Appendix

TABLE A1. RESULTS FROM MODIFIED-DELPHI STUDY WITHIN THE SOC CLINICAL ALGORITHM

Initial recommendations	Base case value
Prescribe non-CHC without medical history	9%
Prescribe CHC without medical history	7%
Conduct medical history	84%
Risk factors identified via medical history	
Personal or familial	
Proportion aware of/reporting personal risk	62%
Prescribe non-CHC with "known FII/FV" risk	47%
‡Additional laboratory testing with "known FII/FV" risk	53%
Proportion aware of/reporting family history	50%
Prescribe non-CHC with family history risk	47%
‡Additional laboratory testing with family history risk	53%
Proportion who refuse laboratory testing	12%
Clinical risk factors (more than one)	
Prescribe CHC % (else, non-CHC)	
Obese + smoker	30%
Obese + 35 years to 40 years old	27%
Obese + 40 years old or older	21%
Obese + smoker + 35 years to 40 years old	1%
Obese + smoker + 40 years old or older	4%
Smoker + 35 years to 40 years old	18%
Smoker + 40 years or older	6%
Clinical risk factors (single risk factor)	
Prescribe non-CHC with "BMI" risk	64%
Prescribe CHC with "BMI" risk	36%
Prescribe non-CHC with "higher age" risk*	49%
Prescribe CHC with "higher age" risk*	34%
Additional laboratory testing with "higher age" risk*	17%
Prescribe non-CHC with "smo" risk	31%
Prescribe CHC with "smo" risk	69%
‡After laboratory testing....	
IF positive thrombophilia → non-CHC	100%
IF negative thrombophilia + more than a single clinical risk factor → non-CHC	Refer to "Clinical risk factors (more than one)" above

IF negative thrombophilia + family history	
Prescribe non-CHC	46%
Prescribe CHC	54%
IF negative thrombophilia with "higher age" risk*	
Prescribe non-CHC	42%
Prescribe CHC	58%
IF negative thrombophilia with "smo" risk	
Prescribe non-CHC	37%
Prescribe CHC	63%
IF negative thrombophilia with "BMI" risk	
Prescribe non-CHC	66%
Prescribe CHC	34%

BMI=body mass index, CHC=combined hormonal contraceptive, FII=Factor II, FV=Factor V, smo=smoking

TABLE A2. POPULATION CHARACTERISTICS

Inputs				**Mean estimate**	**Source**
Age distribution of first-time users in Switzerland from 15-29 years old					
less than 16 years old				10%	Modified-Delphi study
16-19 years old				34%	
20-24 years old				40%	
25-29 years old				16%	
Smokers				35%	Firmann et al., 2008[1]
Family history				15.0%	McDaid et al., 2017[2]
Prevalence of protein C/S (prothrombin G20210A)				0.2%	NIH US National Library of Medicine[3],[3]
	Frequency				
Genetic polymorphisms	ho	he	wt		
PP1, FV	0.16%	5.9%	93.95%		Firmann et al., 2008[1]
PP2, FII	0.0%	2.4%	97.60%		dbSNP [4]
PP3	8.7%	13.0%	78.30%		dbSNP[4]
PP4	14.5%	47.4%	38.14%		Firmann et al., 2008[1]
PP5	0.96%	16.3%	82.7%		Firmann et al., 2008[1]
PP6	2%	23.8%	74.1%		Firmann et al., 2008[1]
PP7	13.4%	46.8%	39.8%		Firmann et al., 2008[1]
PP8	30.6%	49%	20.4%		Firmann et al., 2008[1]
PP9	19.3%	47.5%	33.2%		Firmann et al., 2008[1]

* The genetic polymorphisms listed as PP1, PP2, etc. refer to the 9 genes identified for additional CHC risk. dbSNP=Database of single nucleotide polymorphisms (SNPs) and multiple small-scale variations

that include insertions/deletions, microsatellites, and non-polymorphic variants, FII= Factor II, FV= Factor V.

TABLE A3. BODY MASS INDEX (BMI) BY AGE

Age range	Underweight (BMI < 18.5)	Normal weight (18.5 <= BMI < 25)	Overweight (25 <= BMI < 30)	Obese (BMI >= 30)	Source
less than 24 years old	11.60%	74.30%	10.20%	3.90%	Swiss Federal Statistical Office[5]
25-34 years old	9.90%	71.10%	13.90%	5.00%	
35-39 years old (35 to 44 in Swiss table)	4.50%	68.90%	19.50%	7.10%	
Greater than 40 years old	4.90%	65.55%	21.40%	8.20%	

TABLE A4. DURATION OF COMBINED HORMONAL CONTRACEPTIVE (CHC) USE ACCORDING TO AGE OF FIRST-TIME USERS

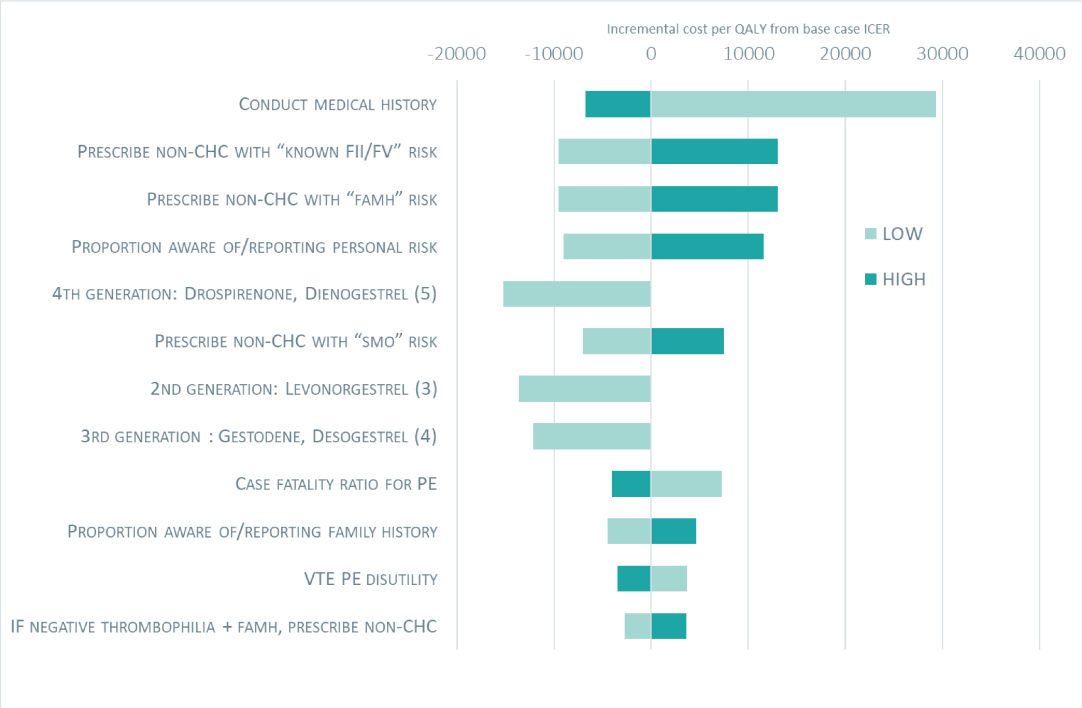
Age range	None	> 2 years	2 - 5 years	6 - 10 years	11 to 15 years	< than 15 years
	0	**1**	**3.5**	**8**	**13**	**24.5**
less than 16 years old	-	23%	-	15%	31%	31%
16-19 years old	**-**	-	8%	31%	46%	15%
20-24 years old	**-**	-	15%	54%	15%	15%
25-28 years old	**-**	8%	38%	31%	15%	8%
29-34 years old	**-**	8%	62%	31%	-	-
35-39 years old	**-**	38%	23%	38%	-	-
40 years old or greater	23%	23%	38%	15%	-	-

DESCRIPTION OF PRODUCTIVITY (INDIRECT COSTS)

For the societal perspective, the incorporation of productivity costs was required for the cost-effectiveness modelling. We approached this using the human capital approach, where the calculated loss is based on the salaries of the individuals impacted by the disease. We asked two Swiss hematologists to estimate the total time out of work (i.e. lost productivity of employees) that a patient with VTE may experience. These questions were developed by the study team and provided to the two hematologists in the format of a questionnaire. The number of DVT disability days in Switzerland on average were reported to be 42 days with ranges 28 to 90 days, while the PE disability days were reported to be 60 days with ranges 28 to 90 days. These ranges equate to an equivalent of three months, and hence this was the time in which productivity loss was incurred in our base-case approach. Although there may be some cases of longer-term disability, we did not consider these due to lack of data.

In order to calculate the average salary per year for females in Switzerland we utilized data from the Swiss Federal Office of Statistics (SFOS).[6,7,8] A number of elements were considered: a) population data on the size of the female population across different age groups[6] b) the average employment level of women in Switzerland based on age category[7], c) labour force participation rate based on age and gender[7], and d) salary based on gender[8]. These three components were combined to calculate the average daily salary for females in Switzerland in 2016 to be CHF 143. After these steps were performed, we combined the data on average daily salary with the time out of work data derived from the hematologist questionnaire, and estimated the lost wages per case due to disability for PE and DVT in Switzerland. The estimated mean productivity losses per disability claim due to DVT and PE amounted to CHF 4,286 and 6,122 respectively.

FIGURE A1: TORNADO DIAGRAM FOR THE ONE-WAY SENSITIVITY ANALYSES



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