werner 2010	35	511	17445	240348	2.0%	0.94 [0.69, 1.30]	2010
Ortoft 2010	55	572	2426	59065	2.2%	2.34 [1.82, 3.02]	2010
Andia 2011	19	189	10	189	1.1%	1.90 [0.91, 3.98]	2011
Lima 2011	4	18	2	36	0.4%	4.00 [0.81, 19.82]	2011
Simoens 2012	12	52	6	104	0.9%	4.00 [1.59, 10.05]	2012
Poon 2012	41	473	1156	25772	2.1%	1.93 [1.43, 2.60]	2012
Frega 2013	26	406	19	379	1.4%	1.28 [0.72, 2.27]	2013
Heinonen 2013	547	7636	30151	658179	2.4%	1.56 [1.44, 1.70]	2013
Frey 2013	111	598	178	1140	2.2%	1.19 [0.96, 1.47]	2013
Guo 2013	10	48	8	39	1.0%	1.02 [0.44, 2.32]	2013
Martyn 2015	20	278	6	191	0.9%	2.29 [0.94, 5.60]	2015
Stout 2015	115	598	178	1129	2.2%	1.22 [0.99, 1.51]	2015
Subtotal (95% CI)		**21318**		**1424023**	**33.9%**	**1.56 [1.36, 1.79]**	
Total events	1724		66607				
Heterogeneity: Tau² = 0.05; Chi² = 78.52, df = 24 (P < 0.00001); I² = 69%							
Test for overall effect: Z = 6.38 (P < 0.00001)							
1.2.5 LA vs No Treatment							
Anderson 1984	7	68	5	70	0.7%	1.44 [0.48, 4.32]	1984
Saunders 1986	14	97	6	97	0.9%	2.33 [0.94, 5.82]	1986
Gunasekera 1992	2	109	1	109	0.2%	2.00 [0.18, 21.73]	1992
Spitzer 1995	16	129	10	97	1.1%	1.20 [0.57, 2.53]	1995
van Rooijen 1999	14	236	38	472	1.4%	0.74 [0.41, 1.33]	1999
Sadler 2004	23	223	19	158	1.4%	0.86 [0.48, 1.52]	2004
Bruinsma 2007	92	1005	163	1840	2.2%	1.03 [0.81, 1.32]	2007
Subtotal (95% CI)		**1867**		**2843**	**7.9%**	**1.04 [0.86, 1.26]**	
Total events	168		242				
Heterogeneity: Tau² = 0.00; Chi² = 5.51, df = 6 (P = 0.48); I² = 0%							
Test for overall effect: Z = 0.37 (P = 0.71)							
1.2.6 CT vs No Treatment							
Hemmingsson 1982	3	115	2	65	0.3%	0.85 [0.15, 4.94]	1982
Crane 2006	1	36	0	22	0.1%	1.86 [0.08, 43.87]	2006
Subtotal (95% CI)		**151**		**87**	**0.4%**	**1.02 [0.22, 4.77]**	
Total events	4		2				
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%							
Test for overall effect: Z = 0.03 (P = 0.98)							
1.2.7 RD vs No Treatment							
Bruinsma 2007	109	760	123	1390	2.2%	1.62 [1.27, 2.06]	2007
Subtotal (95% CI)		**760**		**1390**	**2.2%**	**1.62 [1.27, 2.06]**	
Total events	109		123				
Heterogeneity: Not applicable							
Test for overall effect: Z = 3.91 (P < 0.0001)							
1.2.8 Excisional Treatment NOS vs No Treatment							
El-Bastawissi 1999	118	852	28	250	1.9%	1.24 [0.84, 1.82]	1999
Sjoborg 2007	116	735	34	742	1.9%	3.44 [2.38, 4.98]	2007
Jakobsson 2007	222	2063	12211	261994	2.4%	2.31 [2.04, 2.62]	2007
Albrechtsen 2008	2368	14882	126466	2155505	2.4%	2.71 [2.61, 2.82]	2008
Shanthag 2009	129	1103	6682	94846	2.3%	1.66 [1.41, 1.96]	2009
Fischer 2010	19	85	3	85	0.6%	6.33 [1.95, 20.61]	2010
van de Vijner 2010	14	55	2	55	0.5%	7.00 [1.67, 29.36]	2010
Simoens 2012	2	12	5	24	0.4%	0.80 [0.18, 3.54]	2012
Reilly 2012	146	1521	1816	29978	2.3%	1.58 [1.35, 1.86]	2012
Van Hentenryck 2012	19	106	13	212	1.3%	2.92 [1.50, 5.69]	2012
Castanon 2012 & 2014	449	4776	34739	517923	2.4%	1.40 [1.28, 1.53]	2012
Wuntakal 2013	42	261	22	257	1.6%	1.88 [1.16, 3.06]	2013
Kitson 2014	25	278	10	278	1.2%	2.50 [1.22, 5.11]	2014
Martyn 2015	5	19	0	13	0.1%	7.70 [0.46, 128.32]	2015
Miller 2015	114	1356	1102	17172	2.3%	1.31 [1.09, 1.58]	2015
Subtotal (95% CI)		**28104**		**3079334**	**23.6%**	**2.02 [1.60, 2.55]**	
Total events	3788		183133				
Heterogeneity: Tau² = 0.14; Chi² = 289.41, df = 14 (P < 0.00001); I² = 95%							
Test for overall effect: Z = 5.95 (P < 0.00001)							
1.2.9 Ablative Treatment NOS vs No Treatment							
El-Bastawissi 1999	4	72	2	22	0.4%	0.61 [0.12, 3.12]	1999
Jakobsson 2007	261	3576	20791	446099	2.4%	1.57 [1.39, 1.76]	2007
Noehr 2009 (singletons & cone depth)	95	2027	3666	107951	2.3%	1.38 [1.13, 1.68]	2009
Shanthag 2009	34	285	1723	24457	2.0%	1.69 [1.23, 2.33]	2009
Reilly 2012	36	522	622	10261	2.0%	1.14 [0.82, 1.57]	2012
Subtotal (95% CI)		**6482**		**588790**	**9.0%**	**1.46 [1.27, 1.66]**	
Total events	430		26804				
Heterogeneity: Tau² = 0.01; Chi² = 5.69, df = 4 (P = 0.22); I² = 30%							
Test for overall effect: Z = 5.54 (P < 0.00001)							
1.2.10 Treatment NOS vs No Treatment							
Kristensen 1985	9	85	755	12792	1.3%	1.79 [0.96, 3.34]	1985
Kristensen 1993	19	130	1213	28124	1.8%	3.39 [2.23, 5.15]	1993
Kirn 2015	16	135	11	135	1.1%	1.45 [0.70, 3.02]	2015
Subtotal (95% CI)		**350**		**41051**	**4.3%**	**2.20 [1.28, 3.78]**	
Total events	44		1979				
Heterogeneity: Tau² = 0.14; Chi² = 5.23, df = 2 (P = 0.07); I² = 62%							
Test for overall effect: Z = 2.85 (P = 0.004)							
Total (95% CI)		**60619**		**5183941**	**100.0%**	**1.78 [1.60, 1.98]**	
Total events	6506		281575				
Heterogeneity: Tau² = 0.12; Chi² = 679.28, df = 79 (P < 0.00001); I² = 88%							
Test for overall effect: Z = 10.63 (P < 0.00001)							
Test for subgroup differences: Chi² = 82.07, df = 9 (P < 0.00001), I² = 89.0%