Supplementary Online Content

Berry DA, Zhou S, Higley H, Mukundan L, Fu S, et al. Association of minimal residual disease with clinical outcome in pediatric and adult acute lymphoblastic leukemia: a meta-analysis [published online May 11, 2017]. *JAMA Oncol*. doi:10.1001/jamaoncol.2017.0580

This supplementary material has been provided by the authors to give readers additional information about their work.

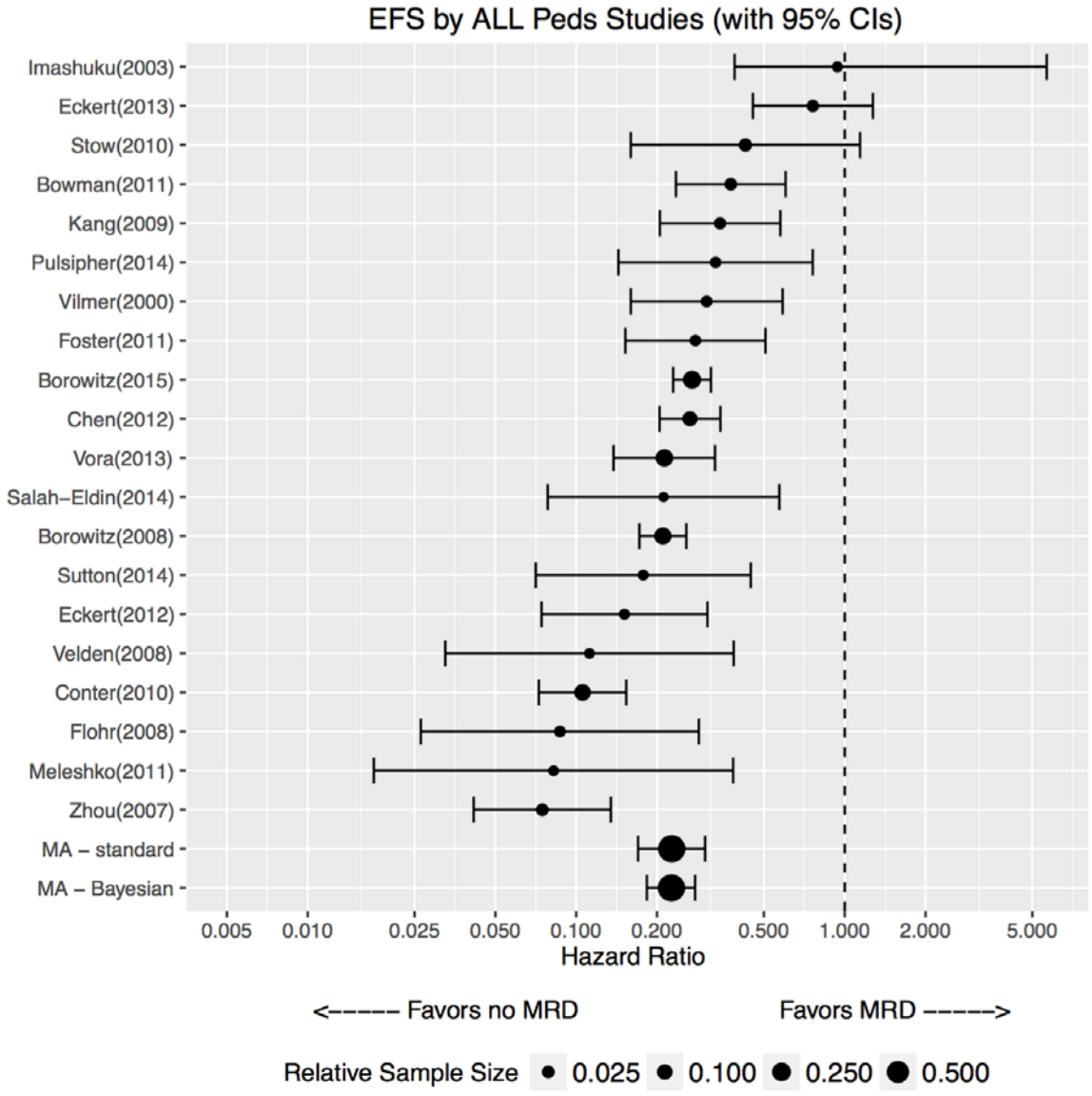
eTable 1. Characteristics of the studies included in this meta-analysis

Age group	First author	Year pu-blish	MRD Detec -tion	MRD cut-off (%)	MRD assess-ment period	Cyto-gen-esis	Cell pheno-type	Total sample size (MRD/no MRD)	Random or cohort	Med. follow -up (yrs)	Survival End Point	PMID
Ped	Vilmer	2000	PCR	0.5	Induction			150(61/89)	Random	6.9	EFS	12796792
Ped	Imashuku	2003	PCR	0.1	Other			67(12/55)	Cohort	1.13	EFS	21596436
Ped	Zhou	2007	PCR	0.1	Induction		B-cell	284(38/246)	Random	5.6	EFS	21370437
Ped	Flohr	2008	PCR	0.01	Induction			129(74/55)	Random	NA	EFS	26124497
Ped	Borowitz	2008	FC	0.01	Induction		B-cell	1971(383/1588)	Random	NA	EFS	23265714
Ped	Velden	2009	PCR	0.01	Induction		B-cell	54(30/24)	Random	4.83	EFS	19880498
Ped	Conter	2010	mixed	0.04	Induction	Ph–		1537 (189/1348)	Random	4.0	EFS	18388178
Ped	Kang	2010	FC	0.01	Induction			191(67/124)	Cohort	NA	EFS	24692146
Ped	Stow	2010	mixed	1	Induction		B-cell	379(63/316)	Cohort	NA	EFS	24924991
Ped	Meleshko	2011	PCR	0.01	Induction			61(22/39)	Cohort	3.5	EFS	24497539
Ped	Bowman	2011	FC	0.01	Induction		B-cell	245(84/161)	Cohort	NA	EFS	20304809
Ped	Foster	2011	FC	0.1	Other			116(18/98)	Cohort	NA	EFS	19212338
Ped	Chen	2012	FC	0.01	Induction		B-cell	964(220/744)	Cohort	NA	EFS	18239620
Ped	Eckert	2013	PCR	0.1	Induction			208(99/109)	Random	4.8	EFS/OS	21360654
Ped	Eckert	2013	PCR	0.1	Induction		B-cell	80(34/46)	Random	NA	EFS/OS	22368272
Ped	Vora	2013	PCR	0.01	Induction			2120(1030/1090)	Random	3.83	EFS	11187917
Ped	Pulsipher	2014	FC	0.01	Other			105(17/88)	Random	2.17	EFS	23775972
Ped	Salah-Eldin	2014	PCR	0.1	Induction		B-cell	46(34/12)	Cohort	1.38	EFS/OS	25312094
Ped	Sutton	2015	PCR	1	Other			69(31/38)	Cohort	4.8	EFS/OS	20154213
Ped	Borowitz	2015	FC	0.1	Induction	Ph–	B-cell	2473(685/1788)	Random	NA	EFS/OS	17485550
Adult	Mortuza	2002	PCR	0.1	Consol'n	Ph–		36(17/19)	Random	NA	EFS	24752047
Adult	Krampera	2003	FC	0.01	Induction		T-cell	47(18/29)	Cohort	1.42	EFS	24740809
Adult	Stirewalt	2003	PCR		Other	Ph+		63 (33/30)	Cohort	0.77	EFS	12652472
Adult	Pane	2005	PCR	0.1	Consol'n	Ph+		42(14/28)	Cohort	1.18	EFS/OS	16195338
Adult	Bruggemann	2006	PCR	0.01	Induction			111(38/73)	Cohort	4.58	EFS	18492099
Adult	Raff	2007	PCR	0.01	Other			105(28/77)	Cohort	1.34	EFS	22442346
Adult	Spinelli	2007	PCR	0.1	Other			37(25/12)	Cohort	1.92	OS	11844835
Adult	Holowieck	2008	FC	0.1	Induction	Ph–		116(38/78)	Cohort	1.42	EFS	19863538
Adult	Bassan	2009	PCR	0.01	Induction			112(54/58)	Cohort	3.0	EFS	15744351
Adult	Patel	2010	PCR	0.01	Induction	Ph–	B-cell	64(20/44)	Random	4.83	EFS	23836561
Adult	Lee	2012	PCR	0.1	Other	Ph+		95(62/33)	Cohort	5.0	EFS	17488684
Adult	Gokbuget	2012	PCR	0.01	Consol'n	Ph–		504(120/384)	Cohort	NA	EFS/OS	24961645
Adult	Ravandi	2013	PCR	0.1	Induction	Ph+		62(26/36)	Cohort	1.05	EFS/OS	22705993
Adult	Tucunduva	2014	mixed	0.1	Other	Ph+		98(59/39)	Cohort	3.0	EFS	19141862
Adult	Beldjord	2014	PCR	0.01	Induction	Ph–	B/T-cell	423(158/265)	Random	4.0	EFS	12492579
Adult	Ribera	2014	FC	0.05	Consol'n	Ph–		161	Cohort	3.75	EFS/OS	17023577
A & P	Vidriales	2003	FC	0.05	Induction			87(44/43)	Cohort	2.42	EFS/OS	21710165
A & P	Zhao	2012	mixed	0.01	Other			139(33/106)	Cohort	2.67	EFS/OS	22430088
A & P	Bachanova	2012	FC	0.1	Other			86(10/76)	Cohort	3.9	EFS/OS	12586618

eTable 2. Hazard ratios of EFS and OS and their respective Bayesian 95% credible intervals for each subgroup of patients in pediatric and adult ALL. Studies not included were either mixtures of subgroups or subgroup status was not indicated in the publications. See forest plots comparing pediatric and adult ALL studies in Figures 4A and 4B.

Subgroup	Event-free Survival (EFS)				Overall Survival (OS)			
	Pediatric ALL (20 studies)		Adult ALL (16 studies)		Pediatric ALL		Adult ALL	
	# studies	HR (95% BCI)	# studies	HR (BCI)	# studies	HR (95% BCI)	# studies	HR (BCI)
Analysis method								
Flow Cytometry	7	0.27 (0.20, 0.36)	3	0.32 (0.20, 0.51)	1	0.27 (0.22, 0.34)	1	0.28 (0.13, 0.61)
PCR	11	0.20 (0.11, 0.35)	12	0.24 (0.18, 0.32)	4	0.23 (0.09, 0.58)	4	0.29 (0.18, 0.49)
Analysis cutoff								
≤ 0.01%	9	0.30 (0.20, 0.46)	7	0.29 (0.21, 0.39)	0	--	1	0.25 (0.18, 0.35)
> 0.01%	11	0.18 (0.11, 0.29)	8	0.21 (0.14, 0.32)	5	0.23 (0.12, 0.47)	4	0.30 (0.18, 0.50)
Period assessed								
Induction	16	0.20 (0.15, 0.28)	7	0.33 (0.24, 0.44)	4	0.25 (0.11, 0.57)	1	0.54 (0.24, 1.20)
Consolidation	0	--	4	0.25 (0.18, 0.36)	0	--	3	0.27 (0.18, 0.40)
Other	4	0.20 (0.15, 0.28)	5	0.18 (0.08, 0.42)	1	0.18 (0.05, 0.63)	1	0.20 (0.04, 0.92)
Ph chromosome								
Ph–	2	0.17 (0.07, 0.42)	7	0.28 (0.22, 0.37)	2	0.27 (0.22, 0.34)	2	0.26 (0.17, 0.40)
Ph+	0	--	5	0.34 (0.22, 0.53)	0	--	2	0.38 (0.19, 0.75)
ALL type								
B-cell	9	0.21 (0.14, 0.30)	2	0.28 (0.17, 0.46)	2	0.18 (0.09, 0.38)	0	--
T-cell	0	--	2	0.31 (0.19, 0.53)	0	--	0	--
Study type								
RCT	11	0.19 (0.12, 0.29)	4	0.31 (0.21, 0.45)	3	0.25 (0.08, 0.74)	0	--
Database	9	0.29 (0.18, 0.45)	12	0.25 (0.18, 0.33)	2	0.21 (0.09, 0.51)	5	0.29 (0.19, 0.44)

eFigure 1. Hazard ratios of EFS and their 95% confidence intervals for the individual studies used in our pediatric ALL meta-analysis



eFigure 2. Hazard ratios of EFS and their 95% confidence intervals for the individual studies used in our pediatric ALL meta-analysis