

Supplemental Material

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eTable 1. Categorization of surgical complications

Surgical site infection*			
Location code**	Location**	Code nature of complication**	Nature of complication**
24	Pelvis	012	Prosthesis infection
40	Hip	083	Deep infection
42	Knee	134	Infected organ
Venous thromboembolism			
24	Pelvis	104	Thrombosis
40	Hip	105	Embolus
41	Femur/upper leg		
42	Knee		
43	Lower leg		
50	Lung		
56	Venous system		
Luxation			
40	Hip	041	Luxation
		086	Disconnection prosthesis
Delirium			
54	Central nervous system	141	Psychological decompensation
58	Total		
Nerve damage			
40	Hip	094	Nerve lesion
41	Femur/upper leg		
43	Lower leg		
57	Arterial system		
Postoperative bleeding			
40	Hip	014	Wound leakage
41	Femur/upper leg	022	Bleeding

42	Knee	100	Secondary
56	Venous system	136	bleeding/hematoma Bleeding organ

* the records registered with the nature of complication 010 (infection around sutures), 011 (superficial infection), 013 (local wound necrosis) and 014 (wound leakage) are checked for occurrence of surgical site infection and added to the outcome surgical site infection when this was the case.

** only depicted when location code or code of the nature of complication occurred in the register.

Furthermore records registered with nature of complication 125 (interruption of sterility) were checked for occurrence of a surgical complication.

eTable 2. Predictors per outcome

	OR*/RR** (95% CI)	Study
Surgical site infection		
Age		
<i>THA (>70years)</i>	0.7** (0.3-1.5)	Almustafa et al (2018) (1)
<i>TKA (>70years)</i>	1.7** (0.9-3.3)	Almustafa et al (2018) (1)
Smoking status	0.16** (0.05-0.52)	Møller et al (2002) (2)
BMI	6.7* (NR)	Namba et al (2005) (3)
	4.8** (1.9-12.0)	Almustafa et al (2018) (1)
	2.53* (1.25-5.13)	Chen et al (2013) (4)
Immunological disorder	-	<i>Clinical reasoning</i>
NSAID's	-	<i>Clinical reasoning</i>
Diabetes mellitus	1.90* (1.32-2.74)	Podmore et al (2018) (5)
Liver disease	2.46* (1.46-4.12)	Podmore et al (2018) (5)
Venous thromboembolism		
Age		
<i>THA(≥75years)</i>	1.82* (1.15-2.87)	Migita et al (2014) (6)
<i>TKA(≥75years)</i>	1.30* (0.99-1.71)	Migita et al (2014) (6)
Sex		
<i>THA(female>risk)</i>	2.31* (1.03-5.18)	Migita et al (2014) (6)
<i>TKA(female>risk)</i>	1.58* (1.08-2.31)	Migita et al (2014) (6)
Diabetes mellitus	1.26* (0.92-1.72)	Podmore et al (2018) (5)
<i>(TKA)</i>	1.36* (1.07-1.72)	Yang et al (2015) (7)
Thromboembolic event (<i>TKA</i>)	1.11* (0.36-3.46)	Migita et al (2014) (6)
Obesity		
<i>THA(BMI>30)</i>	0.89* (0.36-2.20)	Migita et al (2014) (6)
<i>TKA(BMI>30)</i>	0.90* (0.58-1.38)	Migita et al (2014) (6)
Postoperative bleeding		
Age		
<i>THA(>70 years)</i>	2.61** (1.50-4.53)	Quintero et al (2016) (8)

<i>TKA(>70years)</i>	2.25** (1.03-4.94)	Quintero et al (2016) (8)
BMI	-	<i>Clinical reasoning</i>
Heart disease	-	<i>Univariate analysis</i>
Vitamin K antagonists	-	<i>Clinical reasoning</i>
Smoking status	-	<i>Univariate analysis</i>
Luxation		
Age	1.27* (1.02-1.57)	Kunutsor et al (2019) (9)
Smoking status	1.08* (0.96-1.21)	Kunutsor et al (2019) (9)
BMI	1.38* (1.03-1.85)	Kunutsor et al (2019) (9)
Rheumatoid arthritis	1.50* (1.05-2.15)	Kunutsor et al (2019) (9)
Disease of the central nervous system	2.54* (1.86-3.48)	Kunutsor et al (2019) (9)
Delirium		
Age	2.20* (1.80-2.71)	Huang et al (2019) (10)
Disease of the central nervous system (<i>dementia</i>)	7.44* (3.54-14.60)	Huang et al (2019) (10)
Heart disease (<i>congestive</i>)	0.83* (0.39-1.61)	Huang et al (2019) (10)
Nerve damage		
Age (<45 vs 65-74)	7.17* (1.17-44.00)	Shetty et al (2016) (11)
BMI (<BMI >risk)	0.96* (0.77-1.21)	Kawano et al (2018) (12)
Sex (<i>female > risk</i>)	Not reported	Shetty et al (2016) (11)
Smoking status	1.90* (1.06-3.38)	Shetty et al (2016) (11)
Dysplasia	3.69* (1.65-8.28)	Farrell et al (2005) (13)
*results reported as odds ratio (OR); ** results reported as risk ratio (RR).		

eTable 3. Categorization of comorbidities

Categorization of comorbidities	
Comorbid category*	Included comorbid conditions**
Bleeding diseases	Hemophilia
Blood quality	Anemia
Cancer	Prostate cancer Leukemia Breast cancer Lymph node cancer Bowen's disease
Central nervous system	Parkinson's disease Dementia TIA CVA
Cognitive impairment	Down syndrome
Diabetes mellitus	Diabetes mellitus
Heart disease	Ischemia of the heart Valve damage blood regurgitation Valve damage reduced blood flow Valve replacement Cardiomyopathy decreased contraction Cardiomyopathy decreased relaxation Heart decompensation Heart attack Angina pectoris Atrial fibrillation
High blood pressure	Hypertension
Hyper hormonal	Hyper hormonal
Hypo hormonal	Hypo hormonal

Immunological disorder	Scleroderma Rheumatoid arthritis Gout Psoriasis Artritides Dermal barrier disease General immune disorder Organ transplantation
Inflammation	Chronic bladder infection
Kidney disease	Kidney insufficiency
Liver disease	Liver cirrhosis
Lung disease	Chronic bronchitis Asthma COPD Emphysema Dyspnea
Mood sickness	Depression Psychosis
Obesity	Obesity
Peripheral nervous system	Nerve compression Lumbar vertebral stenosis
Poor peripheral blood flow	Atherosclerosis Claudication intermittent
Thromboembolic event	Deep venous thromboembolism Pulmonary embolism

* the comorbid categories are used for analysis.

** comorbid conditions are depicted when the frequency was ≥ 10 or when the comorbid condition was considered as a relevant comorbid condition in terms of outcome prediction.

eTable 4. Categorization of drug groups

Categorization of medication use	
Drug category	Drugs groups according to the Dutch pharmacotherapeutic compass (14)
Acenocoumarol	Acenocoumarol*
Antifibrinolytica	Antifibrinolytica
Antimycotics	Antimycotic antibiotics Others
Antiretroviral agents	Antiretroviral agents
Bisfosfonates	Bisfosfonates
Colchicine group	Colchicine group
Directly working oral anticoagulants	Directly working oral anticoagulants
DMARD's biologicals	Immunosuppressives selective Immunosuppressives others
Factors in blood coagulance	Factors in blood coagulance
Fenprocoumon	Fenprocoumon*
Imidazoles	Cutane imidazoles Others
Immunosuppressives	Interferons Interleukin antagonists Monoclonal antibodies
Local antibacterial agents	Cutaneous antibacterial agents Ocular antibacterial agents
Local corticosteroids	Cutane corticosteroids Nasal corticosteroids Corticosteroides for inhalation
Low molecular weight heparins	Low molecular weight heparins
Methotrexate	Methotrexate

NSAID's**	Coxib's Others
Oncology related detoxificants	Oncology related detoxificants
Salicylates	Analgetic salicylates Trombocytic salicylates
Statins	Statins
Systemic antibacterial agents	Cephalosporins Macrolides Penicillin's Tetracyclines Carbapenems Ceftriaxone Glycopeptides Aminoglycosides Rifamycins tuberculose Sulfonamides and trimethoprimides Triazoles Fluoroquinolones Others
Thrombocyte-aggregationblockers	P2y12 blockers Others
Xanthineoxidase inhibitor	Xanthineoxidase inhibitor

* according the Dutch pharmacotherapeutic compass, acenocoumarol and fenprocoumon belong to the drug group 'vitamin k antagonists'. Based on expert opinion, acenocoumarol and fenprocoumon were included separately in the analysis because of the differences in half-life.

** Non-Steroidal Anti-Inflammatory Drugs

eTable 5. Original prediction models and adjusted coefficients

Prediction model for estimation of risk for surgical site infection

Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-7.305	-7.272	-
Age (years)	0.031	0.031	1.032 (1.005-1.059)
BMI (kg/m ²)	-0.002	-0.002	0.998 (0.937-1.063)
Smoking status (yes/no)	0.769	0.757	2.145 (0.883-5.213)
Immunological disorder (yes/no)	0.905	0.891	2.474 (1.186-5.158)
Diabetes mellitus (yes/no)	0.918	0.904	2.494 (1.125-5.529)
Liver disease (yes/no)	2.382	2.345	10.659 (2.441-46.555)
NSAID's (yes/no)	0.629	0.619	1.877 (0.946-3.725)
To calculate the absolute risk of surgical site infection: $P_{(\text{surgical site infection})} = 1 / (1 + e^{-\text{linear part}}) \times 100\%$; Linear part = $-7.272 + (0.031 \times \text{age} - 0.002 \times \text{BMI} + 0.757 \times \text{smoking status} + 0.891 \times \text{immunological disorder} + 0.904 \times \text{diabetes mellitus} + 2.345 \times \text{liver disease} + 0.619 \times \text{NSAID's})$. *adjustment for over-fitting by shrinkage factor (SF) (SF = 0.984); the intercept was re-estimated.			

Prediction model for estimation of risk for venous thromboembolism

Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-4.764	-4.790	-
Age (years)	-0.009	-0.008	0.991

			(0.966-1.018)
Gender (male/female)	-0.170	-0.168	0.844 (0.377-1.888)
Obesity (yes/no)	1.396	1.376	4.040 (1.462-11.159)
Diabetes mellitus (yes/no)	0.841	0.829	2.317 (0.870-6.173)
Thromboembolic event (yes/no)	1.523	1.501	4.586 (1.521-13.826)
To calculate the absolute risk of venous thromboembolism: $P_{(\text{venous thromboembolism})} = 1/(1+e^{-\text{linear part}}) \times 100\%$; Linear part = $-4.790 + (-0.008 \times \text{age} - 0.168 \times \text{gender} + 1.376 \times \text{obesity} + 0.829 \times \text{diabetes mellitus} + 1.501 \times \text{thromboembolic event})$.			
*adjustment for over-fitting by shrinkage factor (SF) (SF = 0.986); the intercept was re-estimated.			

Prediction model for estimation of risk for postoperative bleeding.

Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-7.182	-7.172	-
Age (years)	0.033	0.033	1.034 (1.006-1.062)
BMI (kg/m ²)	0.012	0.012	1.012 (0.954-1.073)
Smoking status (yes/no)	-0.023	-0.023	0.952 (0.336-2.701)
Heart disease (yes/no)	0.737	0.729	2.086 (1.040-4.183)
Vitamin K antagonist use (yes/no)	0.796	0.787	2.220 (1.022-4.821)
To calculate the absolute risk of postoperative bleeding: $P_{(\text{postoperative bleeding})} = 1/(1+e^{-\text{linear part}}) \times 100\%$;			

Linear part = $-7.172 + (0.033 \times \text{age} + 0.012 \times \text{BMI} - 0.023 \times \text{smoking status} + 0.729 \times \text{heart disease} + 0.787 \times \text{vitamin K antagonist use})$.

*adjustment for over-fitting by shrinkage factor (SF) (SF = 0.989); the intercept was re-estimated.

Prediction model for estimation of risk for luxation.

Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-5.976	-5.800	-
Age (years)	0.014	0.013	1.014 (0.991-1.038)
BMI (kg/m ²)	0.022	0.021	1.023 (0.951-1.099)
Smoking status (yes/no)	0.521	0.491	1.667 (0.651-4.268)
Rheumatoid arthritis (yes/no)	0.572	0.538	1.752 (0.408-7.530)
Disease of central nervous system (yes/no)	0.113	0.106	1.113 (0.324-3.822)
To calculate the absolute risk of luxation: $P_{(\text{luxation})} = 1/(1+e^{-\text{linear part}}) \times 100\%$; Linear part = $-5.800 + (0.013 \times \text{age} + 0.021 \times \text{BMI} + 0.491 \times \text{smoking status} + 0.538 \times \text{rheumatoid arthritis} + 0.106 \times \text{disease of central nervous system})$. *adjustment for over-fitting by shrinkage factor (SF) (SF = 0.941); the intercept was re-estimated.			

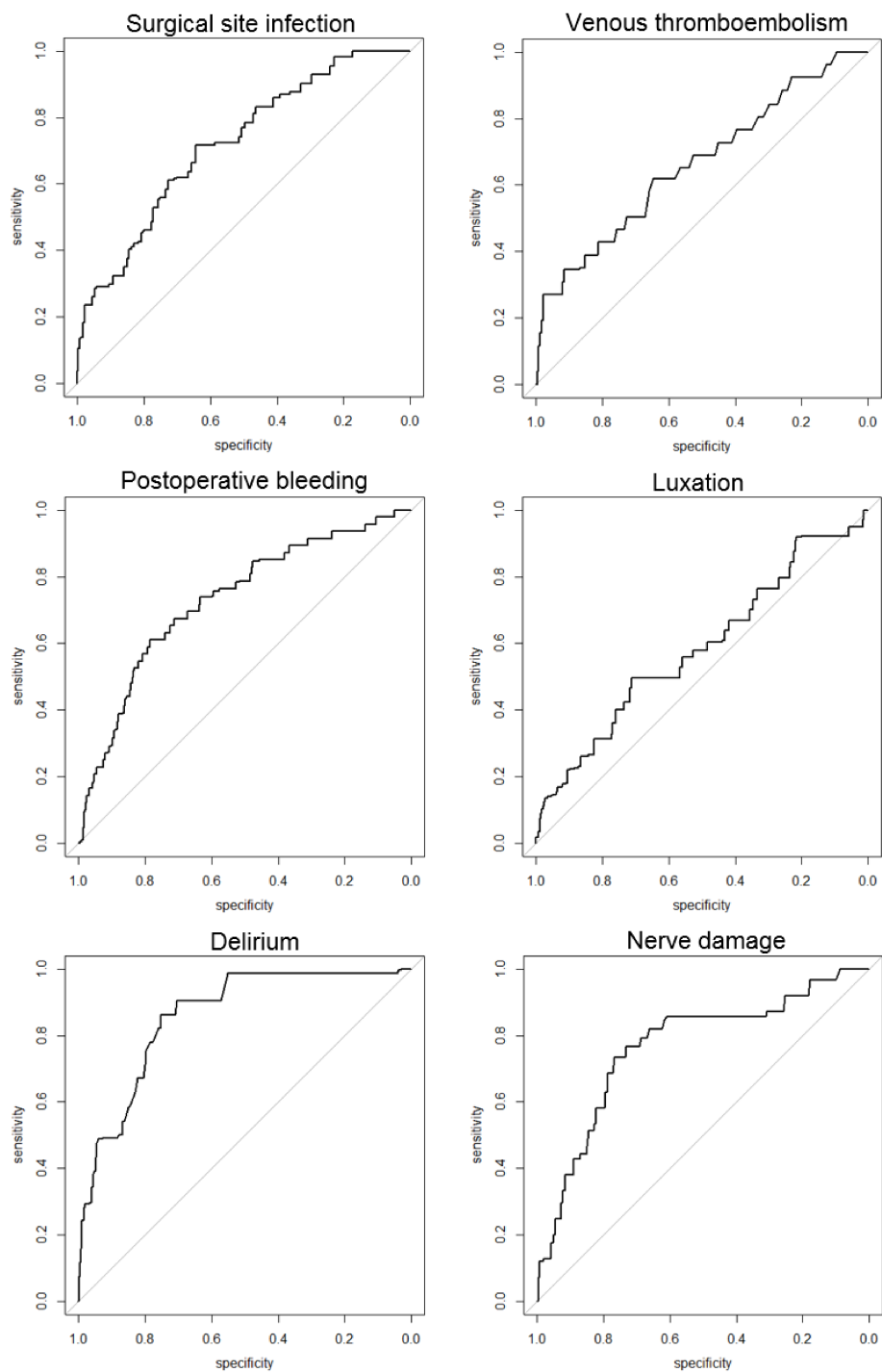
Prediction model for estimation of risk for delirium.

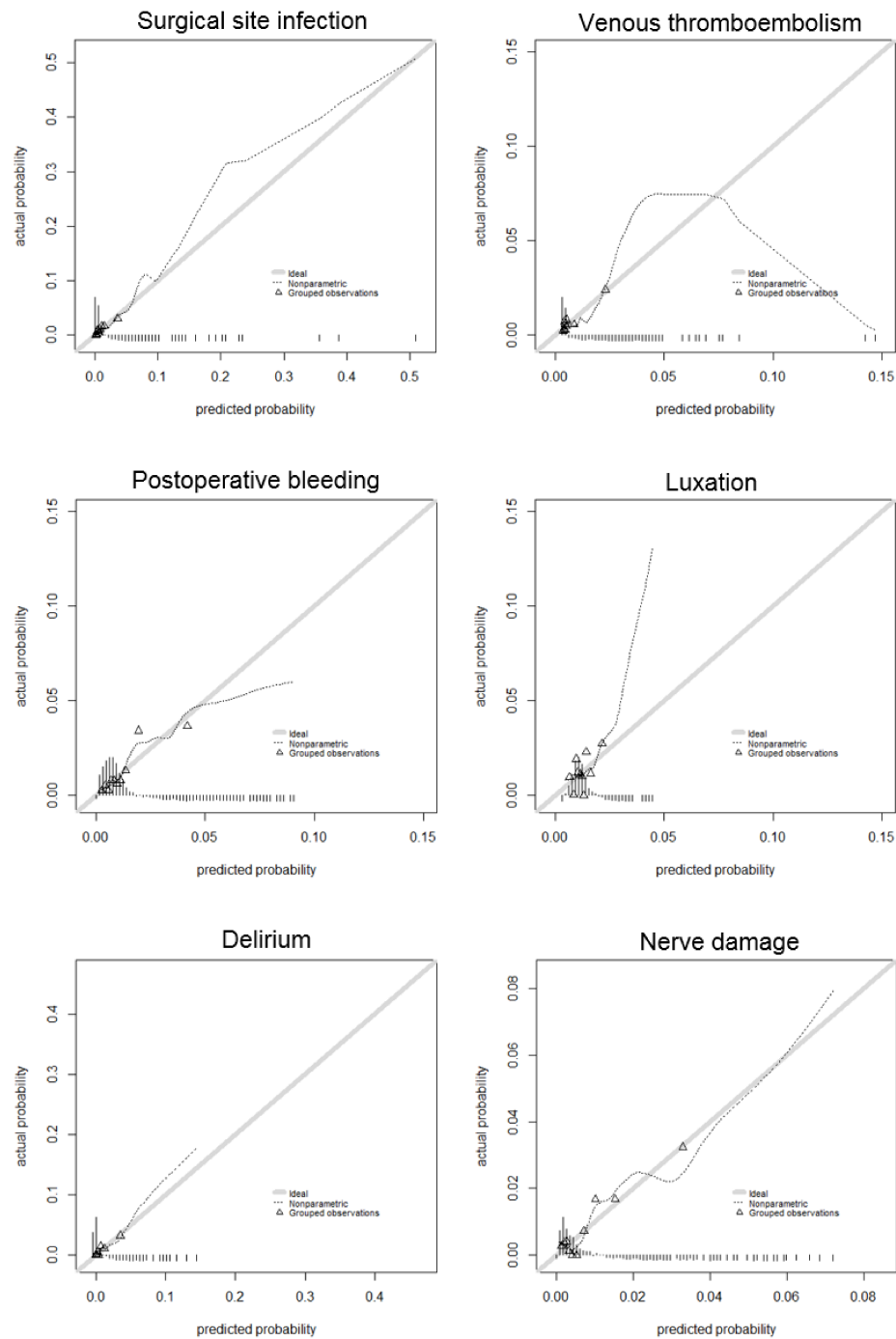
Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-14.368	-14.307	-
Age (years)	0.129	0.127	1.137 (1.067-1.212)
Heart disease (yes/no)	0.351	0.348	1.422

			(0.590-3.428)
Disease of central nervous system (yes/no)	0.904	0.898	2.465 (0.936-6.490)
<p>To calculate the absolute risk of delirium: $P_{(\text{delirium})} = 1/(1+e^{-\text{linear part}}) \times 100\%$;</p> <p>Linear part = $-14.307 + (0.127 \times \text{age} + 0.348 \times \text{heart disease} + 0.898 \times \text{disease of central nervous system})$.</p> <p>*adjustment for over-fitting by shrinkage factor (SF) (SF = 0.993); the intercept was re-estimated.</p>			

Prediction model for estimation of risk for nerve damage.

Variable	Regression coefficient	Regression coefficient (adjusted with SF)*	Odds Ratio (95% CI)
Intercept	-2.209	-2.250	-
Age (years)	-0.052	-0.051	0.949 (0.926-0.974)
Gender (man/woman)	-0.258	-0.254	0.772 (0.319-1.868)
Smoking status (yes/no)	0.580	0.572	1.754 (0.510-6.029)
Dysplasia (yes/no)	-0.009	-0.009	0.993 (0.217-4.552)
<p>To calculate the absolute risk of nerve damage: $P_{(\text{nerve damage})} = 1/(1+e^{-\text{linear part}}) \times 100\%$;</p> <p>Linear part = $-2.250 + (-0.051 \times \text{age} - 0.254 \times \text{gender} + 0.572 \times \text{smoking status} - 0.009 \times \text{dysplasia})$.</p> <p>*adjustment for over-fitting by shrinkage factor (SF) (SF = 0.987); the intercept was re-estimated.</p>			

eFigure 1. ROC curves and Calibration plots**eFigure 1.1.** Receiver Operating Characteristic curves of the prediction models for surgical site infection, venous thromboembolism, postoperative bleeding, luxation, delirium and nerve damage



eFigure 1.2. Calibration plots with actual probability against the predicted probability for the models for surgical site infection, venous thromboembolism, postoperative bleeding, luxation, delirium and nerve damage. The triangles indicate quantiles ($g=10$) of patients with a similar predicted probability of success. The grey diagonal line represents perfect agreement between predicted and actual probability

REFERENCES

1. Almustafa MA, Ewen AM, Deakin AH, Picard F, Clarke JV, Mahmood FF. Risk Factors for Surgical Site Infection Following Lower Limb Arthroplasty: A Retrospective Cohort Analysis of 3932 Lower Limb Arthroplasty Procedures in a High Volume Arthroplasty Unit. *The Journal of Arthroplasty*. 2018;33(6):1861-7.
2. Moller AM, Villebro N, Pedersen T, Tonnesen H. Effect of preoperative smoking intervention on postoperative complications: a randomised clinical trial. *Lancet*. 2002;359(9301):114-7.
3. Namba RS, Paxton L, Fithian DC, Stone ML. Obesity and perioperative morbidity in total hip and total knee arthroplasty patients. *J Arthroplasty*. 2005;20(7 Suppl 3):46-50.
4. Chen J, Cui Y, Li X, Miao X, Wen Z, Xue Y, et al. Risk factors for deep infection after total knee arthroplasty: a meta-analysis. *Arch Orthop Trauma Surg*. 2013;133(5):675-87.
5. Podmore B, Hutchings A, van der Meulen J, Aggarwal A, Konan S. Impact of comorbid conditions on outcomes of hip and knee replacement surgery: a systematic review and meta-analysis. *BMJ Open*. 2018;8(7):e021784.
6. Migita K, Bito S, Nakamura M, Miyata S, Saito M, Kakizaki H, et al. Venous thromboembolism after total joint arthroplasty: results from a Japanese multicenter cohort study. *Arthritis Res Ther*. 2014;16(4):R154-R.
7. Yang G, Meng F, Liu Y, Kong L, Shen Y. Diabetes mellitus and risk of deep vein thrombosis after total knee replacement: a meta-analysis of cohort studies. *Int J Clin Exp Med*. 2015;8(6):9086-92.

8. Quintero JI, Cardenas LL, Navas M, Bautista MP, Bonilla GA, Llinas AM. Primary Joint Arthroplasty Surgery: Is the Risk of Major Bleeding Higher in Elderly Patients? A Retrospective Cohort Study. *J Arthroplasty*. 2016;31(10):2264-8.
9. Kunutsor SK, Barrett MC, Beswick AD, Judge A, Blom AW, Wyld V, et al. Risk factors for dislocation after primary total hip replacement: a systematic review and meta-analysis of 125 studies involving approximately five million hip replacements. *The Lancet Rheumatology*. 2019;1(2):e111-e21.
10. Huang J, Sprung J, Weingarten TN. Delirium following total joint replacement surgery. *Bosn J Basic Med Sci*. 2019;19(1):81-5.
11. Shetty T, Nguyen JT, Wu A, Sasaki M, Bogner E, Burge A, et al. Risk Factors for Nerve Injury After Total Hip Arthroplasty: A Case-Control Study. *J Arthroplasty*. 2019;34(1):151-6.
12. Kawano S, Sonohata M, Kitajima M, Mawatari M. Risk Factors for the Development of Nerve Palsy Following Primary Total Hip Arthroplasty. *Open Orthop J*. 2018;12:164-72.
13. Farrell CM, Springer BD, Haidukewych GJ, Morrey BF. Motor nerve palsy following primary total hip arthroplasty. *J Bone Joint Surg Am*. 2005;87(12):2619-25.
14. ZorginstituutNederland. Farmacotherapeutisch Kompas. 2020 [Available from: <https://farmacotherapeutischkompas.nl>].