Online only supplementary tables

Table S1. Demographic characteristics of the participants

Years of experience in paediatric cardiology	**n/total**	**%**
<1 year	0/100	0
1-5 years	4/100	4
> 5-10 years	13/100	13
> 10 years	83/100	83
Type of unit	**n/total**	**%**
Paediatric Cardiology	91/100	91
Paediatric critical care	3/100	3
Neonatology	1/100	1
Other	5/100	5
Total number of paediatric beds in the hospital	**n/total**	**%**
≤50	22/100	22
51-100	23/100	23
101-150	24/100	24
151-200	8/100	8
>200	17/100	17

Participants that selected the answer option "other" when asked about the type of unit in which they were working, reported working in a cardiology department that provides medical care also to adult patients or in a combined paediatric cardiology- critical care department.

Note that 6 of the participants did not answer the question on how many paediatric beds the hospital they work in has.

Table S2. ACE-I use for the management of cardiac diseases related to heart failure development

Cardiac disease	**n/ total**	**%**
Dilated cardiomyopathy (DCM)	95/100	95*
Congenital heart diseases (CHD)	97/100	97
None	0/100	0
Other	8/100	8

This was a multiple-choice question and also more than one condition could be typed in the box that displayed for participants that selected the answer option "other". Conditions reported under "other" included cardiac transplant, myocarditis, dyskinetic Kawasaki, rheumatic valvulopathy with valvar regurgitation and heart failure, iatrogenic heart failure.

* Please note, even though only 95% of the participants selected the answer option DCM in this question, 100% of the participants reported using ACE-I as therapy for symptomatic DCM related heart failure, either as initial or add-on therapy (table 1.). This means 5 of the participating physicians did not provide consistent answers in this regard.

ACE-I, Angiotensin-converting enzyme inhibitor.

Table S3. ACE-I use in patients with congenital heart defects after heart surgery

Post-surgery time	**n/total**	**%**
< 1 month	9/97	9
1 to 3 months	34/97	35
>3 months to 6 months	28/97	29
>6 months	7/97	7
No use after surgery	16/97	16

Note that 3 of the 97 participants to whom this question was applicable did not answer it.

ACE-I, Angiotensin-converting enzyme inhibitor.

Table S4. Aspects potentially related to the practice of prescribing ACE-I to newborns (0 – 27 days)

Hospital size: number of paediatric beds*	Use of ACE-I in newborns		p
	No	Yes	
Small hospital (< 100 paediatric beds)	13	26	0,158
Big hospital (≥100 paediatric beds)	11	44	

Years of working experience in paediatric cardiology	Use of ACE-I in newborns		p
	No	Yes	
Short working experience ≤ 10 years	3	14	0,548
Long working experience > 10 years	23	60	

Type of ACE-I formulation in use reported	Use of ACE-I in newborns		p
	No	Yes	
Liquid formulation	11	36	0,651
Other than liquid formulations	15	38	

P values were calculated with the use of Fisher's exact test.

*6 participants did not enter any response to this question. Similar results were obtained when other cut-off values were used to define big hospital (eg. ≥50 beds p = 0,559, ≥200 beds p = 0,786).

We did not observe any country dependent pattern; however, sample size was insufficient for a statistical test to be applied.

ACE-I, Angiotensin-converting enzyme inhibitor.

Table S5. Rationale for first-choice ACE-I selection

Reasons	Captopril In Newborns		Captopril In infants and toddlers		Enalapril In children		Enalapril In adolescents	
	n/ total	%	n/ total	%	n/ total	%	n/ total	%
More experience with use	50/54	93	55/63	87	38/55	69	43/55	78
Most appropriate formulation available	25/54	46	29/63	46	25/55	45	22/55	40
More convenient to parents/ patients	7/54	13	11/63	17	34/55	62	33/55	60
Recommended in guidelines/ books	24/54	44	29/63	46	20/55	36	22/55	40
Established in hospital protocols	25/54	46	29/63	46	16/55	29	12/55	22
No specific reason	0/54	0	0/63	0	0/55	0	1/55	2
Other	2/54	4	1/63	2	2/55	4	1/55	2

Age groups were defined as follows: newborns 0 to 27 days, infants and toddlers 28 days to 23 months, children 2 to 11 years and adolescents 12 years to 18 years [European Medicines Agency: CPMP/ICH/2711/99 ICH Topic E 11 Clinical Investigation of Medicinal Products in the Paediatric Population. http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002926.pdf, Last accessed February 2014].

Reasons entered under "other" for captopril included "less adverse events" and "licensed for hypertension in paediatrics". For enalapril these included "2 doses", "better efficacy expected" and "less adverse events"

One of the 55 participants that reported using enalapril in children did not answer this question.

Table S6. ACE-I starting dose by age group (mg/kg/dose)

ACEI	Newborns n median (range) mean (SD)	Infants and toddlers n median (range) mean (SD)	Children n median (range) mean (SD)	Adolescents n median (range) mean (SD)
Captopril	**n=49** 0.15 (0.01 - 1.00) 0.22 (0.22)	**n=52** 0.20 (0.03 - 1.00) 0.26 (0.24)	**n=22** 0.28 (0.05 - 1.00) 0.33 (0.27)	**n=5** 0.10 (0.10 - 0.50) 0.18 (0.18)
Enalapril	**n=11** 0.05 (0.005 - 0.10) 0.06 (0.03)	**n=17** 0.05 (0.02 - 0.10) 0.06 (0.03)	**n=42** 0.10 (0.01 - 0.20) 0.08 (0.04)	**n=41** 0.10 (0.01 - 0.25) 0.09 (0.05)
Lisinopril	**n= 2** 0.08 (0.05 - 0.10) 0.08 (0.04)	**n=5** 0.10 (0.05 - 0.10) 0.08 (0.03)	**n=6** 0.10 (0.05 - 0.20) 0.13 (0.06)	**n=10** 0.10 (0.05 - 0.30) 0.13 (0.08)
Perindopril	NA	NA	**n=1** 0.05 0.05	**n=3** 0.10 (0.05 - 0.10) 0.08 (0.03)
Ramipril	NA	**n=1** 0.10 0.10	**n=2** 0.06 (0.01 - 0.10) 0.06 (0.06)	**n=5** 0.05 (0.01 - 0.10) 0.06 (0.04)

Where a participant entered a range of doses, the reported minimum dose value was considered to be the starting dose. Answers were excluded from analysis if: (1) the exact requested information (starting dose in mg/kg/dose) was not provided, (2) target dose reported was smaller than starting dose or (3) the dose entered was considered not to be compatible with current knowledge (10 times or more above the larger doses that have been reported in literature for children and/or adults). The number of participants whose answers could be taken into consideration for the calculations in each case is indicated.

One participant selected trandolapril as first-choice ACE-I in adolescents, however his starting dose answer had to be excluded from analysis (dose per kg not compatible with current knowledge).

NA, not applicable; an ACE-I was not selected by any participant as first-choice within a certain age group and thus, no dosage data were requested.

ACE-I, Angiotensin-converting enzyme inhibitor.

Table S7. ACE-I target/maintenance dose by age group (mg/kg/day)

ACEI	Newborns n median (range) mean (SD)	Infants and toddlers n median (range) mean (SD)	Children n median (range) mean (SD)	Adolescents n median (range) mean (SD)
Captopril	**n=48** 1.50 (0.01 - 7.50) 1.58 (1.23)	**n=54** 2.00 (0.20 - 6.00) 1.99 (1.14)	**n=24** 2.00 (0.30 - 6.00) 2.30 (1.56)	**n=6** 1.25 (0.50 - 5.00) 1.75 (1.64)
Enalapril	**n=14** 0.15 (0.03 - 1.00) 0.27 (0.29)	**n=21** 0.40 (0.10 - 1.00) 0.41 (0.26)	**n=45** 0.40 (0.10 - 1.50) 0.42 (0.32)	**n=44** 0.40 (0.10 - 1.50) 0.43 (0.27)
Lisinopril	**n=3** 0.20 (0.20 - 0.25) 0.22 (0.03)	**n=6** 0.40 (0.20 -1.00) 0.53 (0.38)	**n=8** 0.34 (0.20 - 1.00) 0.48 (0.34)	**n=9** 0.33 (0.10 - 1.00) 0.39 (0.27)
Perindopril	NA	NA	**n=1** 0.08 0.08	**n=3** 0.13 (0.10 - 0.15) 0.13 (0.03)
Ramipril	NA	**n=1** 0.20 0.20	**n=2** 0.13 (0.05 - 0.20) 0.13 (0.11)	**n=6** 0.13 (0.05 - 0.30) 0.15 (0.09)

Where a participant entered a range of doses, the median value was recorded as the maintenance dose. Answers were excluded from analysis if: (1) the exact requested information (maintenance dose in mg/kg/day) was not provided, (2) target dose reported was smaller than starting dose or (3) the dose entered was considered not to be compatible with current knowledge (10 times or more above the larger doses that have been reported in literature for children and/or adults). The number of participants whose answers could be taken into consideration for the calculations in each case is indicated.

One participant selected trandolapril as first-choice ACE-I in adolescents, however his starting dose answer had to be excluded from analysis (dose per kg not compatible with current knowledge).

NA, not applicable; an ACE-I was not selected by any participant as first-choice within a certain age group and thus, no dosage data were requested.

ACE-I, Angiotensin-converting enzyme inhibitor.

Table S8. Captopril starting (mg/kg/dose) and maintenance/target dose (mg/kg/day)

Captopril starting dose (mg/kg/dose)													Captopril maintenance dose (mg/kg/day)											
Neonates			**Infants and toddlers**			**Children**			**Adolescents**				**Neonates**			**Infants and toddlers**			**Children**			**Adolescents**		
	n/total	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**			**n/total**	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**
0.01	3/49	6	0.03	1/52	2	0.05	1/22	5	0.10	4/5	80		0.01	1/48	2	0.20	2/54	4	0.30	1/24	4	0.50	1	17
0.02	2/49	4	0.05	2/52	4	0.10	7/22	32	0.50	1/5	20		0.05	1/48	2	0.30	1/54	2	1.00	5/24	21	1.00	2	33
0.03	1/49	2	0.10	21/52	40	0.20	2/22	9					0.10	1/48	2	0.50	1/54	2	1.20	1/24	4	1.50	2	33
0.05	5/49	10	0.15	1/52	2	0.25	1/22	5					0.20	1/48	2	0.75	1/54	2	1.25	1/24	4	5.00	1	17
0.10	13/49	27	0.20	8/52	15	0.30	3/22	14					0.30	2/48	4	0.85	1/54	2	1.50	2/24	8			
0.15	2/49	4	0.25	2/52	4	0.50	6/22	27					0.60	2/48	4	1.00	8/54	15	2.00	6/24	25			
0.20	8/49	16	0.30	5/52	10	1.00	2/22	9					0.65	1/48	2	1.05	1/54	2	2.50	1/24	4			
0.25	2/49	4	0.33	1/52	2								0.75	1/48	2	1.20	1/54	2	3.00	3/24	13			
0.30	4/49	8	0.50	8/52	15								1.00	10/48	21	1.25	1/54	2	4.00	1/24	4			
0.33	1/49	2	1.00	3/52	6								1.20	1/48	2	1.50	8/54	15	5.00	1/24	4			
0.50	6/49	12											1.25	1/48	2	2.00	10/54	19	6.00	2/24	8			
1.00	2/49	4											1.50	9/48	19	2.25	2/54	4						
													2.00	8/48	17	2.50	3/54	6						
													2.25	2/48	4	3.00	9/54	17						
													2.50	1/48	2	3.50	1/54	2						
													3.00	4/48	8	4.00	2/54	4						
													4.00	1/48	2	4.50	1/54	2						
													7.50	1/48	2	6.00	1/54	2						

Table S9. Enalapril starting (mg/kg/dose) and maintenance/target dose (mg/kg/day)

Enalapril starting dose (mg/kg/dose)											Enalapril maintenance dose (mg/kg/day)										
Neonates			**Infants and toddlers**			**Children**			**Adolescents**			**Neonates**			**Infants and toddlers**			**Children**			**Adolescents**		
	n/total	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**		**n/total**	**%**
0.005	1/11	9	0.02	1/17	6	0.01	1/42	2	0.01	1/41	2	0.03	1/14	7	0.10	1/21	5	0.10	5/45	11	0.10	3/44	7
0.03	1/11	9	0.03	1/17	6	0.03	2/42	5	0.025	1/41	2	0.10	5/14	36	0.15	2/21	10	0.15	4/45	9	0.15	3/44	7
0.05	6/11	55	0.05	9/17	53	0.04	1/42	2	0.03	3/41	7	0.15	2/14	14	0.175	1/21	5	0.175	1/45	2	0.20	5/44	11
0.10	3/11	27	0.10	6/17	35	0.05	16/42	38	0.05	9/41	22	0.20	2/14	14	0.20	4/21	19	0.20	4/45	9	0.25	2/44	5
						0.10	20/42	48	0.10	24/41	59	0.30	1/14	7	0.25	1/21	5	0.25	2/45	4	0.30	4/44	9
						0.20	2/42	5	0.20	2/41	5	0.50	1/14	7	0.40	3/21	14	0.30	4/45	9	0.40	6/44	14
									0.25	1/41	2	0.75	1/14	7	0.50	6/21	29	0.35	2/45	4	0.475	1/44	2
												1.00	1/14	7	0.75	1/21	5	0.40	6/45	13	0.50	15/44	34
															1.00	2/21	10	0.50	10/45	22	0.75	1/44	2
																		0.60	1/45	2	0.80	1/44	2
																		0.75	1/45	2	1.00	2/44	5
																		0.80	1/45	2	1.50	1/44	2
																		1.00	2/45	4			
																		1.50	2/45	4			

Table S10. Supply of ACE-I formulations prescribed when the adults' tablets are not suitable

Source	**n /total**	**%**
Provided by hospital pharmacy	66/100	66
Provided by community pharmacy	73/100	73
Prepared by parents	12/100	12
Other	2/100	2
Source (combinations)	**n /total**	**%**
Only provided by hospital pharmacy	21/100	21
Only provided by community pharmacy	28/100	28
Only prepared by parents	3/100	3
Only "other"	1/100	1
Hospital pharmacy + community pharmacy	37/100	37
Parents + hospital pharmacy	2/100	2
Parents + community pharmacy	2/100	2
Hospital pharmacy + community pharmacy + "other"	1/100	1
Parents + community pharmacy + hospital pharmacy	5/100	5

More than one response was possible to this question.
"Licensed liquid formulations" was entered under "other".

Table S11. Types of formulations of ACE-I prescribed when the adults' tablets are not suitable

Type of formulation	**n/total**	**%**
Liquid	47/100	47
Capsules	44/100	44
Powder	27/100	27
Other	5/100	5
Type of formulation (combinations)	**n/total**	**%**
Only liquid	31/100	31
Only capsules	27/100	27
Only powder	16/100	16
Only other	3/100	3
Liquid + capsules	11/100	11
Liquid + powder	5/100	5
Powder + capsules	5/100	5
Capsules + other	1/100	1
Powder + other	1/100	1

More than one response was possible to this question.
"Tablets" were entered under "other".

Table S12. Drugs used for asymptomatic heart failure related to dilated cardiomyopathy

Drug class	n/total	%
ACE-I	81/89	91
ARB	6/89	7
Beta-blockers	49/89	55
Loop Diuretic	17/89	19
Thiazide Diuretic	6/89	7
Aldosterone antagonists	25/89	28
Cardiac glycosides	2/89	2
Other	1/89	1

This was a multiple-choice question. Note that one of the 89 participants that reported using drug therapy for patients with asymptomatic heart failure due to dilated cardiomyopathy did not answer this question.

Acetylsalicylic acid was the drug reported under "other".
ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers.

Table S13. Drug regimens used for the therapy of asymptomatic dilated cardiomyopathy related heart failure

Drug combinations	n/total	%
Single-drug regimen		
ACE-I	26/89	29
Aldosterone antagonist	1/89	1
Beta-blocker	3/89	3
Two-drug regimen		
ACE-I + Aldosterone antagonist	3/89	3
ACE-I + ARB	1/89	1
ACE-I + Beta-blocker	26/89	29
ACE-I + Loop diuretic	3/89	3
Aldosterone antagonist + Loop diuretic	2/89	2
Beta-blocker + Thiazide diuretic	1/89	1
Three-drug regimen		
ACE-I + ARB + Beta-blocker	2/89	2
ACE-I + Aldosterone antagonist + Beta-blocker	5/89	6
ACE-I + Aldosterone antagonist + Loop diuretic	2/89	2
Four-drug regimen		
ACE-I + Aldosterone antagonist + ARB + Beta-blocker	1/89	1
ACE-I + Aldosterone antagonist + Beta-blocker + Loop diuretic	3/89	3
ACE-I + Aldosterone antagonist + Beta-blocker + Thiazide diuretic	1/89	1
ACE-I + Aldosterone antagonist + Beta-blocker + Cardiac glycoside	1/89	1
ACE-I + Aldosterone antagonist + Loop diuretic + Thiazide diuretic	1/89	1
ACE-I + Beta-blocker + Loop diuretic + Acetylsalicylic acid	1/89	1
Five-drug regimen		
ACE-I + Aldosterone antagonist + ARB + Beta-blocker + Loop diuretic	1/89	1
ACE-I + Aldosterone antagonist + Beta-blocker + Loop diuretic + Cardiac glycoside	1/89	1
ACE-I + Aldosterone antagonist + Beta-blocker + Loop diuretic + Thiazide diuretic	2/89	2
Six-drug regimen		
ACE-I + Aldosterone antagonist + ARB + Beta-blocker + Loop diuretic + Thiazide diuretic	1/89	1

Note that one of the 89 participants that reported using drug therapy for patients with asymptomatic heart failure due to dilated cardiomyopathy did not answer this question.
ACE-I, angiotensin-converting enzyme inhibitors; ARB, angiotensin II receptor blockers.