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# SOCIO-ECONOMIC ASSESSMENT OF PATIENT BLOOD MANAGEMENT PRACTICAL IMPLEMENTATION IN SURGICAL TREATMENT OF CORONARY HEART DISEASE (I20–I25)

Aim	To evaluate possible social and economic benefits of correcting preoperative iron deficiency/iron deficiency anemia as a comorbidity in a model population in the process of transition from the routine practice to the optimized preparation of patients to elective surgery (as exemplified by several circulatory diseases: I20 – I25, class IX ICD 10).
Material and methods	By building imitation models depending on the patient blood management (PBM) practice, changes in years of life lost/saved adjusted for disability were evaluated, including in monetary terms, in relation to the annual number of operations performed for ischemic heart disease (IHD) (I20 – I25) in the age group of 17 years and older, as well as a potential effect of PBM on the applied health economics.
Results	With implementation of the PBM systemic measures in cardiac surgery, the potentially prevented annual social and economic damage will amount to more than 38 thousand years of life saved and more than 20.2 billion rubles in monetary terms. Furthermore, it will be possible to exclude 9435 hemotransfusion from the cardiosurgical practice, which will annually save more than 2.3 thousand liters of blood with a total cost of 77.7 million rubles in favor of clinical situations that have no alternative.
Conclusion	The implementation of PBM in cardiac surgery, the discipline with the highest levels of preoperative iron deficiency/anemia and the use of blood components, will not only improve the clinical outcomes and cost-effectiveness of surgical interventions, but will also prevent social and economic damage to the country.
Keywords	Social and economic damage; iron deficiency; anemia; patient blood management (PBM); cardiovascular surgery; hemotransfusion; applied health economics
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#### Introduction

Coronary artery disease (CAD), which is associated in about 70% of cases with chronic heart failure (CHF) [1], is a socially sensitive disease. This is due to the very high rates of annual fatal and non-fatal losses in the Russian Federation of 19.2 million DALYs (16.0% of all countrywide losses, 51.5% of losses due to cardiovascular diseases). DALY (disability-adjusted life years) is a composite measure (DALY=YLL + YLD) used to assess the loss of potential years of life as a result of premature death by YLL (years of life lost) and the impact of disability (expected/mean number of years lost due to a disease) by YLD (years lost due to disability). One DALY is a lost year of healthy life adjusted for a specific disease/health status [http://ghdx.healthdata.org/gbd-

results-tool, 2018]. The prevalence of chronic CAD (3.857.1 per 100 thousand peopleaged 18 or more [2]) results in more than three hundred thousand surgical interventions every year [3] (~42.9% of all cardiovascular interventions and ~73.7% of all heart surgeries) [2]. Thus, there is a need for medical technologies to be implemented in cardiology practice to reduce the risk of adverse surgical outcomes.

According to the consensus of leading cardiologists and transfusiologists [4], one such technology is multimodal individual patient blood management (PBM). This consists of three factors: improving erythropoiesis including correcting iron deficiency/iron deficiency anemia (ID/IDA); preventing blood loss; and optimizing physiological tolerability of anemia [5].

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Iron deficiency and anemia in patients with CAD/CHF are clinically significant concomitant diseases [6]. The timely detection and correction of pre-operative ID/IDA in all patients requiring operation is a good clinical practice [4] which minimizes the risk of postoperative complications / death and reduces the need for hemotransfusion. It also significantly saves associated health costs and overall economic losses of a country [7-9]. In 2019, the Russian Federal Government incurred expenses of 4.16 billion rubles connected with the budget line «Collecting, processing, storing and securing donated blood and its components». The consolidated expenses of the budget of the Russian Federation subject and the territorial state non-budgetary fund amounted to 28.5 billion RUB (Federal Treasury of the Russian Federation, https:// www.roskazna.ru/ispolnenie-byudzhetov/federalnyjbyudzhet/). In 2019, the total volume of transfusions was 956.7 thousand liters [3].

According to foreign researchers, the potential costeffectiveness of PBM is due mainly to the reduction of transfusions, the frequency of postoperative complications, and the duration of hospital stay [10]. Using PBM in cardiac surgery to eliminate the risk of independent factor triad (anemia, blood loss, hemotransfusions) prevents 14.45% of post-operative complications and 3.04% of deaths. Given the hospitalization costs, the savings are 14.139 EUR per prevented complication and 57.883 EUR per prevented complication-related death [11].

In Russia, the economic consequences of preoperative iron deficiencies have not yet been thoroughly analyzed. In this regard, the data calculated based on local foreign indicators, concerning the potential reduction of socio-economic losses and the actual economic benefits in the case of PBM, will contribute to the earlier systematic implementation of PBM in the Russian clinical practice. This includes cardiac surgery, which is a medical field with significantly higher levels (odds ratio (OR) 2.75, p<0.001) of blood component use compared to other areas [12–14].

#### Aim

To estimate the possible socio-economic benefits of correcting pre-operative iron deficiency/iron deficiency anemia as a concomitant diagnosis in the model population when moving from the existing practice to an improved practice of preparing patients for scheduled surgeries (using the examples of some diseases of the circulatory system: I20 – I25, class IX ICD 10). The factor of pre-operative ID/IDA in cardiac surgery is briefly described in the Appendix.

#### Material and methods

## Approaches to the assessment considering incurred/prevented socio-economic losses

DALY (Global burden of disease, GBD [15]) was selected to quantify the socio-economic impact of surgical outcomes in cardiosurgical patients (I20-I25) with perioperative ID/IDA depending on applying/non-applying PBM. The monetary expression of losses (resources spent by the society due to morbidity, disability, or mortality, and taking into account reduced working age due to a disease/decrease in life expectancy [16]) was calculated by multiplying the estimated mean cost of one year of mean life expectancy [17, 18] by the total years lost due to the disease.

A model was constructed to analyze the potential changes in lost/saved years of life in relation to the annual number of surgeries for CAD (I20 – I25) in seventeen-year-old and older patients [3]. Since the global indicators, mortality, and risk factors associated with iron deficiency are estimated in GBD as a condition associated with alimentary iron deficiency, the study objectives were also achieved by constructing several econometric models that enabled the necessary calculations to be made at a high level of significance.

Initially, the most recent available GBD data was used to calculate the number of years lost per ID/IDA case (due to the inability to reliably estimate the perioperative mortality directly caused by ID/IDA, YLL was excluded from the calculations and the losses were estimated only using YLD, Formula 1):

$$YLD'=YLD_{i}/n_{i}$$
 (1),

where n is the number of ID/IDA cases, i is a corresponding country.

The nominal value of one YLD was multiplied by the number of surgeries in patients with ID/IDA, in order to estimate the years of life lost. The monetary estimation of health and human life was used to calculate the monetary expression of YLD, and its total value in terms of the cost of the losses incurred. The total monetary equivalent of socio-economic losses, as the total of YLDs for all the I20 – I25 surgeries in patients with ID/IDA, was calculated using Formula 2:

The monetary equivalent of socio-economic losses=YLDs × calculated an equivalent of the mean cost of one year of human life (2).

The problem of the absence of potential values of the indicators assessed when implementing PBM in the Russian Federation was resolved by modeling the possible changes in the Russian healthcare system. This was based on the assumption that they would correspond to German values. Between 1990–2017, the reduction of



losses per case in YLD and YLL, including due to the use of PBM, was 26.11 and 3.06%, respectively.

Depending on the order of surgeries, the potential losses from implementing PBM were calculated in a differentiated manner (Formula 3). In the case of scheduled surgeries, the specific values of YLD calculated for Germany were used. In the case of emergency surgeries, not conditionally assuming pre-operative correction of ID/IDA, the actual specific losses were used, i.e., those calculated for the Russian Federation.

$$YLDs_{ID/IDA}=YLD'_{Germany} \times N \times SS+YLD'_{RF} \times N \times (1 SS) (3),$$

where  $\rm YLD_{\rm sID/IDA}$  are losses caused by scheduled and emergency surgeries for I20-I25 in patients with ID/IDA after the potential implementation of PBM in the Russian Federation.  $\rm YLD'_{\rm Germany}$  are specific losses per ID/IDA case after possible implementation of PBM in the Russian Federation (at the level of specific losses in Germany). N is the number of surgeries for I20 – I25 in patients with ID/IDA.  $\rm YLD'_{RF}$  are specific losses per ID/IDA case before potential implementation of PBM in the Russian Federation. SS is the percentage (%) of scheduled surgeries of the total number of surgeries for I20 – I25 in patients with ID/IDA. (1 SS) is the percentage (%) of emergency surgeries for I20 I25 in ID/IDA patients.

# Approaches to the assessment considering the impact of PBM on some financial indicators in health care

In order to assess the potential impact of PBM on the applied health care economics, a simulation model was used to analyze current and possible perioperative management of CAD patients (I20-I25). The model assessed the number and cost for two comparison parameters: number of red blood cell (RBC) suspension transfusion procedures; and the mean duration of hospital stay. The material analyzed included the cumulative data of 1,133 medical records of patients subjected to surgical treatment for CAD in Bakulev National Medical Research Center for Cardiovascular Surgery in 2019. Given the annual volume of surgeries performed in the Russian Federation for I20-I25 (310,988 [3]), error in the analysis of 1,133 cases does not exceed 0.57% with the 95% confidence interval. This allows the whole population analyzed to be assessed based on the sample results.

The calculation of savings made based on the duration of hospital stay assumed that after implementing the PBM program this indicator would be the same in anemia patients as in those without anemia at present, without sex-specific calculations. The potential benefit of reducing the mean duration of hospital stay per patient was

calculated by multiplying the difference in the number of days before and after the possible implementation of PBM, by the cost of a 24-hour hospital stay in a surgical department.

$$S_{B/D} = C_{SD} \times \Delta DS_{SD}$$
 (4),

where EB/D are the potential savings from reducing the mean duration of hospital stay per patient with mild anemia. CSD is the cost rate of one day in a surgical department.  $\Delta DS_{SD}$  is the difference in the duration of hospital stay between a patient with mild anemia and a patient without anemia in a surgical department.

In order to calculate the cost of hospital stay, the cost rates effective in Moscow in 2019 were used [19]. The cost of one day in a standard surgical ward of 418.37 RUB.

The cost of transfusion was calculated on the basis that intraoperative transfusions were performed 2.73 times more often in a group of 51,111 patients who underwent surgeries for CAD (310,988×95%×17.3%=51,111), than in patients without anemia. Based on the cost of one liter of blood/blood components (the calculations were based on the assumption of equal value of 1 liter of any blood component) of 34,148.30 RUB and the difference in the mean single volumes of transfusion (167.8 mL), the cost of transfusion per recipient and the total cost of transfusions of blood/blood components for all anemia patients surgically operated for I20 – I25 were calculated as follows:

$$C_{RBCS} = V_{RBCS} \times C_{RBCS} L (5),$$

where  $C_{RBCS}$  is the cost of RBC suspension per patient with mild anemia.  $V_{RBCS}$  is the volume of RBC suspension transfused per patient with mild anemia.  $C_{RBCS}L$  is the cost of one liter of RBC suspension; and

$$S_{RBCS} = C_{RBCS} \times P_{SO}$$
 (6),

where  $S_{RBCS}$  are the potential savings of RBC suspension in patients with mild anemia.  $P_{SO}$  is the number of surgically operated patients with mild anemia for CAD.

The estimated cost of transfusions was assessed both as expenses incurred without the correction of preoperative anemia and as potential savings if some PBM activities were performed.

#### Statistical analysis

Data analysis was performed using SPSS 21.0. The normality of distribution was evaluated using the Kolmogorov-Smirnov test. Quantitative variables are expressed as the median (Me), and the interquartile range and qualitative variables are represented as the absolute and relative values (n (%)).

The quantitative data was compared between two independent samples using the Mann–Whitney test. Chi-scared ( $\chi^2$ ) test was used to compare qualitative variables. The prognosis was estimated in a binary logis-



tic model. The differences were statistically significant at p<0.005.

#### Results

#### Assessment of incurred/prevented socio-economic losses

In order to make an evaluation based on the available publications and expert data, all surgical interventions performed for I20-I25 were grouped by order of implementation (emergency/scheduled) followed by calculating the percentage of patients with pre-operative ID/IDA (Table 1).

Table 2 shows the results of the calculation of the number of years lost per ID/IDA case (YLD) by means of Formula 1.

The monetary estimation used the calculated cost of one year of mean life expectancy based on data obtained from the following agencies: the Federal Treasury; the Pension Fund; the Ministry of Labor and Social Protection; and the Federal Service of State Statistics. This data was equal to the values of 2019 as shown in Table 3.

According to the calculations provided, the potential annual losses due to the failure to correct ID/IDA in due time in 70% of patients (217,692) requiring surgery for I20 – I25 during 12 months amount to more than 50 thousand years lost and more than 26 billion RUB in monetary terms (Table 4). At the same time, the high weighted mean specific monetary equivalent of YLD' (per thousand surgeries with concomitant anemia) entails high specific losses regarding all 310,988 surgeries for I20 – I25. The systematic introduction of PBM in cardiac surgical

departments followed by changes in the specific YLD' from current Russian values (0.23 for both sexes) to those similar to the German values (0.05 for both sexes) may produce a more than threefold reduction in the years of life lost (YLD) and their monetary expression (Table 4).

### Assessment of the impact of PBM on some health care indicators

Our analysis showed that, of the total number of CAD surgeries, anemia was reported as a concomitant condition in the pre-operative period in 196 (17.3%) patients (149 males, 76%), with lower mean hemoglobin and RBC levels when compared to patients without anemia (Table 5).

Patients with pre-operative anemia had lower hemoglobin levels on day 1 (p=0.0001) and day 5 (p=0.0001) after surgery with comparable intraoperative blood loss. This was despite the higher frequency and volume of RBC suspension transfusions when compared to patients without pre-operative anemia (OR=3.99, 95% CI[2.86; 5.58], p=0.0001) (Table 6).

Patients with uncorrected pre-operative anemia remain in hospital for a little longer than patients without initial anemia and spend more hours on ventilation and more days in ICU (Table 7). A complicated post-operative period, and especially the development of acute coronary syndrome, is also more common in patients with pre-operative anemia (Table 8). At the same time, both anemia and the transfusion of RBC-containing components of donated blood are prognostic of adverse surgery outcomes (Table 9).

Table 1. Annual volume of surgeries (I20-I25), Russian Federation, 2019

Discipline	Total, n¹	Scheduled surgeries, %2	Surgeries with ID/IDA, %2	Surgeries with ID/IDA, n <sup>3</sup>
Cardiac surgery (I20-I25)	310 988	95	70	217 692

<sup>&</sup>lt;sup>1</sup> – statistics; <sup>2</sup> – expert assessment; <sup>3</sup> – calculation.

**Table 2.** Calculated specific values of global indicators, 2017

Indicators	RF	Germany	
mulcators	Both sexes	Both sexes	
YLD', years of life	0.23	0.05	

**Table 3.** Estimated mean cost of one year of mean life expectancy, 2019

Population	Cost, RUB
Male	578,075.01
Female	473,003.20
Mean	521,546.38

Table 4. Losses due to perioperative ID/IDA, Russian Federation, 2019

Discipline	YLD, years	Monetary equivalent of YLD,	YLD () per 1,000 surgeries (all surgeries)	YLD () per 1,000 surgeries with anemia
Cardiac surgery (I20-I25), before PBM	50,190	26,176,501,239.83	69,808,843.39	120,245,802.96
Cardiac surgery (I20-I25), with PBM*	11,838	5,971,263,441.58	19,200,944.86	27,429,921.24
$\Delta_{ m beforePBM-withPBM}$	38,352	20,205,237,798.25	76.41%	_

<sup>\* –</sup> scheduled surgeries – 95%.



Table 5. Hematologic parameters in patients with CAD depending on the presence of anemia

Parameters	Patients without anemia	Patients with anemia					
1 arameters	ratients without allellia	Total	Male	Female			
Hemoglobin, g/L	144 [137; 152]	120 [114; 127]	124 [116; 128]	115 [110; 118]			
RBC,×10 <sup>9</sup> /L	5.0 [4.7; 5.3]	4.3 [4.0; 4.6]	4.3 [4.0; 4.6]	4.3 [3.9; 4.6]			
MCV<80 fL	11 (1.2%)	20 (10.9%)	13 (9.4%)	7 (15.9%)			
MCH<27 pg	93 (10.2%)	59 (32.2%)	35 (25.2%)	24 (54.5%)			

**Table 6.** Blood loss, hemoglobin levels, and transfusion of RBC-containing components of donated blood during and after coronary artery bypass grafting

Parame	Patients	Pa	itients with anemi	a	
raiame	without anemia	Total	Male	Female	
Intraoperative blood loss, mL		400 [400; 500]	400 [400; 500]	400 [400; 500]	400 [400; 600]
Transfusion of RBC-containing components of donated blood	Patients, n (%)	143 (15.3%)	82 (41.8%)	55 (36.9%)	27 (57.4%)
	Volume of transfusions, mL	0 [0;0]	0 [0;338]	0 [0; 333]	300 [0; 621]
Hemoglobin levels, g/L	Day 1	111 [99;123]	96 [89;105]	97 [89;107]	92 [87;103]
	Day 5	110 [99;121]	95 [88;108]	96 [88;109]	95 [88;104]

**Table 7.** Need for mechanical ventilation, duration of ICU, and hospital stay after coronary artery bypass grafting depending on the presence of initial anemia

Status	Duration of hospital stay, days				Duration of ICU s	Duration of ventilation, hours		
	Me [Q1-Q3]	p	min	max	Me [Q1-Q3]	p	Me [Q1-Q3]	p
Without anemia	9 [8; 12]	0.089	6.0	14.6	0.8 [0.7-0.9]	0.024	10 [7–13.5]	0.018
With anemia	10 [8; 13]	0.069	6.7	14.9	0.8 [0.7–1]	0.024	11 [7–17]	0.018
Total sample/ difference	10 [8; 12] 0.7 0.3		0.3					

With the above factors in mind, the results of calculations made using the simulation model to analyze the current and potential perioperative CAD patient management show that individual patient blood management at all stages of surgery for I20-I25 would be of benefit to applied health care economics. Thus, it would be possible to save more than 10 million RUB, or 205 thousand RUB per 1,000 surgically operated patients with anemia. This would be achieved by reducing the duriation of hospital stay (Table 10), while more than 2.2 thousand liters of blood coild be saved with a total cost of 77.6 million RUB, or 1.52 million RUB per 1,000 surgeries in patients with anemia. This would be achieved by excluding 9,435 transfusions (Table 11).

#### Discussion

The discrepancy between the published (70%) and actual clinical (17.3%) data in the prevalence of ID/IDA in patients who underwent surgery for I20 – I25 raises the issue of the quality of pre-operative examination and the evaluation of its results. In routine Russian practice, prelatent and latent forms of iron deficiency, as well as its symptomatic form (iron deficiency anemia), are clearly underdiagnosed. This makes it difficult to

assess possible intra- and postoperative risks and related economic losses. According to the available findings, surgical interventions for I20 – I25 are performed only in patients with mild anemia (Hb>90 g/L), showing that patients with moderate anemia (according to the WHO [20]) are also included in this group. The issue of surgery in moderate to severe anemia, which is undoubtedly the case in all classes of CHF in CAD, is also considered. Although it cannot be excluded that anemia is treated as an outpatient procedure before surgery, and only when hemoglobin is>90 g/L, physicians find it possible to refer patients for surgical treatment.

According to the medical records analyzed, iron metabolism in patients with mild (and in fact moderate in some cases) anemia in the pre-operative period is not studied and it is not corrected after hospitalization. At the same time, a combination of low hemoglobin levels and RBC count with reduced RBC indices (MCV<80 fL and MCH<27 pg, respectively) was observed in at least 25% of surgically operated male patients and 54% of surgically operated female patients. This is indicative of microcytic hypochromic anemia, most often caused by iron deficiency, which decreases the heart muscle performance and is an independent prognostic factor of



Table 8. Effects of pre-operative anemia on the prognosis of early post-operative complications

Variable	With anemia. n (%)	Without anemia. n (%)	OR	95% CI	p
Acute coronary syndrome	5 (2.6%)	8 (0.9%)	3.1	1.0-9.5	0.05
Heart failure	2 (1%)	7 (0.7%)	1.4	0.3-6.7	0.696
Neurological complications	5 (2.6%)	13 (1.4%)	1.9	0.7-5.3	0.243
Infections	6 (3.1%)	13 (1.4%)	2.3	0.6-6.0	0.106
Respiratory failure	3 (1.5%)	7 (0.7%)	2.1	0.5-8.1	0.296

Table 9. Effects of RBC-containing blood component transfusions on early post-operative complications

Variable	With transfusions, n (%)	Without transfusions, n (%)	OR	CI	p
Acute coronary syndrome	7 (3.1%)	6 (0.7%)	4.8	1.6-14.3	0.005
Heart failure	5 (2.2%)	4(0.4%)	5.1	1.4-19.0	0.016
Neurological complications	9 (3.9%)	9 (1%)	4.1	1.6-10.5	0.003
Infections	9 (3.9%)	10 (1.1%)	3.7	1.6-10.5	0.005
Respiratory failure	5 (2.2%)	5 (0.5%)	4.1	1.1-14.2	0.028

Table 10. Potential savings by reducing the mean duration of hospital stay, scheduled surgeries

Degree of anemia	Patients	Savings, K/day		Cost difference per patient, ₽	Total savings, ₽
		mean	25,555	209.19	5,345,814.49
Легкая	<b>Легкая</b> 51111	min	15,333	125.51	1,924,493.22
		max	35,778	292.86	10,477,796.39

Table 11. Potential savings (loss prevention) by reducing the number of transfusions

Degree of anemia	the number		Specific (pe decrease in trans	<b>1</b> /	Potential savings of RBC suspension	
or anemia	of recipients	of transfusions	mL	₽	L	₽
Легкая	13545	9435	167.8	5730.08	2272.9	77615671.07

an adverse CHF outcome. Given that normocytic anemia is also possible in iron deficiency, and hypochromia may develop in normal-volume RBCs, the failure to perform pre-operative testing for iron reduces the possibility of adequate and objective assessment of concomitant conditions in CAD patients and their timely correction. This can contribute to the development of complications in the early and late postoperative periods.

The uneven recovery of hemoglobin in the postoperative period suggests the presence of undiagnosed iron deficiency typical of CAD in more patients than calculated in the analysis of medical records (17.3%). Thus, on day 1 after surgery, hemoglobin decreases by the mean amount of 37.7 units in patients with its initially high levels and by 22.1 units in patients with initial anemia. The recovery of hemoglobin levels slows down later. On day 5, hemoglobin is reduced by the mean of 33.9 units patients without initial anemia, which is 1.8 times higher than in patients with initial anemia (the mean of 21.6 units). Such changes can be explained by undiagnosed

pre-operative iron deficiency, which suppresses aerobic energy formation in tissues, reduces the blood oxygen capacity, causes hypoxia and low hemoglobin levels even with small blood loss.

It is reasonable to discuss the incidence of ID/IDA in patients who have undergone surgery for I20 – I25 given the results of the assessment of preventable annual socioeconomic losses when PBM is introduced in the cardiac surgery practice (more than 38 thousand years and more than 20.2 billion RUB saved). This calculation is based on ID/IDA in patients with CAD (70%), which is most often mentioned indicator in the literature. Given the evidence of the underestimated incidence of ID/IDA in real-world clinical practice, the percentage of 17.3% should be also be considered underestimated, and approaches to iron deficiency verification should be treated as inadequate.

However, despite certain inconsistencies, the benefits of individual patient blood management for the applied health care economics have been shown to be quite convincing in terms of the the two assessed parameters: the number of RBC suspension transfusions; and the mean duration of hospital stay. If PBM is included in routine cardiac surgical practice, the actual potential savings in surgeries for I20 – I25 will amount to 1.6–1.7 million RUB per 1,000 patients with anemia on only two of its results (reduction of the mean duration of hospital stay and the number of transfusions). The the positive results in the case of pre-operative anemia correction were a reduction in values similar to those in patients without initial anemia. In a more detailed analysis of intraoperative transfusions, the target values in patients without initial anemia will obviously differ, and therefore the savings will be higher.

Although pre-operative hemoglobin level is a significant risk factor for allogenic transfusions (OR=3.99), the fact of RBC transfusion is associated with neither initial hemoglobin nor blood loss, and differences between transfusions in patients with and without anemia vary only in the number of RBC doses transfused. With minor diversities in surgical techniques of bypass grafting of three to four coronary arteries under cardiopulmonary bypass, comparable mean blood loss volumes in different patient groups and blood volumes transfused indicate that intra-operative transfusion is an

unquestioned and common practice in cardiovascular surgery. If systemic PBM is implemented during surgeries for I20 – I25, 9,435 transfusions may be excluded, thus achieving an annual saving of more than 2.3 thousand liters of blood with a total cost of 77.7 million RUB in favor of clinical situations that have no alternatives.

Given the cost of hospital stay, even with a minimal difference in the duration of stay of patients with and without anemia (a mean of 0.5 days), the implementation of PBM activities during surgeries for I20-I25 may save 5–10 million RUB.

#### Limitations

The study had several limitations as discussed above. The most significant limitation was the use of borrowed German values of specific YLD' in ID/IDA, as well as the frequency of transfusions and the duration of hospital stay hypothetically comparable to those for patients without pre-operative ID/IDA. This was due to the absence of the systemic PBM practice in the Russian Federation.

A significant limitation was the exclusion of potential/prevented losses and their monetary values YLL from the assessment. This can be associated with the inability to reliably estimate the level of perioperative mortality directly caused by ID/IDA.







- 1) ЕДИНСТВЕННЫЙ НЕДЕКСТРАНОВЫЙ ВЫСОКОДОЗНЫЙ ПРЕПАРАТ ЖЕЛЕЗА ДЛЯ ВНУТРИВЕННОГО ВВЕДЕНИЯ
- 2) БОЛЕЕ НИЗКАЯ# ИММУНОГЕННОСТЬ<sup>2</sup> И УБЕДИТЕЛЬНАЯ ДОКАЗАТЕЛЬНАЯ БАЗА
- 3 УТИЛИЗАЦИЯ СОЗРЕВАЮЩИМИ ЭРИТРОЦИТАМИ ДО ~90% ВВЕДЕННОГО ЖЕЛЕЗА В ТЕЧЕНИЕ 6-9 ДНЕЙ<sup>3</sup>
- 4) ИННОВАЦИОННЫЙ ВЫСОКОСТАБИЛЬНЫЙ КОМПЛЕКС ЖЕЛЕЗА С КАРБОКСИМАЛЬТОЗОЙ<sup>1</sup>
- 5) ВОЗМОЖНОСТЬ ВВЕДЕНИЯ ДО 1000 МГ ЖЕЛЕЗА А ОДНУ 15-МИНУТНУЮ ИНФУЗИЮ БЕЗ ВВЕДЕНИЯ ТЕСТ-ДОЗЫ

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There is reason to believe that the losses are underestimated due to the lack of late postoperative patient observation data (30–60–90–365 days). The analysis of the correlation between ID/IDA and morbidity/mortality within 12 months after surgery was excluded for the same reason

The insufficient verification of pre-operative iron deficiencies led to the initial shift of patients with moderate/severe anemia to the groups of patients with mild/no anemia. This also led to a significant discrepancy between the published (70%) and practical (17.3%) ID/IDA rate and prevented the differences in the application losses with or without ID/IDA from being assessed more accurately.

#### Conclusion

Although the international professional community recognizes patient blood management as a commercially feasible and clinically effective concept, there are some organizational challenges in promoting evidence-based algorithms in Russian clinical practice. Given all the assumptions, it appears that the calculations made on the example of the highest levels of pre-operative iron deficiency/iron deficiency anemia and the use of blood component, demonstrated the possibility of significant socio-economic benefits and actual savings. This may be a significant reason for the early introduction of PBM as an approach to extend the range of laboratory diagnosis, improve clinical performance, and cost-effectiveness of surgical interventions.

#### Appendix. The factor of pre-operative ID/IDA in cardiac surgery

Pre-operative iron deficiency alone and especially in combination with anemia, has a significant impact on the outcomes of cardiac surgeries [21]: 90-day mortality (OR=3.5); the number of lethal outcomes and serious complications (OR=2.5); and the number of major cardiac and cerebrovascular events (OR=2.1) increase.

The risk of adverse outcomes is more likely with the higher functional class of CHF in patients with CAD, since iron deficiency not only significantly increases the incidence of anemia [22] (from 8–33% in class I–II to 19–68% in class III–IV CHF [23, 24]), but also reduces heart muscle performance, and increases the frequency of myocardial ischemia episodes [25]. Mortality increases 1.27-fold in mild anemia, 1.48-fold in moderate anemia, and 1.82 times in severe anemia when compared to patients without anemia [26].

Post-operative risks in CAD are even greater in the case of intraoperative transfusions, the reliable predictor of which is the combination of anemia (26-69.6%) of cases [27-29] and high blood loss typical of cardiac surgery [30]. Adjusted OR for infections in patients subject to hematotransfusion compared to those who were not is 3.38, ischemic outcomes – 3.35, up to 30-day mortality  $(\sim20\%)$  of lethal outcomes – 6.69, from 31-day to one-year mortality  $(\sim20\%)$  – 2.59, and over-one-year mortality  $(\sim60\%)$  – 1.32. With hematotransfusion being an effective medical technique necessary to treat life-

threatening anemia, its use in 59% is unreasonable and is considered appropriate only in 11.8% of cases [31]. This is due to the short-term effect, the significant likelihood of complications, additional risk due to volume overload and/or development of ischemia-related complications in CHF patients [32].

As the WHO recommended [33, 34], in order to review the traditional paradigm of blood component transfusion, many foreign clinics adhere to the guidelines [35] on restrictive intraoperative transfusions in stable patients in Hb from 70 to 80 g/L, while trying to elevate hemoglobin levels by intravenous administration of iron supplements in the pre-operative period. In Russian cardiosurgical practice, the recognition that myocardial ischemia with low hemoglobin levels may deteriorate, while the tolerance of anemia in coronary insufficiency may decreases [36], is grounds enot so much for preoperative anemia correction but for hemotransfusions aimed at achieving a Hb level of 100 g/L. This is prognostically more favorable for such patients. Even in the case of effective surgical/pharmacological hemostasis and the absence of complications during cardiovascular surgeries, the incidence of intra-operative transfusions does not decrease by less than 30-40% [37].

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