Appendix A: Clinical data on cases of testicular ascent

Clinical data on cases of testicular ascent

References	No. Cases	Mean Age (yrs)	Position (at surgery)				No. Hernias/ Testes	No. Side (unilat/bilat)
			Prescrotal/ High Scrotal	Superficial Inguinal Pouch	Inguinal	Abdominal		
Myers and Officer[10]	7	6.6	—	—	—	—	—	3/4
Atwell[28]	10	9.4	7	1	2	—	10/11	9/1
Schiffer et al[29]	3	6.7	—	2	—	—	—	3/0
Belman[30]	6	—	1	4	1	—	3/6	—
Robertson et al[31]	13	8.1	—	—	—	—	10/13	13/0
Eardley et al[32]	34	7.5	15	19	3	—	24/39	29/5
Mayr et al[33]	19	7.0	5	9	13	—	14/27	19/2
Rabinowitz and Hulbert[34]	21	7.2	2	19	2	—	12/23	19/2
Gracia et al[35]	36	7.0	8	5	32	1	18/46	11/8
Clarnette et al[36]	25	7.6	—	—	—	—	10/33	17/8
Rusnack et al[37]	91	7.4	79	11	—	1	39/91	91/0
Total No. (%)	265		117 (48)	70 (29)	53 (22)	2	140/289 (48)	77 (23)

* As published in *Journal of Urology*
Barthold JS and Gonzalez R: The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy. J Urol 2003; 170: 2396.

Appendix B: Evidence table of studies examining the association of CAG repeats in the AR gene and cryptorchidism

Sasagawa2000	Ferlin2005	Silva-Ramos2006	Radpour2007
Study characteristics			
Tokyo, Japan Case-control	Padova, Italy Case-control, prospectively recruited.	Porto, Portugal Case-control, prospectively recruited from two hospitals.	Tehran, Iran Case-control
Sample characteristics			
48 Japanese Pts w/crypto (age 1-32, mean 13 yrs); 17 BL, 29 UL UDT and 2 w monorchia). Controls: 100 males w/ proven fertility	105 ex-cryptorchid men (55 UL; 50 BL) who presented no other obvious causes of testicular damage. Age 23–42 yrs, age at orchidopexy 1-12 years . Precise location of testes at surgery could not be determined in all cases. 115 fertile non-cryptorchid controls whose wives were pregnant.	42 cryptorchid boys (age 3 -77; mean 20.9 yrs); 7 BL, 35 UL (6 w/ clinically patent processsus vaginalis (PPV) in the contra-lateral; 3 UL ectopic; 2 UL intra-abdominal). Six w/ family hx of crypto. (Cases should not present any other genital malformation). 31 controls (hospital staff) w/o personal or family hx of genital abnormalities; age 22-69 yrs, mean 42 yrs.	76 unrelated Iranian males w/ crypto (27 UL; 49 BL) w/o spontaneous descent. 190 healthy fertile controls. All studied patients were 46,XY males. Patients with visible cytogenetic aberrations were excluded.
Measurement of CAG repeats			
Genomic DNA from peripheral leukocytes amplified by PCR (30 cycles). Repeat length analysis by GeneScan.	Genomic DNA extracted from peripheral blood leuco-cytes. AR exon 1 amplified in two different PCR reactions under the same standard conditions with 8% dimethylsulphoxide and same cycle.	Genomic DNA extracted from blood samples stored at -20°C & amplified by PCR.	Genomic DNA from peripheral blood lymphocytes was amplified by PCR in 2 different reactions. Genotyping done blinded to case-control status.
Cryptorchidism ascertainment			
Not indicated.	Cohort of men previously orchidopexied.	Sole inclusion criterion was the presence of crypto.	Ultrasound examination of the testes.
CAG repeats among cryptorchidism cases (mean ± SD; second line range and median)			
23.4 ± 0.48 (overall) Range: 16 – 32; median: 23	21.8 ± 2.9 (overall 105 crypto) Range: 12 – 29; median: 22	22.4 ± 3.2 (overall) (p-v=0.206) Range: 15 – 29; median: 22.5	21.9 ± 2.5 (overall) Range: 17 – 30; median: 21
23.7 ± 0.64 (31 UL) Range: 18 – 32; median: 24	21.8 ± 3.0 (55 UL) Range: 12 – 29; median: 21	22.1 ± 3.3 (35 UL) (p-v=0.474) Range: 15 – 29; median: 21	21.5 ± 0.8 (27 UL) Range: 17 – 29; median: 21
23.8 ± 0.69 (17 BL) Range: 16 – 28; median: 23; (SE rather than SD provided)	21.8 ± 2.7 (50 BL) Range: 13 – 27; median: 22	24.7 ± 1.8 (7 BL) (p-v=0.019) Range: 21 – 26; median: 25.5 25.2 ± 2.9 (6 UL w/ PPV) Range: 20 – 29; median: 25	22.4 ± 1.6 (49 BL) Range: 19 – 30; median: 22
CAG repeats among controls			
23.5 ± 0.29 Range: 15 – 32; median: 23	21.6 ± 3.3 Range: 9 – 31; median: 22	21.5 ± 2.7 Range: 16 – 26; median: 22	21.8 ± 2.8 Range: 16 – 28; median: 21

Appendix C - Evidence table of studies examining the association of ESR1 SNPs and cryptorchidism

Yoshida2005	Galan2007	Wang2008
Study characteristics		
Tokyo, Japan, 1995-2003 Case-control	Florence, Italy Case-control	USA (Wilmington, DE) Case-control
Sample characteristics		
63 Japanese cryptorchid males, aged 1–13 yr, (median, 5.0 yrs) and 47 control males, aged 4–12 yr (median, 7.5 yrs) 47 UL: inguinal region in 39; abdominal cavity in 7; 1 vanishing testis. 16 BL: both testes inguinal region in 15; abdominal cavity in 1 Individuals recruited from the urban or suburban area of Tokyo or Yamagata City. They were free of particular residential environments, specific dietary habits, and intake of drugs with hormonal effects.	118 cryptorchid males of Italian origin (Central Italy); 71 UL, 47 BL The Italian control group includes 168 men from Central Italy with normal sperm parameters and no hx of cryptorchidism.	152 cryptorchid males who had non-syndromic UL (120) or BL (32) UDT, and had no other discernible congenital abnormalities UDT located in the prescrotal region, external ring, or superficial inguinal pouch, inguinal canal or abdominal area 160 unrelated control subjects All Pts & controls recruited from A.I. duPont Hospital for Children [Wilmington] Exclusion criteria: boys with a hx of prematurity, and those with retractile testes, or that spontaneously descended within the first 6 months of life.
Sample and genetic analysis methods		
30 SNPs were measured along the ESR1 gene. Leukocyte genomic DNA was amplified by PCR with primers designed to amplify a 300-bp region around e/SNP. Genotyping performed by 5' nuclease assay (TaqMan method). Haplotype analysis performed to identify one associated with cryptorchidism phenotype.	Germline DNA extracted from peripheral blood. For controls, DNA from frozen semen was used too. Five polymorphisms for the AGATA haplotype were genotyped by PCR protocols. Genotyping quality controls were performed.	Genomic DNA was obtained from peripheral blood leukocytes, buccal swab, or tissues from orchidopexy or circumcision. Puregene DNA purification kits were used for DNA extraction. TaqMan SNP Genotyping Assays was used to genotype the 5 SNPs (SNP10-SNP14). Haplotype association analysis performed using PLINK v1.01.
Cryptorchidism ascertainment		
Not specified	Not specified	Not specified
Control selection		
Controls (came from the urban or suburban area of Tokyo or Yamagata City) were found to have no discernible abnormality by cytogenetic, skeletal, and endocrine studies	Of the 168 men, 109 fathered at least one child spontaneously or had normal fertilization after IVF for pure female (tubal) factor infertility, whereas 59 men were students from the local university.	The 160 controls were healthy male infants and children presenting for circumcisions or voiding problems. Each boy had full descent of the testes, no significant testicular retractility, and no additional urogenital anomalies or known syndromes.
Haplotype frequency distribution and association		
15 of 30 SNPs presented certain degree of heterozygosity. These were in HWE. Within block covering SNPs 10-14, four major haplotypes accounted for 95% (patients) and 93% (controls) of all haplotypes. AGATA haplotype frequency was greater in patients than in controls. SNP 12: A vs G OR=1.99 (95% CI 1.07, 3.67)	SNP10-13 did not deviate from HWE but SNP14 deviated in both cases and controls. SNP12 frequencies: GG GA AA Crypto 101 (85.6) 17 (14.4) 0 (0.0) Control 124 (73.8) 43 (25.6) 1 (0.6) OR=0.50 (95% CI 0.28, 0.90)	No difference in distribution of race was found between cases and controls. SNPs in Caucasian group were in HWE. No difference for SNP12 in Caucasians. Severe cases were more likely to have a GG genotype than moderate cases, OR=8.8 (1.1, 69.7). G allele OR=9.3 (1.2, 73.4). Mild cases were also less likely to have GG genotype and G allele compared to severe case but not significantly.

Appendix D - Evidence table of studies assessing the association between maternal alcohol consumption and cryptorchidism

Damgaard2007	Jensen2007	Strandberg-Larsen2009	Mongraw-Chaffin2008
Study characteristics			
Copenhagen, Denmark 1997-00, Turku, Finland 1997-99. Prospective birth cohort study. Eligible women (2,229 Danish and 2,728 Finnish) residing in hospital referral areas were consecutively recruited during early pregnancy. Inclusion criteria: both parents and grandparents of the unborn child had to be born and raised in Denmark or Finland.	Aarhus, Denmark 1984-87. Prospective collection of prenatal exposures and obstetric information from a 16–19 years of follow-up in a nationwide patient register. Population-based random sample (n = 15,434) of boys born January 1984 and December 1987 drawn in the Danish Civil Registration system to assess comparability of the cohort.	Copenhagen, Denmark 1996–2002 (The Danish National Birth Cohort). Partial overlap (22%) with Damgaard's Danish cohort. Pregnant women invited to participate by their GP at first antenatal visit. Fifty percent of GP participated and 60% of invited women consented. Analysis limited to women who gave birth to a singleton boy and completed first interview.	Berkeley, CA, USA 1959-1967 Prospective study ≥40-yr f-up of 20,754 pregnancies occurring b/w 1959-67 in CA. Cases were matched to three controls from the same cohort on birth year and race. If more than three controls were available, these were selected at random from the pool of matches.
Sample characteristics			
Denmark, 1,042 boys (1,029 mothers), Finland 1,454 boys (1,446 mothers). 128 cryptorchid boys at birth [matched w/ 2,368 healthy controls] (94 Danish, 34 Finnish) Only 33 (19 Danish, 14 Finnish) [matched w/ 2,215 healthy controls] remained cryptorchid at 3 mos.	5,716 boys, 270 cases of crypto diagnosed, 185 of these underwent orchiopexy. Mothers: average gestational alcohol intake of five or more drinks per week. Age, parity, alcohol consumption smoking habits, infertility treatment.	41,268 live-born singleton, 1,598 cases. Of these, 355 boys were diagnosed with crypto but had no maternal report. Of the 810 boys diagnosed with crypto, ["diagnosis of crypto"] 398 had orchiopexy ["orchipexy"]	84 cases at birth persisting to at least age 2 yrs among 7,574 live-born sons whose mothers were interviewed in early pregnancy.
Alcohol consumption ascertainment			
Quantitative data on alcohol consumption, smoking, and caffeine intake obtained by questionnaire and/or interview once during the third trimester of pregnancy, before pregnancy outcome known. For a sub-group (n = 465) [no specification on who they were – cohort and/or controls], information on alcohol consumption was obtained twice during pregnancy by interviews.	Pregnant women attending their last scheduled regular antenatal care visit (~36th gestational wk), filled in a comprehensive self completed questionnaire, and returned it by mail. Alcohol/wk [units = 12g. of alcohol]. Binge episodes [intake of 8+ units of alcohol on one occasion]	Maternal alcohol consumption assessed in two computer-assisted telephone interviews around gestational weeks 17 and 32. One drink = one bottle of beer (0.33 l), one glass of wine, or one glass of spirits, each approx. 12 g of alcohol. Total = sum of weekly intake. Binge drinking: 5+ drinks on a single occasion since the onset of pregnancy.	In structured interview, mother's alcohol consumption ascertained by asking how many glasses of beer, wine, or whiskey she drank in a week. Total drinks of alcohol consumed per wk were obtained by adding the number of glasses drunk per week for the 3 beverages.
Cryptorchidism ascertainment			
Examination at birth and 3 months. Preterm boys examined at expected delivery date. Gestational age based on routine US at 18–20 wks. When not available (2.1%), last menstrual period used. Data on birth weight and parity obtained from birth records. Testis considered cryptorchid if found in a high scrotal, supra-scrotal or inguinal position or if non-palpable. Retractile testes considered a normal variant. Majority were transient cryptorchid cases but still presented slightly elevated gonadotropin levels at 3 months.	Cases ascertained by clinical examination at birth and at 3 mos. Most cases were transient (spontaneous descent within 3 months). Among persistent cases no excess risk was observed (only 33 observations). All diagnosis or surgical procedures during hospital admissions of these boys in the yrs. 1984–2003 were extracted from the Danish National Patient Register. Two endpoints: boys having a crypto diagnosis without orchiopexy ('no orchiopexy') and boys with a diagnosis who also underwent	Maternal report at 6 or 18 months and/or crypto dx in National Hospital Discharge Registry (NHDR), 398 of 1,598 were verified by orchiopexy (identified in the NHDR).	Condition should be present at 2 yrs of age to examine risk factors for persistent crypto.

Damgaard2007	Jensen2007	Strandberg-Larsen2009	Mongraw-Chaffin2008
	orchiopexy ('orchiopexy').		
Univariate estimate			
Drinks/week continuous (*): (n= 2,477) 1.26 (1.13–1.40) Binge [five or more alcoholic drinks at one occasion/ day] episodes: Yes 1.25 (0.85, 1.87) (*) Additionally, several OR from 0 drink to ≥ 9 drinks per week Drinks/wk OR (95% CI) 0 Ref 0.1-4.9 1.69 (1.16, 2.45) ≥ 5 4.97 (2.00, 12.40)	Risk ratios, ref (<1 drink/wk) a) All cases (n=270) 1-4 0.9 (0.7, 1.1) 5-9 0.7 (0.4, 1.3) ≥10 0.8 (0.2, 2.5) b) Surgery (n=185) 1-4 0.8 (0.6, 1.1) 5-9 0.6 (0.3, 1.2) ≥10 0.7 (0.2, 3.0) c) No surgery (n=85) 1-4 1.0 (0.6, 1.5) 5-9 1.1 (0.5, 2.4) ≥10 0.9 (0.1, 6.7) Binge episodes (Ref=No) RR for binge drinking a) All cases 1.2 (0.9, 1.7) b) Surgery 1.3 (0.9, 1.9) c) No surgery 1.0 (0.6, 1.8)	Hazard ratio, ref (0 drinks/wk) a) Maternal report of crypto dx 0.5-1.5 0.87 2-3.5 0.82 4+ 0.63 b) Crypto dx c) Surgery 0.5-1.5 0.92 0.89 2-3.5 0.87 0.77 4+ 0.61 0.77 Binge drinking episodes a) Maternal report of crypto dx 1 0.90 2 0.89 3+ 0.99 b) Crypto dx c) Surgery 1 0.86 0.74 2 0.79 0.56 3+ 0.94 0.93	Odds ratio 3.3 drinks/wk 1.05 (0.86, 1.29)
Multivariate estimate			
MV odds ratio (OR) adjusted for country, smoking, caffeine intake, maternal age, social class, parity, birth weight. Ref: 0 drinks/wk. Drinks/week continuous: (n=2,477) 1.17 (1.03, 1.34) Binge episodes: Yes 1.18 (0.77, 1.83) Drinks/wk OR (95% CI) 0.1-4.9 0.95 (0.61, 1.49) ≥ 5 3.10 (1.05, 9.10)	MV risk ratios (RR) adjusted for maternal and paternal age at delivery, time to index pregnancy, infertility txt, parity, SES group, mother's daily smoking, birth weight, gestational age, placental weight. Ref: < 1 drink/wk a) All cases (n=270) 1-4 0.9 (0.7, 1.2) 5-9 0.7 (0.4, 1.3) ≥10 0.7 (0.2, 2.2) b) Surgery (n=185) 1-4 0.8 (0.6, 1.2) 5-9 0.5 (0.2, 1.2) ≥10 0.6 (0.1, 2.7) c) No surgery (n=85) 1-4 1.0 (0.6, 1.6) 5-9 1.1 (0.5, 2.6) ≥10 0.8 (0.1, 6.0) Binge episodes No (Ref) a) All cases (n=270) Yes 1.3 (0.9, 1.8) b) Surgery (n=185) Yes 1.4 (0.9, 2.1) c) No surgery (n=85) Yes 1.0 (0.5, 1.8)	MV hazard ratio (HR) adjusted for maternal age, parity, time to pregnancy, infertility txt, self-reported diabetes, smoking, occupational status. Ref: 0 drinks/wk a) Maternal report of crypto dx 0.5-1.5 0.89 (0.79, 0.99) 2-3.5 0.82 (0.69, 0.99) 4+ 0.63 (0.41, 0.94) b) Crypto dx 0.5-1.5 0.93 (0.80, 1.08) 2-3.5 0.87 (0.68, 1.12) 4+ 0.58 (0.32, 1.06) c) Surgery 0.5-1.5 0.91 (0.73, 1.13) 2-3.5 0.79 (0.54, 1.15) 4+ 0.77 (0.36, 1.63) Binge drinking a) Maternal report of crypto dx 1 0.88 (0.77, 1.02) 2 0.85 (0.70, 1.06) 3+ 0.94 (0.73, 1.21) b) Crypto dx 1 0.83 (0.68, 1.01) 2 0.73 (0.53, 1.01) 3+ 0.85 (0.60, 1.21) c) Surgery 1 0.70 (0.52, 0.94) 2 0.50 (0.29, 0.85) 3+ 0.81 (0.49, 1.34)	MV odds ratio (OR) adjusted for smoking, caffeine consumption, body mass index, son's birth weight. 3.3 drinks/wk 0.99 (0.83, 1.20)

Appendix E - Definitions

Pediatricians are physicians who are board certified in pediatrics.

Primary Care Providers, in the context of these guidelines, are any licensed healthcare professionals who provide primary care services to patients.

Providers include, in the context of these guidelines, any licensed health care professional involved in the care of patients with suspected cryptorchidism such as: allied health professionals (Nurse Practitioners, Registered Nurses, Physicians' Assistants), physicians: pediatricians (including subspecialists), urologists and general surgeons (including subspecialists), or other licensed health professionals with specialized training and/or medical expertise in this area.

Specialists refer to a physician or allied health professional or other licensed health professional with specialized training/expertise, who are trained in a particular specialty of medicine including urology, endocrinology, or pediatric subspecialty.

Surgical Specialists refer to any physician who is trained or who has expertise in a specific branch of surgery, including (in the context of this guideline) urologic surgery, pediatric general surgery, or pediatric urology.

Appendix F - Distribution of nonpalpable testes location as identified by diagnostic laparoscopy

Group	Absent/Unknown Vanishing/Atrophic	Inguinal	Internal ring/Peeping	Intra-abdominally/ Above internal ring
#1: ≤16 year-old[68-100]	Meta-analytic mean*=33.2%, I^2=92% Minimum=3.4%	Skewed distribution with 44% null	Skewed distribution with 44% null	Meta-analytic mean*=40.3%, I^2=91% Minimum=8.8 %
#2: Prepubertal + older males or unknown[101-115]	Skewed distribution with meta-analytic mean*=32.5%, I^2=92% Minimum=13.5%	Skewed distribution with 33% null	Zero-inflated distribution with 47% null. Non-null values centered at 35%.	Meta-analytic mean*=36.9%, I^2=78% Minimum=21.6%

***Meta-analytic mean indicates that estimate of the mean was obtained using meta-analysis. I^2 indicates the degree of heterogeneity.**

These cohorts were divided into two groups (see Table 3). Group #1 includes boys 16 years-old and younger (34 cohorts).[69-100] Group #2 includes cohorts with a large proportion of prepubertal boys (mean or median age is small), as well as some cases where the male is older than 16.[101-115] Two cohorts in Group #2 do not report the age distribution.[110,113] Therefore, the distribution of the location of testes was estimated separately for these two sets of cohorts.

In Group #1, a total of 3,166 testes were assessed for an average of 93 testes per study; for Group #2, 1,525 testes were assessed and yielded an average of 102 testes per study. For the purpose of determining the distribution, absent/ unknown testes and vanishing or atrophic were all combined because it is suspected that these are not well differentiated in some studies. Eight studies[101-103,106,112,114,115] showed differentiation between absent and vanishing testes; the average rate of absent/unknown testes in these cohorts was 3%.

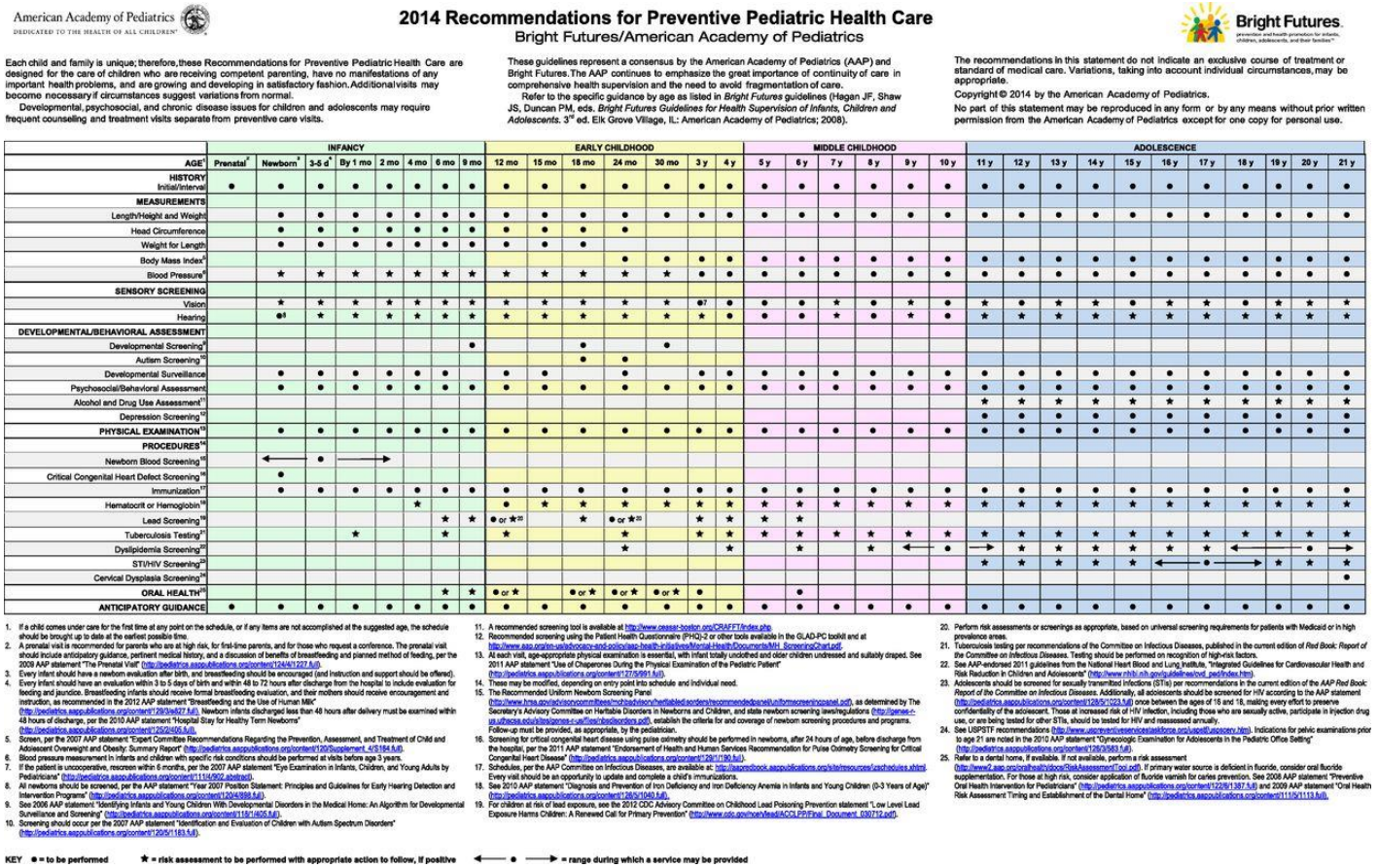
Distributions were similar between the two groups, excluding older cohorts. In these cases, the minimum percent of intra-abdominally located testes was higher in Group #2 than in Group #1 (21.6% vs. 8.8%). Similarly, the minimum percent of absent or vanishing testes was also higher in Group #2 than in Group #1 (13.5% vs 3.4%). These data suggests more intra-abdominally testes will be present in older boys.

This meta-analysis shows that in any cohort of diagnostic laparoscopy for nonpalpable testes, at least 8% of testes will be located intra-abdominally and a small percent of testes will be absent/vanishing/atrophic (3.4%).

References for Appendix F

Full citations available in *Evaluation and Treatment of Cryptorchidism: AUA Guideline*.

Appendix G. Academy of Pediatrics 2014 Recommendations for Preventative Pediatric Health Care



American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

2014 Recommendations for Preventive Pediatric Health Care
Bright Futures/American Academy of Pediatrics

Bright Futures
promotion and health promotion for infants, children, adolescents, and their families™

Each child and family is unique; therefore, these Recommendations for Preventive Pediatric Health Care are designed for the care of children who are receiving competent parenting, have no manifestations of any important health problems, and are growing and developing in satisfactory fashion. Additional visits may become necessary if circumstances suggest variations from normal.

Developmental, psychosocial, and chronic disease issues for children and adolescents may require frequent counseling and treatment visits separate from preventive care visits.

These guidelines represent a consensus by the American Academy of Pediatrics (AAP) and Bright Futures. The AAP continues to emphasize the great importance of continuity of care in comprehensive health supervision and the need to avoid fragmentation of care.

Refer to the specific guidance by age as listed in *Bright Futures* guidelines (Hagan JF, Shaw JS, Duncan PM, eds. *Bright Futures Guidelines for Health Supervision of Infants, Children and Adolescents*. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2008).

The recommendations in this statement do not indicate an exclusive course of treatment or standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

	INFANCY								EARLY CHILDHOOD							MIDDLE CHILDHOOD						ADOLESCENCE										
AGE[1]	Prenatal[2]	Newborn[3]	3-5 d[4]	By 1 mo	2 mo	4 mo	6 mo	9 mo	12 mo	15 mo	18 mo	24 mo	30 mo	3 y	4 y	5 y	6 y	7 y	8 y	9 y	10 y	11 y	12 y	13 y	14 y	15 y	16 y	17 y	18 y	19 y	20 y	21 y
HISTORY Initial/interval	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
MEASUREMENTS																																
Length/Height and Weight		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Head Circumference		●	●	●	●	●	●	●	●	●	●	●																				
Weight for Length		●	●	●	●	●	●	●	●	●	●																					
Body Mass Index[5]												●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Blood Pressure[6]		★	★	★	★	★	★	★	★	★	★	★	★	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
SENSORY SCREENING																																
Vision		★	★	★	★	★	★	★	★	★	★	★	★	●[7]	●	●	●	★	●	★	●	★	●	★	★	●	★	★	●	★	★	★
Hearing		●[8]	★	★	★	★	★	★	★	★	★	★	★	★	●	●	●	★	●	★	●	★	★	★	★	★	★	★	★	★	★	★
DEVELOPMENTAL/BEHAVIORAL ASSESSMENT																																
Developmental Screening[9]								●			●		●																			
Autism Screening[10]											●	●																				
Developmental Surveillance		●	●	●	●	●	●		●	●		●		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Psychosocial/Behavioral Assessment		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Alcohol and Drug Use Assessment[11]																						★	★	★	★	★	★	★	★	★	★	★
Depression Screening[12]																						●	●	●	●	●	●	●	●	●	●	●
PHYSICAL EXAMINATION[13]		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
PROCEDURES[14]																																
Newborn Blood Screening[15]		←———	●	———→																												
Critical Congenital Heart Defect Screening[16]		●																														
Immunization[17]		●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●
Hematocrit or Hemoglobin[18]						★			●	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★
Lead Screening[19]							★	★	● or ★[20]		★	● or ★[20]		★	★	★	★															
Tuberculosis Testing[21]				★			★		★			★		★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★	★
Dyslipidemia Screening[22]												★			★		★		★	←—	●	—→	★	★	★	★	★	★	←———		●	—→
STI/HIV Screening[23]																						★	★	★	★	★	←—	●	—→	★	★	★
Cervical Dyslasia Screening[24]																																●
ORAL HEALTH[25]							★	★	● or ★		● or ★	● or ★	● or ★	●			●															
ANTICIPATORY GUIDANCE	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●	●

1. If a child comes under care for the first time at any point on the schedule, or if any items are not accomplished at the suggested age, the schedule should be brought up to date at the earliest possible time.
2. A prenatal visit is recommended for parents who are at high risk, for first-time parents, and for those who request a conference. The prenatal visit should include anticipatory guidance, pertinent medical history, and a discussion of benefits of breastfeeding and planned method of feeding, per the 2009 AAP statement "The Prenatal Visit" (http://pediatrics.aappublications.org/content/124/4/1227.full).
3. Every infant should have a newborn evaluation after birth, and breastfeeding should be encouraged (and Instruction and support should be offered).
4. Every infant should have an evaluation within 3 to 5 days of birth and within 48 to 72 hours after discharge from the hospital to include evaluation for feeding and jaundice. Breastfeeding infants should receive formal breastfeeding evaluation, and their mothers should receive encouragement and instruction, as recommended in the 2012 AAP statement "Breastfeeding and the Use of Human Milk" (http://pediatrics.aappublications.org/content/129/3/e827.full). Newborn infants discharged less than 48 hours after delivery must be examined within 48 hours of discharge, per the 2010 AAP statement "Hospital Stay for Healthy Term Newborns" (http://pediatrics.aappublications.org/content/125/2/405.full).
5. Screen, per the 2007 AAP statement "Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity: Summary Report" (http://pediatrics.aappublications.org/content/120/Supplement_4/S164.full).
6. Blood pressure measurement in infants and children with specific risk conditions should be performed at visits before age 3 years.
7. If the patient is uncooperative, rescreen within 6 months, per the 2007 AAP statement "Eye Examination in Infants, Children, and Young Adults by Pediatricians" (http://pediatrics.aappublications.org/content/111/4/902.abstract).
8. All newborns should be screened, per the AAP statement "Year 2007 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs" (http://pediatrics.aappublications.org/content/120/4/898.full).
9. See 2006 AAP statement "Identifying Infants and Young Children With Developmental Disorders in the Medical Home: An Algorithm for Developmental Surveillance and Screening" (http://pediatrics.aappublications.org/content/118/1/405.full).
10. Screening should occur per the 2007 AAP statement "Identification and Evaluation of Children with Autism Spectrum Disorders" (http://pediatrics.aappublications.org/content/120/5/1183.full).
11. A recommended screening tool is available at http://www.ceasar-boston.org/CRAFFT/index.php.
12. Recommended screening using the Patient Health Questionnaire (PHQ)-2 or other tools available in the GLAD-PC toolkit and at http://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Mental-Health/Documents/MH_ScreeningChartLogE.
13. At each visit, age-appropriate physical examination is essential, with infant totally unclothed and older children undressed and suitably draped. See 2011 AAP statement "Use of Chaperones During the Physical Examination of the Pediatric Patient" (http://pediatrics.aappublications.org/content/127/5/991.full).
14. These may be modified, depending on entry point into schedule and individual need.
15. The Recommended Uniform Newborn Screening Panel (http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpaneluniformscreening/panel.pdf), as determined by The Secretary's Advisory Committee on Heritable Disorders in Newborns and Children, and state newborn screening laws/regulations (http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/hrsadisorders.pdf), establish the criteria for and coverage of newborn screening procedures and programs. Follow-up must be provided, as appropriate, by the pediatrician.
16. Screening for critical congenital heart disease using pulse oximetry should be performed in newborns, after 24 hours of age, before discharge from the hospital, per the 2011 AAP statement "Endorsement of Health and Human Services Recommendation for Pulse Oximetry Screening for Critical Congenital Heart Disease" (http://pediatrics.aappublications.org/content/128/1/190.full).
17. Schedules, per the AAP Committee on Infectious Diseases, are available at: http://aapredbook.aappublications.org/site/resources/zschedules.xhtml. Every visit should be an opportunity to update and complete a child's immunizations.
18. See 2010 AAP statement "Diagnosis and Prevention of Iron Deficiency and Iron Deficiency Anemia in Infants and Young Children (0-3 Years of Age)" (http://pediatrics.aappublications.org/content/126/5/1040.full).
19. For children at risk of lead exposure, see the 2012 CDC Advisory Committee on Childhood Lead Poisoning Prevention statement "Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention" (http://www.cdc.gov/nceh/lead/ACCLPP/Final_Document_030712.pdf).
20. Perform risk assessments or screenings as appropriate, based on universal screening requirements for patients with Medicaid or in high prevalence areas.
21. Tuberculosis testing per recommendations of the Committee on Infectious Diseases, published in the current edition of *Red Book: Report of the Committee on Infectious Diseases*. Testing should be performed on recognition of high-risk factors.
22. See AAP-endorsed 2011 guidelines from the National Heart Blood and Lung Institute, "Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents" (http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm).
23. Adolescents should be screened for sexually transmitted infections (STIs) per recommendations in the current edition of the *AAP Red Book: Report of the Committee on Infectious Diseases*. Additionally, all adolescents should be screened for HIV according to the AAP statement (http://pediatrics.aappublications.org/content/128/5/1233.full) once between the ages of 15 and 18, making every effort to preserve confidentiality of the adolescent. Those at increased risk of HIV infection, including those who are sexually active, participate in injection drug use, or are being tested for other STIs, should be tested for HIV and reassessed annually.
24. See USPSTF recommendations (http://www.uspreventiveservicestaskforce.org/uspstf/uspscerv.htm). Indications for pelvic examinations prior to age 21 are noted in the 2010 AAP statement "Gynecologic Examination for Adolescents in the Pediatric Office Setting" (http://pediatrics.aappublications.org/content/126/3/583.full).
25. Refer to a dental home, if available. If not available, perform a risk assessment (http://www2.aap.org/oralhealth/docs/RiskAssessmentTool.pdf). If primary water source is deficient in fluoride, consider oral fluoride supplementation. For those at high risk, consider application of fluoride varnish for caries prevention. See 2008 AAP statement "Preventive Oral Health Intervention for Pediatricians" (http://pediatrics.aappublications.org/content/122/6/1387.full) and 2009 AAP statement "Oral Health Risk Assessment Timing and Establishment of the Dental Home" (http://pediatrics.aappublications.org/content/111/5/1113.full).

KEY ● = to be performed ★ = risk assessment to be performed with appropriate action to follow, if positive ←—● —→ = range during which a service may be provided

* As published in *PEDIATRICS*

Committee on Practice and Ambulatory Medicine, Bright Futures Periodically Schedule Workgroup. From the American Academy of Pediatrics Policy Statement: 2014 Recommendations for Pediatric Preventive Health Care. Pediatrics 2014; 133; 568.

Appendix H: Quality Assessment of Individual Studies

Quality was assessed using three published tools, depending on the study design. Two reviewers independently assessed the quality of each study, and then results were adjudicated. For randomized controlled trials (RCTs), we used the Cochrane Risk of Bias tool[1] for cohort studies, the Newcastle-Ottawa Quality Assessment Scale[2]; and for prognostic studies of imaging, the Quality Assessment of Diagnostic Accuracy Studies-Revised (QUADAS-2) tool[3]. The results of these tools were then translated to the Agency for Healthcare Research and Quality standard of "good," "fair," and "poor" quality designations using conversion thresholds developed by the team, as no explicit guidance exists.

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain
Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

References for Appendix H

[1] Higgins JPT, Altman DG, Sterne JAC. Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration; 2011.
[2] Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed January 24, 2012.
[3] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011 Oct 18;155(8):529-36. PMID: 22007046.