

VENOUS THROMBOEMBOLISM DISEASE: DIRECT COSTS ASSOCIATED WITH ITS TREATMENT IN ARGENTINA.

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BACKGROUND

- Venous thromboembolism (VTE), which includes deep vein thrombosis and pulmonary embolism, causes substantial morbidity, disability, and mortality.^{1,2}
- Complete and valid estimates of VTE-associated medical care utilization and costs are essential to inform allocation of scarce resources, target efforts toward prevention, identify best practices, address future care needs, and implement cost-effective treatments.^{2,3}
- However, estimates of direct costs attributable to VTE treatment in developing countries are limited. Also, additional studies are needed in order to incorporate newer treatment patterns, in particular novel oral anticoagulants.^{2,4}

OBJECTIVES

- To determine the direct costs associated with treatment of venous thromboembolism disease (VTE) [deep venous thrombosis (DVT) and pulmonary embolism (PE)] from the payer perspective in institutions of the social security sector (SSS) of Argentina.

METHODS

- Key parameters of resource usage for diagnosis and treatment of VTE, and cost of its complications (bleeding adverse events [AE]) were obtained from clinical guidelines⁵, literature and local expert opinions (Delphi panel).
- Total per-patient direct costs were estimated by micro-costing approach.
- Based on CP guidelines a questionnaire was developed to investigate the therapeutic pathways and resource utilization through a two round Delphi Panel. In each round, 13 VTE experts completed the questionnaire anonymously. Consensus was achieved when 70% of answer fit in the range of mean ± standard deviation.
- Direct costs included diagnosis, drug treatment, laboratory tests, routine medical attention and hospitalization.
- Drug costs were obtained from list of prices of AlfaBeta; cost of resources used was based on tariffs from the SSS of Argentina.
- Costs per patient are presented in Argentinean Peso (AR\$) of November/December (exchange rate 1US\$=37,88AR\$, December 2018).
- EP can be classified as high, moderate or low risk according to the prognosis of the event depending on the hemodynamic state and damage to the right ventricle.⁵

Table 1
DRUG COST CONSIDERED FOR DVT AND PE

DRUGS	PRESENTATION	RETAIL PRICE*
Apixaban (5mg)	Blister for 60 units	\$ 2,956
Rivaroxaban (15mg)	Blister for 28 units	\$ 3,089
Rivaroxaban (20mg)	Blister for 28 units	\$ 3,247
Enoxaparin (60mg)	10 prefilled syringes for 0,6 ml	\$ 6,918
Enoxaparin (80mg)	10 prefilled syringes for 0,8 ml	\$ 9,286
Dabigatran (150 mg)	Blister for 60 units	\$ 4,348
Warfarin (5mg)	Blister for 50 units	\$ 426

*Based on list of prices from AlfaBeta.

Table 2
DAYS OF HOSPITALIZATION ACCORDING TO TREATMENT

	TREATMENT	TYPE	MEAN	SD
Treatment DVT	LMWH + warfarin	Clinic	5.6	1.2
		ICU	0.2	0.4
		Clinic	4.5	1.5
	LMWH + Dabigatran	ICU	0.1	0.3
	Rivaroxaban	Clinic	3.4	1.9
Treatment PE (medium risk)	Apixaban	Clinic	3.4	1.9
		Clinic	4.85	1
		ICU	1.92	1.2
	LMWH + warfarin	Clinic	4.23	1.2
	LMWH + Dabigatran	ICU	2.15	1.5
Treatment PE (low risk)	Rivaroxaban	Clinic	3.08	1
		ICU	2	1.4
		Clinic	3.08	1
	Apixaban	ICU	2	1.4
		Clinic	4.92	1.4
		ICU	0.85	1.5
	LMWH + warfarin.	Clinic	5.15	1.6
		ICU	0.31	0.6
		Clinic	3.23	1.9
	Rivaroxaban	ICU	0.15	0.4
		Clinic	3.23	1.9
		ICU	0.15	0.4

DVT: deep vein thrombosis; PE: pulmonary embolism; SD: Standard deviation; LMWH: Low molecular weight heparin; ICU: Intensive care unit.

Table 3
COST OF RESOURCES ASSOCIATED WITH VENOUS THROMBOEMBOLISM DISEASE (DVT AND PE)

STAGE	CONCEPT	DESCRIPTION	MEAN	SD	MIN	MAX
Diagnosis	Medical attention	History of patient (anamnesis)	\$787	\$118	\$610	\$960
		Dimer -D (blood determination)	\$320	-	\$320	\$320
	Laboratory test	Ecodoppler	\$829	\$165	\$610	\$1,030
		Angio tomography*	\$2,337	\$301	\$2,000	\$2,700
		Chest x-ray*	\$248	\$44	\$203	\$333
		Electrocardiogram*	\$127	\$18	\$105	\$141
		V / Q Centellography*	\$606	\$112	\$470	\$780
Treatment	Medical attention	Clinical medical consultation, hematologist medical consultation	\$787	\$118	\$610	\$960
		Complete blood count: red blood cell count, white blood cell count, hematoctrit, hemoglobin, leukocyte formula.	\$338	\$38	\$289	\$368
	Laboratory test	Quick time	\$148	-	\$148	\$148
		KPTT (Kaolin activated Partial Tromboplastin Time)	\$156	-	\$156	\$156
		Creatinine	\$111	\$57	\$48	\$156
		Creatinine clearance	\$150	-	\$150	\$150
		INR (international normalized ratio)	\$149	\$21	\$115	\$172
		Hepatogram	\$1,930	\$242	\$1,610	\$2,300
		Troponin T o I*	\$420	-	\$420	\$420
	Hospitalization	Atrial Natriuretic Pro-Peptide*	\$580	-	\$580	\$580
		Clinic	\$9,064	\$896	\$7,980	\$10,200
		Intensive care unit (ICU)	\$14,573	\$879	\$13,100	\$15,600

*Applies only to PE

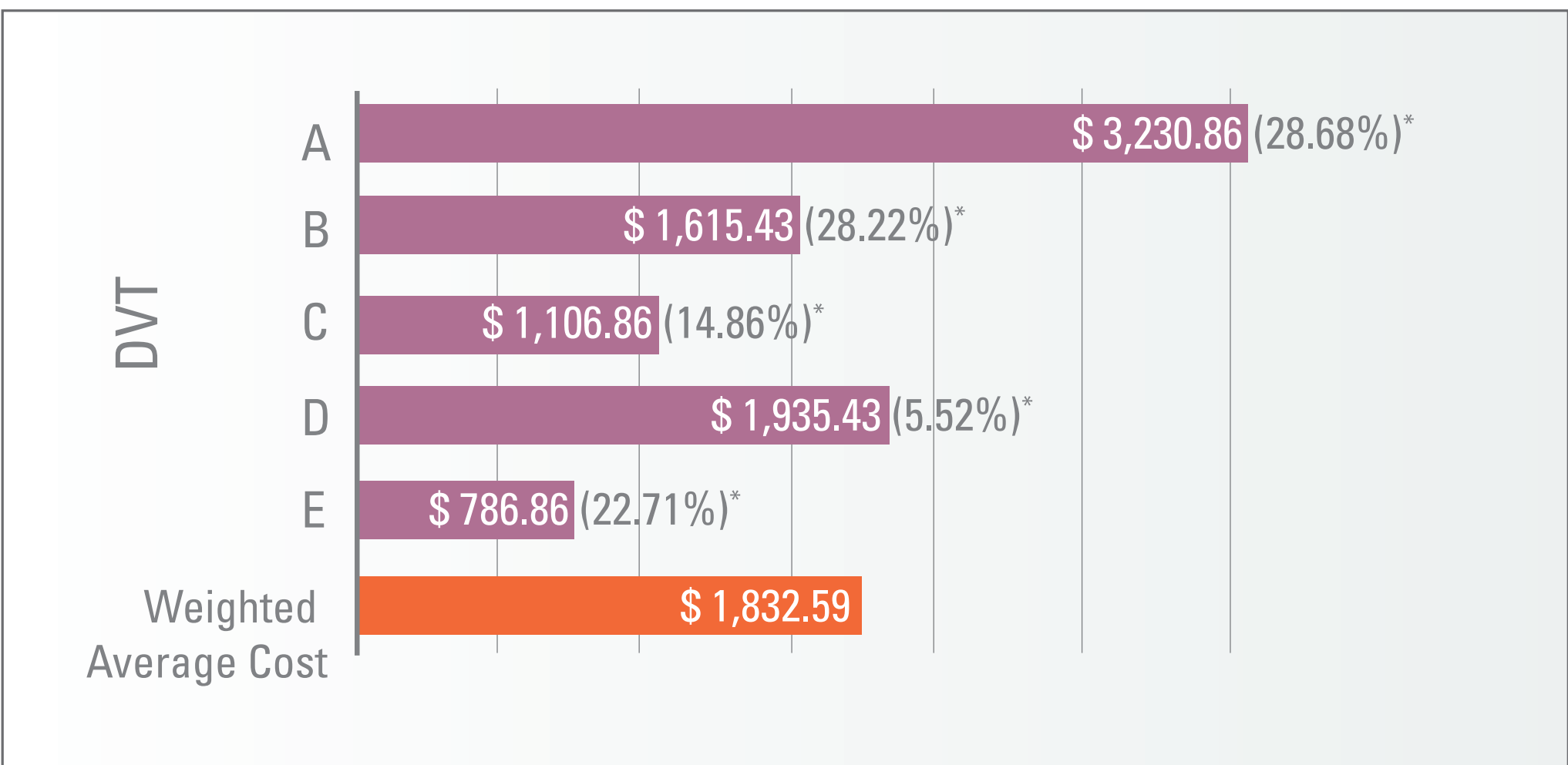
CONCLUSIONS

- This study shows that the direct costs associated with the treatment of VTE in Argentina are high. Cost of outpatient therapy is significantly lower than inpatient care, so if aligned to guidelines, this should be the preferred strategy.
- Furthermore, our study provides relevant information to perform economic evaluations of VTE treatment in Argentina.
- NOACs should be the preferred strategy (in both In-Patient and Out-patients) since they could reduce hospitalization days and therefore costs.

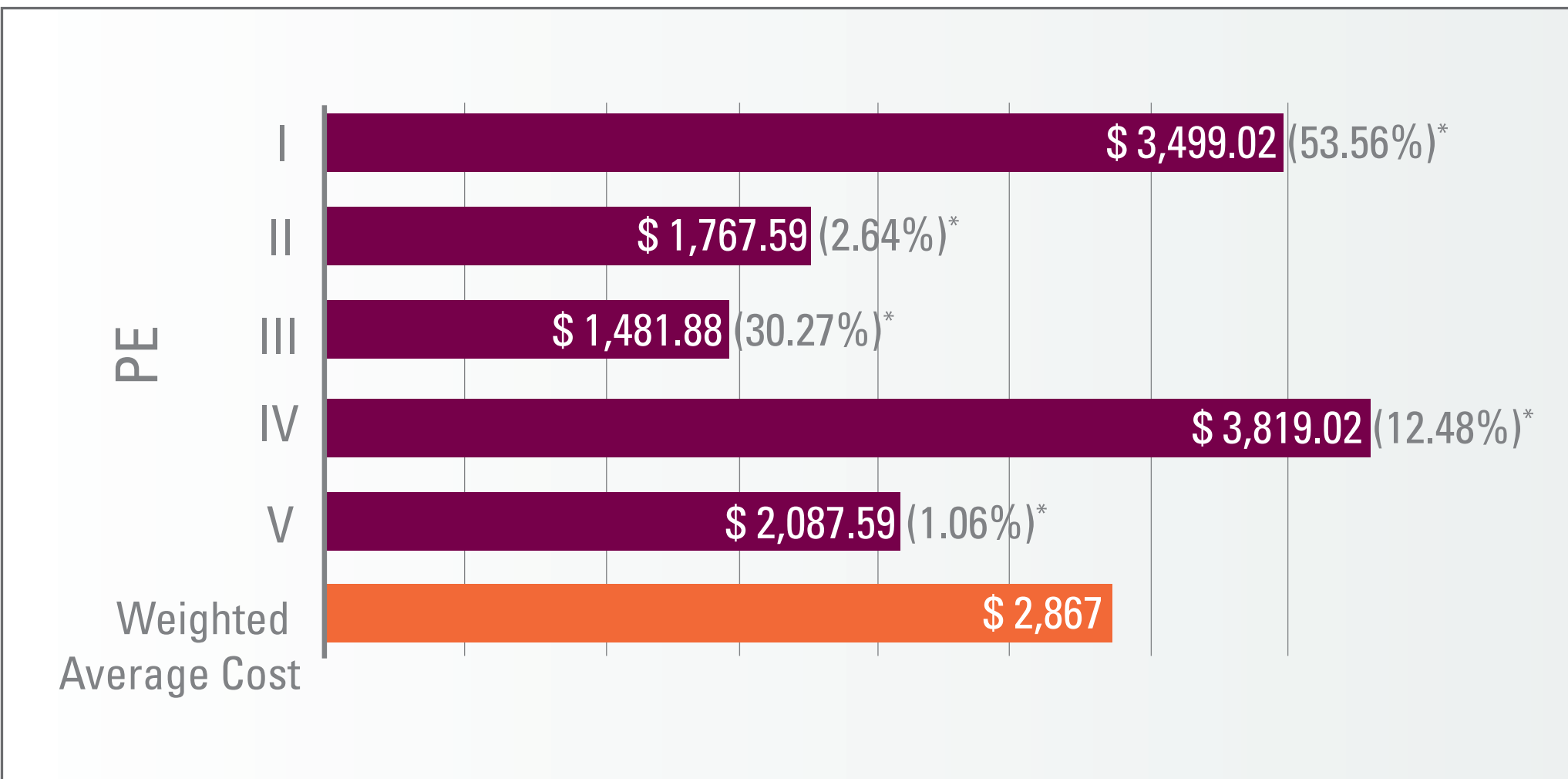
RESULTS

- Per patient cost of diagnosing: DVT AR \$1,833 [range AR \$787 - AR \$3,231] and PE AR\$ 2,868 [AR\$ 1,482 - AR\$ 3,819].

Grafic 1
COST OF DIAGNOSIS



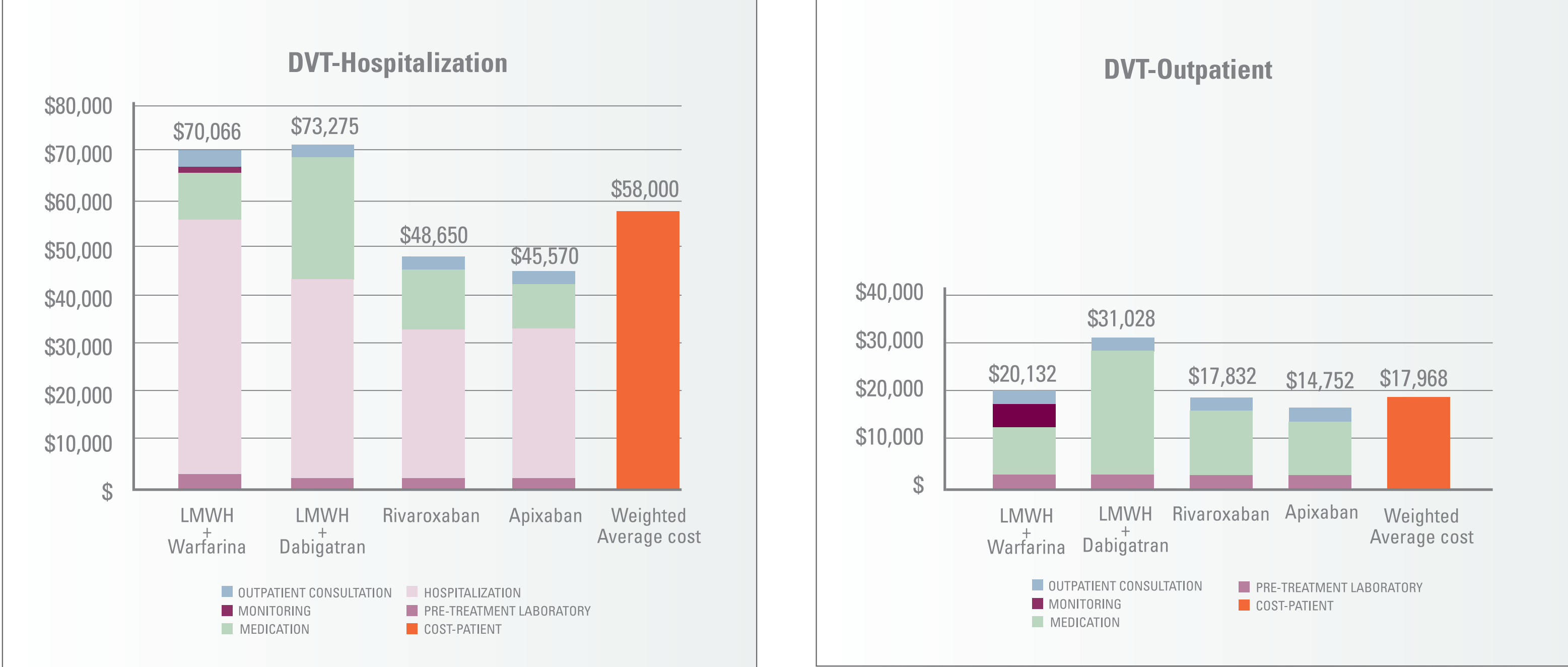
Ref: DVT: Deep venous thrombosis (A): Patient categorized as probable DVT, with indication of Doppler and requiring repeat Doppler; (B): Patient categorized as probable DVT, with indication of doppler; (C) Patient categorized as unlikely DVT, with D-Dimer indication; (D) Patient categorized as unlikely DVT, with D-Dimer indication and with Doppler indication; (E) Patient categorized as unlikely DVT, who does not perform D-Dimer. *PR: Probability



PE: Pulmonary embolism (I) Patient, categorized as probable PE, with indication of helical angio-tomography; (II) Patient, categorized as probable PE, with indication of V / Q Centellography (III) Patient categorized as unlikely PE, with indication of D-Dimer; (IV) Patient categorized as unlikely PE, with indication of D-dimer and helical angio-tomography (V) Patient categorized as unlikely PE, with indication of D-dimer and V / Q Centellography. *PR: Probability

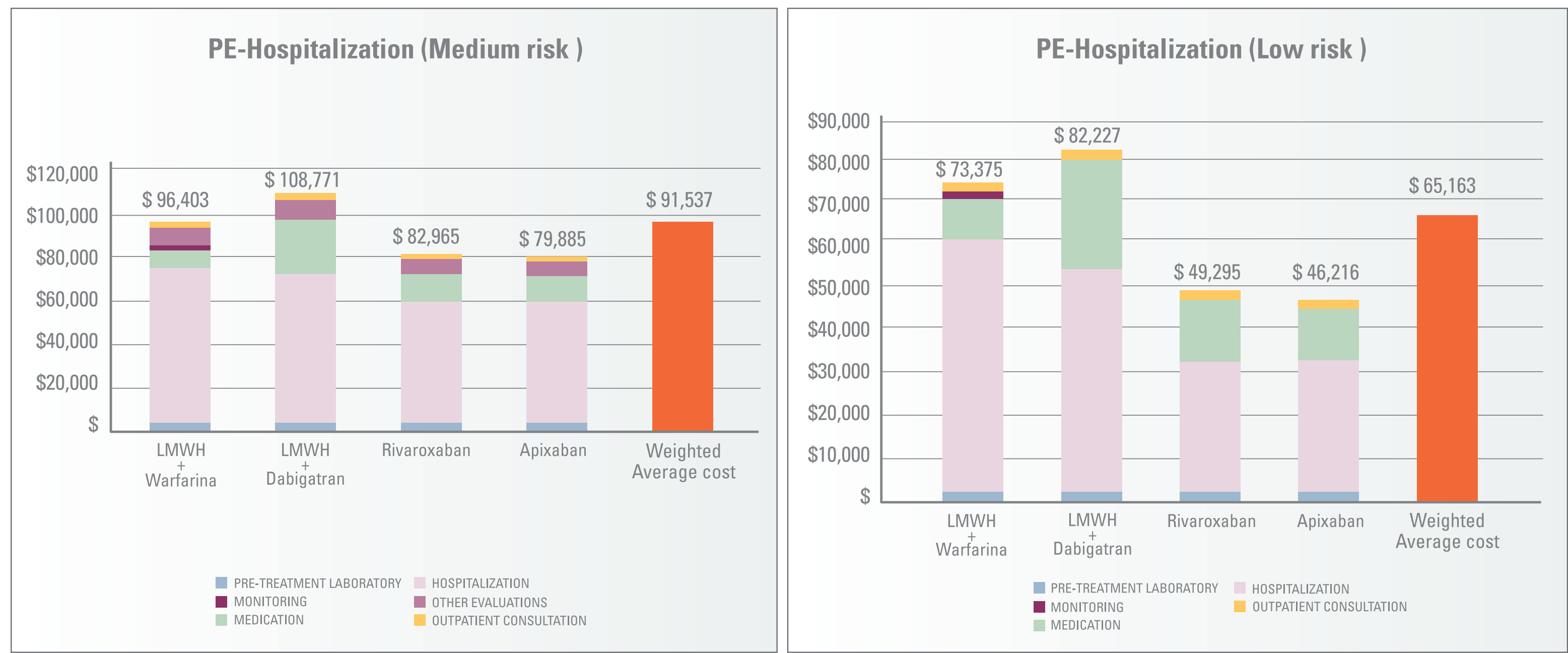
- Per patient cost of PE treatment in candidates for anticoagulation, without considering bleeding complications: i) with intermediate risk AR\$ 91,053 [AR\$ 80,066 - AR\$ 109,228]; ii) with low risk (hospitalized) AR\$ 64,643 [AR \$46,672 - AR\$ 82,534] and iii) with low risk (outpatient) AR\$ 18,748 [AR\$ 14,752 - AR\$ 31,028].

Grafic 2
COST PER PATIENT FOR TREATMENT IN DVT IN HOSPITALIZATION AND OUTPATIENT

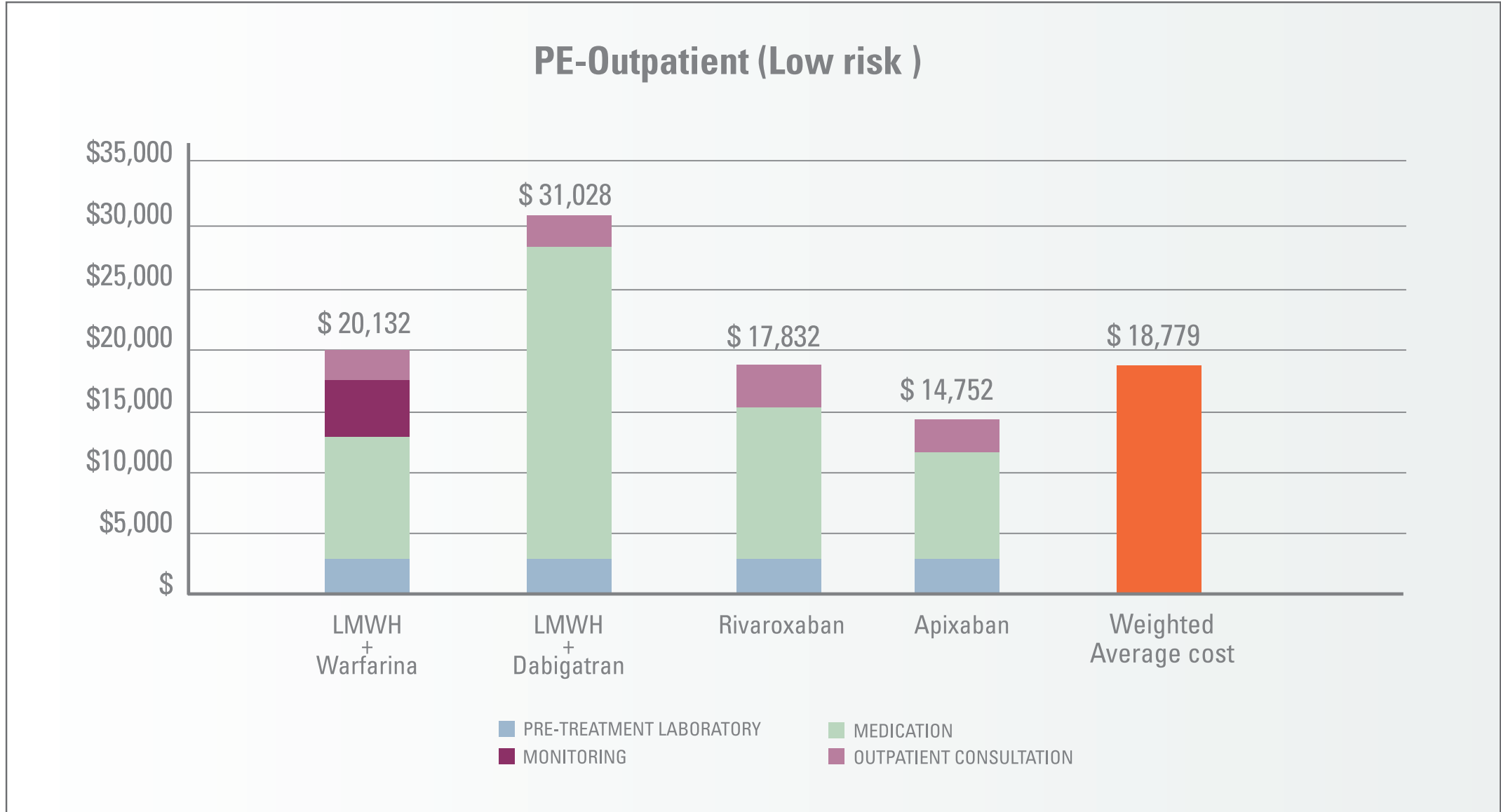


- Per patient cost of DVT treatment in candidates for anticoagulation, without considering bleeding complications: i) hospitalized AR\$ 57,978 [AR\$ 45,571 - AR\$ 73,275], and i) NOT hospitalized (outpatient) AR\$ 17,946 [AR\$ 14,752 - AR\$ 31,028].

Grafic 3
COST PER PATIENT FOR TREATMENT IN PE IN HOSPITALIZATION (MEDIUM AND LOW RISK)



Grafic 4
COST PER PATIENT FOR TREATMENT IN PE OUTPATIENT (LOW RISK)



- Average cost of AE management: major bleeding AR\$ 223,606, clinically relevant non-major bleeding AR\$ 77,358 and minor bleeding AR\$ 27,269.

Table 4
COST OF COMPLICATIONS

ADVERSE EVENT	TREATMENT	INCIDENCE	INPATIENT EVENT COST	OUTPATIENT EVENT COST
Major Bleeding ^(*)	LMWH + warfarin	1.80%	\$ 206,904	
	LMWH + Dabigatran	1.60%	\$ 240,307 ^(§)	
	Rivaroxaban	1.00%	\$ 206,904	-
	Apixaban	0.60%	\$ 206,904	
No major clinically relevant ^(**)	LMWH + warfarin	8.00%		
	LMWH + Dabigatran	4.00%	\$ 77,358	\$ 4,238
	Rivaroxaban	8.60%		
	Apixaban	3.80%		
Minor bleeding ^(***)	LMWH + warfarin	18.80%		
	LMWH + Dabigatran	10.50%	\$ 27,269	\$ 3,017
	Rivaroxaban	11.70%		
	Apixaban	11.70%		

(*) Major bleeding: 100% treated by hospitalization
(**) No Major clinically relevant: 100% of patients hospitalized for VTE are treated for adverse event by prolonging hospitalization, of patients treated on an outpatient basis for VTE, 30% are hospitalized for adverse event and 70% are treated for adverse event on an outpatient basis.
(***) Minor bleeding: Of the 100% of patients hospitalized for VTE, 7.5% are treated for adverse event by prolonging hospitalization and 92.5 are treated on an outpatient basis. 100% of patients treated on an outpatient basis for VTE are treated for adverse event on an outpatient basis.
(§) Requires a reversing agent such as idarucizumab