Discharging Low Risk PE Management Strategies 2017

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Disclosure
Financial Relationships
Geno J. Merli, MD, MACP, FHM, FSVM

- **Jannsen: Research**
- **Bristol-Meyer Squibb/Pfizer: Research**
- **Portola: Research**
- **LoweRisk LLC, Co-Chief Development Officer**

Key Program Components
Outpatient Treatment PE

- **Appropriate patient selection**
- **Appropriate anticoagulant selection**
- **Patient education**
- **Medication procurement**
- **Well defined outpatient follow-up plan**
- **Staff knowledgeable in the process**

National Trends in Home Treatment of Acute Pulmonary Embolism

Paul D. Stein, MD[1], Fadi Matta, MD[1], and Mary J. Hughes, DO[1]

- **54,494 / 915,702 Stable PE Patients seen ED**
- **Highest Group Rx to Home Age < 30 yrs. 12.1%**
- **Lowest Group Rx to Home Age > 80 yrs. 2.9%**
- **66.8% had No Comorbid Conditions**

Conclusion: Younger Patients might be group for home treatment

Nationwide Emergency Department Sample (NEDS)

National Inpatient Sample (NIS)

Healthcare Cost Utilization Project (HCUP)

Agency for Healthcare Research and Quality

European Society of Cardiology
Guideline Dx & Rx Acute PE

PE-Related Early Mortality	Risk Markers*			Potential Treatment Implications
	Clinical (Shock)	RV Dysfunction	Cardiac Injury	
High (>15%)	+	+	+	Thrombolysis
Nonhigh				
Intermediate	−	+	+	Admission
		+	−	
		−	+	
Low	−	−	−	Early discharge or home treatment

Outpatient Rx PE
LMWH Management

Author	No Pts	Intervention	Outcomes
Kovacs	81	Dalteparin	Recurrent VTE: 6.2% Major Bld: 1.2%
Beer	43	Nadroparin	Recurrent VTE: 2.3% Major Bld: 0%
Wells	90	Dalteparin/Tinzaparin	Recurrent VTE: 2.2% Major Bld: 0%
Siragusa	32	LMWH	Recurrent VTE: 5.6% Major Bld: 2.8%
Olsson	100	Tinzaparin	Recurrent VTE: 0% Major Bld: 0%
Davies	156	Tinzaparin	Recurrent VTE: 0% Major Bld: 0%

Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial

Drahomir Aujesky, Pierre-Marie Roy, Franck Verschuren, Marc Righini, Joseph Osterwalder, Michael Egloff, Bertrand Renaud, Peter Verhamme, Roslyn A Stone, Catherine Legall, Olivier Sanchez, Nathan A Pugh, Alfred N'gako, Jacques Cornuz, Olivier Hugli, Hans-Jürg Beer, Arnaud Perrier, Michael J Fine, Donald M Yealy

Enoxaparin 1mg/kg/Q12hrs bridge to warfarin
Outpatient Treatment Group: 171 patients
Inpatient Treatment Group: 168 patients

PE severity index risk class		
I	117 (68%)	109 (65%)
II	54 (32%)	59 (35%)

	Outpatient group	Inpatient group	Difference in percentages ($\%_{outpatient}-\%_{inpatient}$)	Upper 95% CL for difference	p value*
Primary analysis outcomes within 90 days†					
Recurrent VTE	1 (0·6%)‡	0	0·6%	2·7%	0·011
Major bleeding	3 (1·8%)	0	1·8%	4·5%	0·086
Intramuscular	2 (1·2%)	0	1·2%	3·6%	0·031
Menometrorrhagia	1 (0·6%)	0	0·6%	2·7%	0·011
Overall mortality	1 (0·6%)§	1 (0·6%)¶	0%	2·1%	0·005
Primary analysis outcomes within 14 days†					
Recurrent VTE	0	0	0%	1·7%	0·003
Major bleeding	2 (1·2%)	0	1·2%	3·6%	0·031
Intramuscular	2 (1·2%)	0	1·2%	3·6%	0·031
Menometrorrhagia	0	0	0%	1·7%	0·003
Overall mortality	0	0	0%	1·7%	0·003

Localisation of PE‡	Outpatient	Inpatient
Central	24 (14%)	16 (10%)
Lobar	60 (35%)	66 (39%)
Segmental	110 (64%)	100 (60%)
Subsegmental	52 (30%)	44 (26%)
Unspecified	29 (17%)	26 (15%)

Pulmonary Embolism Severity Index

	Points assigned
Age	+1 per year
Male sex	+10
Cancer*	+30
Heart failure	+10
Chronic lung disease	+10
Pulse ≥110 beats per min	+20
Systolic blood pressure <100 mm Hg	+30
Respiratory rate ≥30 breaths per min	+20
Temperature <36°C	+20
Altered mental status†	+60
Arterial oxygen saturation <90%‡	+20

Overall point score for a patient is obtained by summing the patient's age in years with the points for every applicable predictor. A score of <66 is risk class I, 66–85 is risk class II, 86–105 is risk class III, 106–125 is risk class IV, and >125 is risk class V. *History of cancer or active cancer. †Disorientation, lethargy, stupor, or coma. ‡With or without the administration of supplemental oxygen.

Ambulatory management of pulmonary embolism: a pragmatic evaluation

M. J. KOVACS, J. D. HAWEL, J. F. REKMAN and A. LAZO-LANGNER
Division of Hematology, Department of Medicine, University of Western Ontario, London, ON, Canada

Treatment LMWH or UFH Bridge to Warfarin
Outpatient Treatment: 314 pts.
a. 3/314 (0.95%) recurrent PE
b. 3/314 (0.95% major bleeding [day 39, 40, 52]
c. 9/314 (2.9%) deaths secondary to Cancer
first 7 days

Safety of outpatient treatment in acute pulmonary embolism

P. M. G. ERKENS,* E. GANDARA,† P. WELLS,† A. Y.-H. SHEN,† G. BOSE,† G. LE GAL,‡ M. RODGER,†
M. H. PRINS§ and M. CARRIER†

LMWH Bridge to Warfarin
Outpatients Treatment: 260 pts
Inpatient Treatment: 213 pts

Exclusion Criteria
1. BP < 100 mmHg
2. O2 Sat < 92% do not require O2
3. High Bleeding risk
4. Renal Failure
5. Other Co-Morbidities requiring hospitalization: Severe Caner, HF
COPD, CAD, Stroke

Safety Outpt Rx PE

Follow Up	Outpatient	Inpatient	P Value
14 Days			
PE mortality	0 (0%)	5 (2.3%)	0.018
Recurrent VTE	1(0.4%)	4 (1.9%)	0.018
Major Bld	0 (0%)	13 (6.1%)	0
Readmission	4 (1.5%)	4 (1.9%)	1
3 Months			
PE mortality	0 (0%)	5 (2.3%)	0.018
Recurrent VTE	10 (3.8%)	10 (4.7%)	0.654
Major Bld	4 (1.5%)	17 (8.0%)	0.001
Readmission	6 (2.3%)	11 (5.2%)	0.135

Erkens P et al. J Thromb Haemost 2010;8:2412

Hestia vs PESI

Hestia criteria	Simplified Pulmonary Embolism Severity Index
Haemodynamically instable?* Thrombolysis or embolectomy necessary? High risk for bleeding?** Oxygen supply to maintain oxygen saturation >90%>24 h? Pulmonary embolism diagnosed during anticoagulant treatment? Intravenous pain medication >24 h? Medical or social reason for treatment in the hospital >24 h? Creatinine clearance of less than 30 ml/min?*** Severe liver impairment**** Pregnant? Documented history of heparin-induced thrombocytopenia?	Age > 80 years? Cardiopulmonary co-morbidity? History of cancer? Arterial oxyhaemoglobin saturation level <90%? Systolic blood pressure <100 mmHg? Pulse frequency ≥110 beats/min?
If one of the questions is answered with YES, the patient can not be treated at home.	If one of the items is present the patient is regarded as high risk.

* Systolic BP < 100 mmHg, HR > 100/min, needs ICU
** GI bleeding < 14 days, stroke < 4 wks, surgery < 2 wks, bleeding disorder, Thrombocytopenia < 75K, BP systolic > 180 mm Hg, diastolic > 110 mm Hg
*** Calculated CrCl, left to discretion physician

Zondag W, et al Thromb Haemost 2013;109:47

	Hestia criteria	sPESI
	% (95% CI)	% (95% CI)
Proportion identified as low risk	53 (48–58)	59 (54–64)
Proportion identified as high risk	47 (42–51)	41 (36–45)
30-day all cause mortality		
Sensitivity	82 (48–97)	91 (57–100)
Specificity	57 (52–61)	60 (56–65)
Negative predictive value	99 (97–100)	100 (98–100)
Positive predictive value	4 (2–8)	5 (3–10)
30-day adverse events*		
Sensitivity	74 (43–52)	74 (51–89)
Specificity	54 (49–58)	60 (56–65)
Negative predictive value	98 (95–99)	98 (95–99)
Positive predictive value	8 (5–12)	9 (5–14)
*All-cause mortality, recurrent venous thromboembolism and major bleeding.		

**Both selected > 50% patients as Low Risk with good sensitivity
And negative predictive values for 30 day mortality**

Zondag W, et al Thromb Haemost 2013;109:47

Patient Outcomes 14 Days & 3 Months

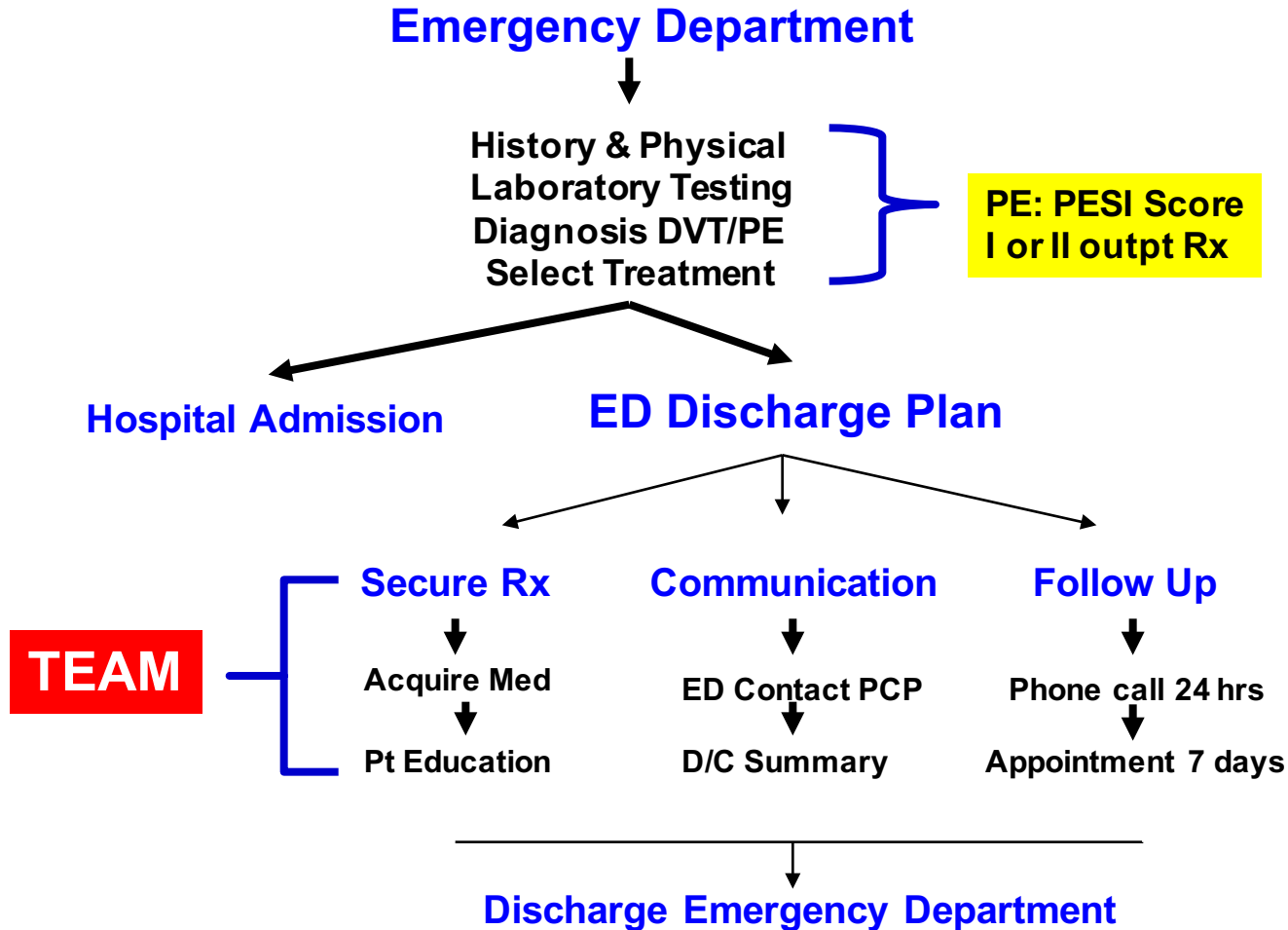|	Overall matched cohort			Class I–II			Class III–IV		
	Inpatients	Outpatients		Inpatients	Outpatients		Inpatients	Outpatients	
	N = 576	N = 505		N = 175	N = 309		N = 401	N = 196	
	% of patients		P value*	% of patients		P value*	% of patients		P value*
Combined events (14 days)	13.0	3.3	0.011	5.1	0.0	0.005	16.5	4.5	0.017
Recurrent VTE	1.7	0.6	0.135	0.6	0.0	0.351	2.2	0.8	0.161
Recurrent VTE including deaths related to PE	9.2	2.0	0.026	2.9	0.0	0.037	12.0	2.8	0.030
Major bleeding	3.8	0.0	< 0.001	2.3	0.0	0.062	4.5	0.0	< 0.001
Mortality all causes	8.2	2.8	0.104	2.3	0.0	0.062	10.7	3.8	0.114
Combined events (3 months)	21.7	6.9	0.001	8.6	1.7	0.002	27.5	8.7	0.001
Recurrent VTE	4.7	3.6	0.586	1.8	1.3	0.733	6.3	4.5	0.557
Recurrent VTE including deaths related to PE	15.7	4.8	0.004	4.6	1.3	0.068	20.5	6.1	0.005
Major bleeding	5.9	0.7	< 0.001	4.1	0.2	< 0.001	6.9	0.9	0.002
Mortality all causes	16.3	3.2	0.005	2.9	0.1	< 0.001	22.8	4.4	0.004

Home Treatment of Pulmonary Embolism in the Era of Novel Oral Anticoagulants

Paul D. Stein, MD,[a] Fadi Matta, MD,[a] Patrick G. Hughes, DO,[a,b,c] Zak N. Hourmouzis, MD,[b] Nina P. Hourmouzis, MD,[b]

983 PE Patients

237 Not Eligible For Home Rx

746 Eligible Home Rx

13 Rxed Home
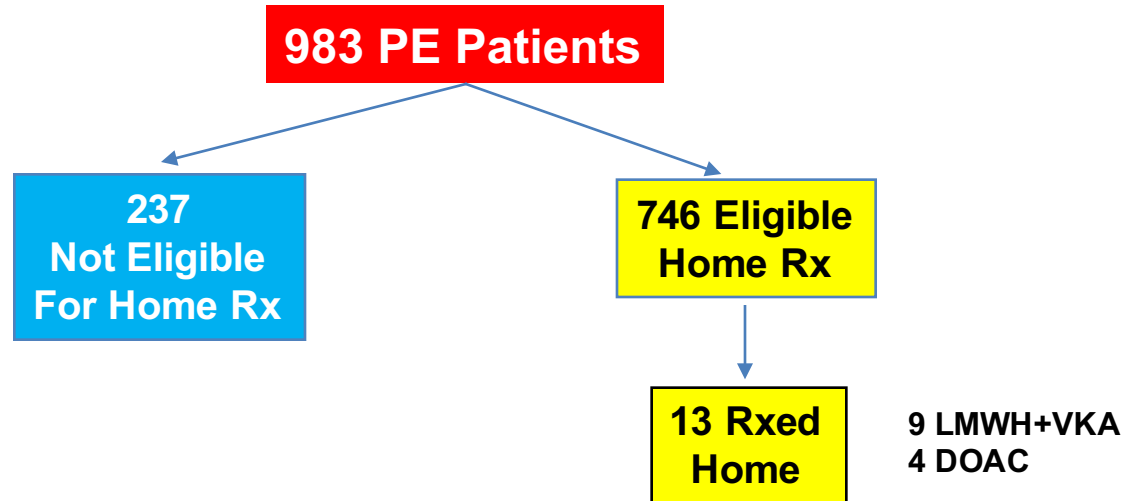
9 LMWH+VKA
4 DOAC

119 D/C < 2 days
76 Pts Rx LMWH + VKA
34 Pts Rx DOAC
9 Pts No Rx

Falconieri L et al Hosp Pract 2014;14:16

Key Program Components
Outpatient Treatment PE

- **Select Scoring System to Risk Stratify Pts**

- **Appropriate anticoagulant selection**

- **Patient education**

- **Medication procurement**

- **Well defined outpatient follow-up plan**

- **Staff knowledgeable in the process**

- **Monitor Monitor Monitor the process**

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Case Management

- **Acquisition of Anticoagulant Medication**
  - **Insured Patient**
    - **Health Insurance Pharmacy Benefit**
    - **Co-Payment**
    - **Patient's Pharmacy**
  - **Uninsured Patient**
    - **Hospital provides anticoagulant**
- **Pharma Company Support Programs**
- **Schedule Follow up appointment with PCP**

Nursing & Pharmacy

- **Standardized Education Materials for patient and family**
- **Use "Teach Back Method"**
- **Education provided by Nursing or Pharmacist**

Physician Communication

- **Contact Primary Care Physician**

- **Discharge Summary to PCP**

- **Discharge Instructions for Patient**

Patient Follow Up

- **Phone Call in 24 hours**
- **Phone Call in 7 days**

Pulmonary Embolism Severity Index

Variable	Score	
	PESI	sPESI
Age (years)	Age (years)	Age ≥80 years = 1
Male sex	+10	
History of cancer	+30	1
History of heart failure*	+10	1*
History of chronic lung disease*	+10	1*
Pulse ≥110 beats/min	+20	1
Systolic blood pressure <100 mm Hg	+30	1
Respiratory rate ≥30 breaths/min	+20	
Temperature <36°C	+20	
Altered mental status	+60	
Oxygenation saturation <90%	+20	1

PESI score

Score	Class	30-day mortality
<65	I	0–1.6%
66–85	II	1.7–3.5%
86–105	III	3.2–7.1%
106–125	IV	4.0–11.4%
>125	V	10.0–24.5%

HESTIA Criteria

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1. Hemodynamically unstable?
2. Thrombolysis or embolectomy necessary?
3. Active bleeding or high risk of bleeding?
4. Oxygen supply to maintain oxygen > 90% > 24 h?
5. Pulmonary embolism diagnosed during anticoagulant treatment?
6. Intravenous pain medication >24 h?
7. Medical or social reason for treatment in hospital >24 h?
8. Creatinine clearance <30 mL/min?
9. Severe liver impairment?
10. Pregnant?
11. Documented history of heparin-induced thrombocytopenia?

If any of the above are answered "yes," the patient should NOT be treated as outpatient. An answer of "no" to all of the above meets criteria for outpatient therapy.

Predictor

    Age >70 years

    History of any of the following: cancer, heart failure, chronic
        lung disease, chronic renal disease, and
        cerebrovascular disease
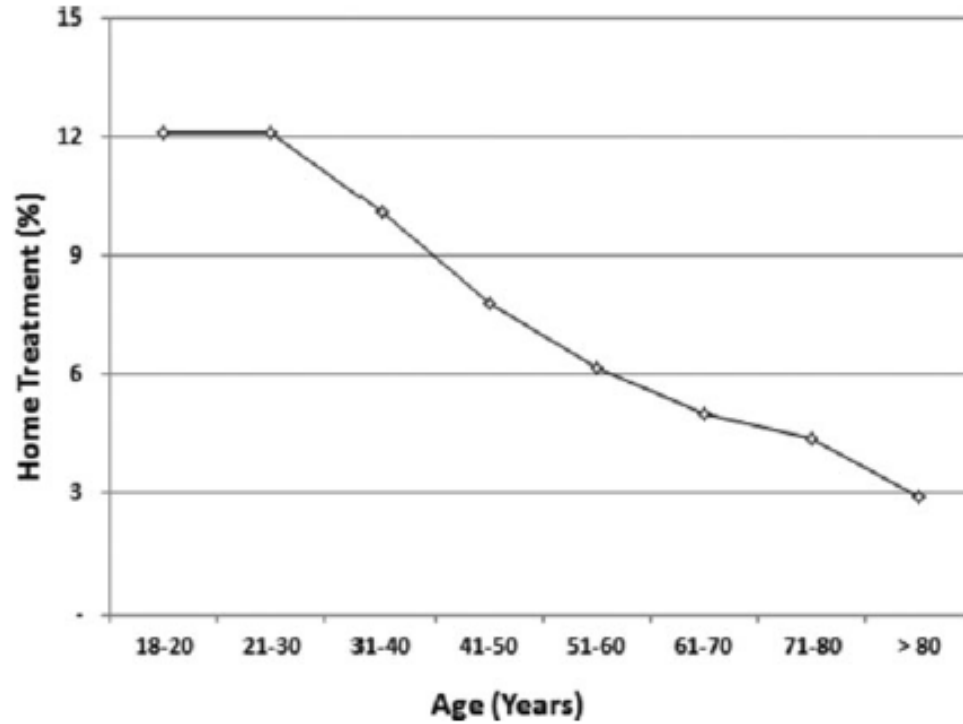
    Pulse $\geq$110 beats/min

    Systolic blood pressure <100 mm Hg

    Altered mental status

    Arterial oxygen saturation <90%

The absence of all the above factors defines patients who are at low risk for pulmonary embolism short-term mortality and adverse medical outcomes.

PE Patients Treated At Home

Stein P et al, Clin Applied Thromb Hemost. 2016;1-7.

	Stable PE (n)	Home Treatment (n)	Home Treatment (%)
Year			
2007	130 896	5099	3.9
2008	138 174	6328	4.6
2009	148 716	8306	5.6
2010	158 011	7567	4.8
2011	171 654	15 978	9.3
2012	168 250	11 215	6.7
All years	915 702	54 494	6.0
Gender			
Male	420 956	24 274	5.8
Female	494 677	30 201	6.1
All patients	915 633[b]	54 475	5.9
Age (years)			
18-20	6617	799	12.1
21-30	44 115	5334	12.1
31-40	74 666	7574	10.1
41-50	128 851	10 014	7.8
51-60	157 937	9842	6.2
61-70	176 956	8823	5.0
71-80	174 837	7754	4.4
>80	151 722	4354	2.9
All ages	915 702	54 494	6.0

Stein P et al, Clin Applied Thromb Hemost. 2016;1-7.

Comparison of two methods for selection of out of hospital treatment in patients with acute pulmonary embolism

Wendy Zondag[1]*; Paul L. den Exter[1]*; Monique J. T. Crobach[2]; Anneke Dolsma[3]; Marjolein L. Donker[4]; Michiel Eijsvogel[5]; Laura M. Faber[6]; Herman M. A. Hofstee[7]; Karin A. H. Kaasjager[8]; Marieke J. H. A. Kruip[9]; Geert Labots[10]; Christian F. Melissant[11]; Michelle S. G. Sikkens[12]; Menno V. Huisman[1]; on behalf of The Hestia Study Investigators

Prospective studies of outpatient treatment for pulmonary embolism.

Study	No of patients	Exclusion criteria for outpatient care	Intervention	Outcomes at 3–13 months
Kovacs 2000 [43]	81	Active bleeding or high bleeding risk, low compliance, renal failure, haemodynamic instability, requirement of oxygen, severe pain requiring parenteral narcotics, or hospitalisation necessary for other reasons	Dalteparin 200 IU/kg sc once daily	VTE recurrence: 6.2% Major bleeding: 1.2% Overall mortality: 4.9%
Beer 2003 [44]	43	Geneva Prognostic Score >2, contraindication to anticoagulants, drug addiction, non-compliance, psychiatric conditions, body weight >110/kg, renal failure, thrombocytopenia, concomitant thrombolysis, prior treatment with oral anticoagulants, or patients presenting on weekends	Nadroparin 171 IU/kg sc once daily	VTE recurrence: 2.3% Major bleeding: 0% Overall mortality: 0%
Wells 2005 [45]	90	Active bleeding or high bleeding risk, no fixed address, history of heparin-induced thrombocytopenia, renal failure, arterial hypotension, hypoxaemia, severe pain requiring intravenous analgesia, or hospitalisation necessary for other reasons	Dalteparin 200 IU/kg or Tinzaparin 175 U/kg sc once daily	VTE recurrence: 2.2% Major bleeding: 0% Overall mortality: 3.3%
Siragusa 2005* [46]	32	Poor clinical condition, other illness requiring hospitalisation, poor compliance, active bleeding or high bleeding risk, renal failure, acute anaemia, or pain requiring parenteral narcotics	Unspecified low-molecular-weight heparin sc once or twice daily.	VTE recurrence: 5.6% Major bleeding: 2.8% Overall mortality: 30.6%
Olsson 2006 [16]	100	Extensive PE based on lung scintigraphy or other reasons necessitating hospitalisation (e.g., intensive pain, status post surgery, active bleeding)	Tinzaparin 175 U/kg sc once daily in a patient hotel close to the hospital	VTE recurrence: 0% Major bleeding: 0% Overall mortality: 0%
Davies 2007 [47]	156	Admission necessary for other medical reason, additional monitoring required, history of prior PE, concomitant major DVT, bleeding disorders or active bleeding, poor compliance, or patient preference	Tinzaparin 175 U/kg sc once daily	VTE recurrence: 0% Major bleeding: 0% Overall mortality: 0%

Jeff FAST ™ Program

Emergency Department

↓

History & Physical
Laboratory Testing
Diagnosis DVT/PE
Select Treatment

Jeff APP

Hospital Admission ← → ED Discharge Plan

Secure Rx — Communication — Follow Up

Acquire Med — ED Contact PCP — Phone call 24 hrs

Pt Education — D/C Summary — Appointment 7 days

Discharge Emergency Department

Falconieri L et al Hosp Pract 2014;14:16

Safety Outpt Rx PE

	Outpatient treatment (n = 260) n (%; 95% CI)	Inpatient treatment (n = 213) n (%; 95% CI)	P-value
14 days follow-up			
Overall mortality	1 (0.4%; 0.0–2.1)*	27 (12.7%; 8.5–17.9)[†]	0.000
PE-specific mortality	0 (0%; 0–1.4)	5 (2.3%; 0.8–5.4)	0.018
Recurrence VTE	1 (0.4%; 0.0–2.1)	4 (1.9%; 0.5–4.7)	0.180
Major hemorrhages[‡]	0 (0%; 0.0–1.4)	13 (6.1%; 3.3–10.2)	0.000
Readmissions VTE/treatment related	4 (1.5%; 0.4–3.9)	4 (1.9%; 0.5–4.7)	1.000
3 months follow-up			
Overall mortality	13 (5%; 2.7–8.4)[§]	57 (26.7%; 20.9–33.2)[¶]	0.000
PE-specific mortality	0 (0%; 0–1.4)	5 (2.3%; 0.8–5.4)	0.018
Recurrence VTE	10 (3.8%; 1.9–7.0)	10 (4.7%; 2.3–8.5)	0.654
Major hemorrhages[†]	4 (1.5%; 0.4–3.9)	17 (8.0%; 4.7–12.5)	0.001
Readmissions VTE/treatment related	6 (2.3%; 0.9–5.0)	11 (5.2%; 2.6–9.1)**	0.135

Erkens P et al. J Thromb Haemost 2010;8:2412

Fifty per cent of patients with pulmonary embolism can be treated as outpatients

T. BAGLIN