Long-term trends in the utilization of beta-blocking agents in the Czech Republic

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SUMMARY

Long-term trends in the utilization of beta-blocking agents in the Czech Republic
To study long term trends in the utilization of beta-blockers (ATC group C07) with regard to a possible influence of the health reform in 1992 on the availability of drugs.
Method: The utilization of C07 was expressed in the defined daily doses per thousand inhabitants and a day (DDD/TID) in the Czech Republic (I), and in DDD per 100 bed days (DDD/100 BD) in the University Hospital (OUH) Ostrava (II). ATC/DDD index: 2004. 10 mg was used as the DDD equivalent for metipranolol. The sources of data were: I. The SUKL database (wholesale data), the UZIS database (prescriptions), and II. The hospital request forms. Observed period: 1985-2007. The statistical analysis of the utilization of the portion of the C07AB group was divided into two parts. a) SUKL x OUH (1985–2007). b) SUKL x OUH, SUKL x UZIS and UZIS x OUH (1998–2005). Statistical tests used: Pearson Correlation *r.* Cross-Correlations Function for lags forward and backward from 1 to 3 years for time series, and paired T-test.
(I) The utilization of plain beta-blockers (C07A) ranged between 39.3 in 1992 and 51.2 DDD/TID in 1998 (SUKL data). Thereafter there has been an increasing trend to up to 80.6 DDD/TID in 2007. The UZIS data give similar outcomes generally on a lower level. (II) The utilization of C07 in OUH ranged between 20-26 DDD/100 BD till 1988. In 1989 there was an amplitude of 69.7 DDD/100 BD, followed by a decrease to 7.6 DDD/100 BD in 1998. During 1999-2004 the utilization was stabilized on the level of 10-14 DDD/100 BD followed by a slight increase to 16.8 during the last three years. The utilization of alpha- and beta-blocking agents was low. The correlation in the utilization of the C07AB portion between all three pairs of data was significantly high at the level of significance $P = 0.000$: SUKL x OUH in the period of 1985–2007: Pearson Correlation $r = 0.995$. In the period of 1998-2005 SUKL x OUH $r = 0.966$, SUKL x UZIS $r = 0.997$, UZIS x OUH $r = 0.976$. The shift of the time series was zero (both periods). The T-test showed a significantly higher proportion of C07AB in OUH, $P < 0.05$.
The selective compounds step-wise replaced the non-selective ones, mainly presented by the domestic metipranolol. The utilization of the selective beta-blocking agents has been still increasing; the most widely utilized ones were metoprolol, betaxolol, atenolol and acebutolol. The utilization of alpha- and beta-blocking agents was low.
Key words: DDD – utilization – beta-blockers – trends

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SOUHRN

Spotřeba betablokátorů (ATC C07) se zřetelem na vliv reformy zdravotnictví v roce 1992 na dostupnost léků.
Celostátní spotřeba byla vyjádřena (I) v definovaných denních dávkách na 1000 obyvatel a den (DDD/TOD), spotřeba ve Fakultní nemocnici Ostrava (FNO) (II) v DDD na 100 ošetřovacích dnů

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(DDD/100OD). ATC/DDD index: 2004. Pro metipranolol použit ekvivalent 10 mg. Zdroje dat: I. SÚKL (údaje od distributorů), ÚZIS (recepty), II. lékárenské žádanky. Období: 1985-2007. Statistická analýza podílu selektivních betalytik (C07AB) byla rozdělena do dvou částí: a) SÚKL x FNO (1985–2007), b) SÚKL x FNO, SÚKL x ÚZIS, ÚZIS x FNO (1998-2005). Statistické testy: Pearsonův korelační koeficient r, vzájemná korelační funkce pro časové řady pro posunutí dopředu i dozadu o 3 roky, párový t-test.
(I) Spotřeba C07A dle SÚKL kolísala mezi 39,3 (1992) a 51,2 DDD/TOD (1998). Poté vzestoupila až na 80,6 DDD/TID (2007). Z ÚZIS obdobné údaje na nižší hladině. (II) Spotřeba C07 ve FNO oscilovala mezi 20-26 DDD/100OD až do 1988. V 1989 stoupla na 69,7 DDD/100OD, následně poklesla na 7,6 DDD/100OD (1998). Mezi 1999-2004 byla ustálená: 10-14 DDD/100OD, poté slabý vzestup na 16,8 v posledních třech letech. Spotřeba alfa a betablokátorů byla velmi nízká. Mezi všemi třemi páry dat byla vysoká korelace v procentuální spotřebě C07AB, P = 0,000; r = 0,995 SÚKL x OUH (1985–2007). V období 1998-2005 SÚKL x FNO r = 0,966, SÚKL x ÚZIS r = 0,997, ÚZIS x FNO r = 0,976. Posun časových řad byl v obou obdobích nulový. T-test ukázal statisticky významně větší podíl C07AB ve FNO, P < 0,05.
Selektivní betablokátory postupně nahradily neselektivní, zastoupené zvl. domácí metipranololem a jejich spotřeba stoupá. Nejužívanějšími byl metoprolol, betaxolol, atenolol a acebutolol.
Klíčová slova: DDD – spotřeba – betablokátory – trend

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Introduction

Drug utilization expresses the exposition to a drug in a relationship to a given population group, in a given period and a given socio-economical background [1)]. There are different data sources available for drug utilization reviews – wholesale data, health insurance companies' data, hospital data etc. The wholesale data give the most complete view about drug utilization in the whole population but the confidential character of newly marketed drugs usually results into presenting agglomerated data without any detailed information about a single drug. The health insurance companies' data might provide full information about drugs reimbursed on the prescription but the information about OTC alone or with prescription drugs is also incomplete. The utilization data from hospitals give more detailed information about the usage of drugs but the general interpretation is limited because of its local character [2)]. The combination of different approaches is thus useful and gives us better information about drug exposures than a single source.

The utilization reviews usually produce similar trends – continuous increases as well as decreases as results of a long-term replacement of older drugs by newer ones. The new information about drugs – such as serious adverse drug reactions or documented treatment benefits resulted either in a decrease or increase in utilization consequently as the information reached the prescribers [3)]. Larger changes might occur after a considerable intervention into the health care system such as an increase of patients' co-payments [4, 5)] or reimbursement changes [6)]. We suggest that the political changes in the Czech Republic (CR) in 1989 that resulted in the major health care reform in 1992 represents such a case.

The aims of the present study are to examine the long term trends in the utilization of beta-blocking agents (C07A ATC group, a prescription only group) in the Czech Republic, and to look for possible changes in their utilization as the consequence of the presumed influence of socio-political changes in CR in 1989 on the drug availability.

EXPERIMENTAL PART

Methods

The utilization of beta-blocking agents was studied in the period of 1985–2007. The data were obtained from a) State Institute for Drug Control (SUKL), b) Institute of Health Information and Statistics (UZIS), and lastly from c) the pharmacy database in the Ostrava University Hospital. The SUKL database represents the wholesale data. The utilization of drugs produced by fewer than three manufacturers was considered to be confidential and thus usually not available [7)]. The UZIS database collects the data from health insurance companies and represents the amount of drugs reimbursed on prescriptions. The UZIS data have been available for the period of 1998–2005 with the exception for the year 2000 when the data were not complete. The data from the Ostrava University Hospital (OUH) represent in-patients utilization. However, the data from 1986 are missing. The utilization was expressed in the defined daily doses (DDD)/1000 inhabitants/day (DDD/TID) at the national level (a, b), and DDD/100 bed days (DDD/100BD) at the University Hospital Ostrava (c).

The DDD values and classification of beta-blocking agents according to the Anatomical-therapeutic-chemical classification (ATC) index 2004 [8)] are summarized in Table 1. For this classification 10 mg was used as the DDD equivalent for metipranolol [9)]. The number of inhabitants was obtained from the Czech Statistical Office web site [10)].

Statistical analysis

The statistical analysis was provided with the aid of SPSS 15.0 software [SPSS Inc.] and divided into two parts. a) We studied the relationship in the utilization of the C07AB group between SUKL and OUH in the period of 1985–2007, with the exception for the year 1986. b) The analyses of the relationship between all three pairs of data – SUKL x UZIS, UZIS x OUH, and SUKL x OUH were provided in the period of 1998–2005, with the exception for the year 2000. The following statistical tests were used for both parts: the association between groups was studied using the Pearson Correlation *r* coefficient. The Cross-Correlations Function for lag forward and backward from 1 to 3 years was created for analyzing the time series. Paired T-test was provided to study the differences in the utilization of C07AB group.

RESULTS

Before 1999 the total utilization of plain beta-blocking agents (C07A) in the Czech Republic (SUKL data) oscillated between 39.3 and 51.2 DDD/TID (Table 2, 3). Thereafter there has been a remarkably increasing trend up to 80.6 DDD/TID in 2007. Selective compounds that have been listed on the market since 1988 replaced the non-selective ones at the middle of the 90s (Fig. 1). Unfortunately it was not possible to evaluate the utilization of single drugs because of the confidential character of these data.

To address this shortcoming we utilized the data from the Ostrava University Hospital, which gives us a better insight following a simple premise that the drug utilized in a local hospital was also utilized at the national level. There were four substances widely used in this hospital before 1992, compared to thirteen ones after 1996 (Table 4). The utilization remained stabilized between 20-26 DDD/100BD before 1989. Of interest is the finding that in 1989 an extraordinary amplitude of 69.7 DDD/100BD took place. All substances (with an exception for labetalol) reached their maximum. Thereafter the utilization declined to 7.6 DDD/100BD in 1998 (Table 5). During the years 1999-2004 it oscillated between 10-14 DDD/100BD. Thereafter a slight increase up to 17 DDD/100BD appeared in 2007.

The selective agents have been dominant since 1996 and replaced the non-selective compounds (Fig. 2). The utilization of alpha- and beta-blocking agents was low. In the first decade, utilization of fixed combinations (difference between C07 and C07A) was noticeable but negligible later on (in the second decade).

We found that the non-selective metipranolol was the

Table 1. The ATC classification of beta blocking agents. O-oral, P-parenteral dose

ATC	Name	DDD (mg)
C07	*Beta blocking agents*	
C07A	*Beta blocking agents*	
C07AA	*Beta blocking agents, non-selective*	
C07AA	metipranolol	10
C07AA03	pindolol	15
C07AA07	sotalol	160
C07AA17	bopindolol	1
C07AB	*Beta blocking agents, selective*	
C07AB02	metoprolol	150
C07AB03	atenolol	75
C07AB04	acebutolol	400
C07AB05	betaxolol	20
C07AB07	bisoprolol	10
C07AB08	celiprolol	200
C07AB09	esmolol	2.5
C07AG	*Alpha and beta blocking agents*	
C07AG01	labetalol	600
C07AG02	carvedilol	37.5

Table 2. The utilization of beta blocking agents in the Czech Republic in DDD / 1000 TID in the period of 1985–1994 (SUKL data)

ATC code	ATC name	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994
C07AA	*Betabloking agents, non-selective*	*45.3*	*47.2*	*47.6*	*48.1*	*46.7*	*47.8*	*39.3*	*35.8*	*35.9*	*36.6*
C07AA03	pindolol								0.18	0.12	0.16
C07AB	*Betabloking agents,selective*				*1.0*			*2.0*	*3.5*	*7.8*	*14.2*
C07AB02	metoprolol							1.7	2.4	4.2	6.3
C07AB03	atenolol								1.0	3.3	5.0
C07AG	*Alpha and beta blocking agents*								*0.02*	*0.02*	*0.03*
C07AG01	labetalol								0.02	0.02	0.03
C07A	*Beta blocking agents*	*45.4*	*47.5*	*48.1*	*49.1*	*48.2*	*49.8*	*41.2*	*39.3*	*43.8*	*50.8*

Table 3. The utilization of beta blocking agents in the Czech Republic in DDD/TID in the period of 1995–2007 (SUKL data)

ATC code	ATC name	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
C07AA	*Beta blocking agents, non-selective*	*27.6*	*22.2*	*19.1*	*16.8*	*15.7*	*13.4*	*11.8*	*10.3*	*9.1*	*7.2*	*6.7*	*3.9*	*3.4*
C07AA03	pindolol	0.13	0.14	0.13										
C07AA07	sotalol					0.52	0.61	0.66	0.70	0.77	0.78	0.87	0.89	1.00
C07AB	*Beta blocking agents, selective*	*20.7*	*22.6*	*28.8*	*34.3*	*38.4*	*42.6*	*50.9*	*55.8*	*61.3*	*63.0*	*69.9*	*64.9*	*74.5*
C07AB02	metoprolol	6.7	7.8	8.6	9.1	10.7	12.5	16.4	18.7	21.5	24.2	26.5	24.3	28.4
C07AB03	atenolol	6.2	7.1	7.9	9.0	10.2	10.7	11.8	11.1	11.1	9.3	9.2	7.6	8.1
C07AB04	acebutolol			1.5	2.4	3.6	4.4	4.8	4.9	5.1	5.1	5.6	5.4	5.7
C07AB05	betaxolol										19.0	22.6	21.4	24.8
C07AB07	bisoprolol									1.5	2.3	3.2	3.8	4.9
C07AB08	celiprolol						0.01	1.3						
C07AG	*Alpha and beta blocking agents*	*0.03*	*0.02*	*0.04*	*0.14*	*0.29*	*0.35*	*0.46*			*1.1*	1.6	2.1	2.6
C07AG01	labetalol	0.03	0.02	0.02	0.02	0.02	0.02	0.002					<0.001	<0.001
C07AG02	carvedilol				0.12	0.27					1.1	1.6	2.1	2.6
C07A	*Beta blocking agents*	*48.3*	*44.9*	*47.9*	*51.2*	*54.3*	*56.3*	*63.2*	*66.7*	*71.1*	*71.3*	*78.2*	*70.0*	*80.6*

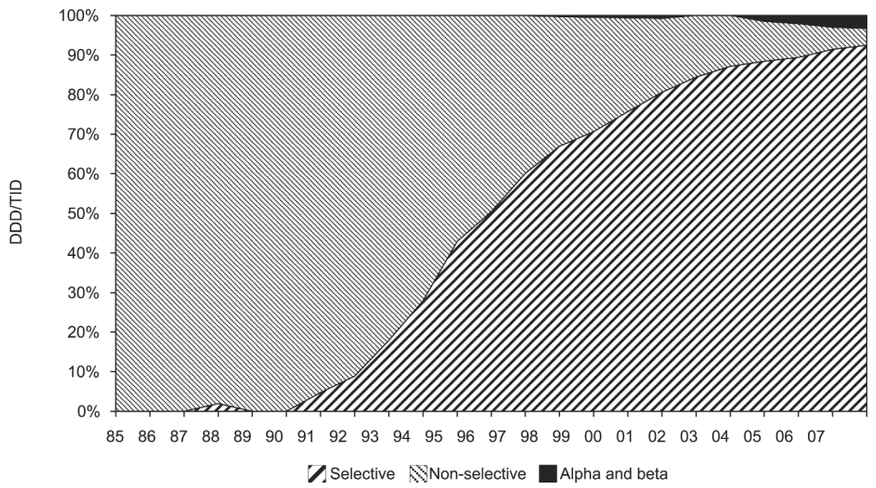

Fig. 1. The utilization of betablocking agents in the Czech Republic (SUKL)

most dominant compound in the 80s, its utilization highly exceeding the utilization of other drugs. However, during the early 90 s its utilization declined. Nevertheless it remained to be the most widely utilized drug till 1997 and its utilization was still above the average in 1999. Among the selective beta-blocking agents the most widely utilized were metoprolol, betaxolol, atenolol and acebutolol. The selective metoprolol was used only partially in the 80 s, but it became the most widely used agent during the 90s. For example, in 1993 it exceeded the average use but sharply increased beginning with 1998 and became the most widely utilized during the last decade.

In the period of 1985-2007 the analysis of association shows a significantly high correlation in the utilization of the portion of C07AB at the level of significance P = 0.000, Person Correlation r = 0.995. Paired T-test showed a significantly higher proportion of the utilization of this group in OUH, P = 0.000). The shift of time series was zero.

The UZIS data show a similar pattern of the utilization as the data from the Ostrava University Hospital (Table 6) with the dominance of metoprolol, betaxolol, atenolol and until 2002 also acebutolol.

In the period of 1998–2005 the analysis of association shows a significantly high correlation in the utilization of the C07AB portion between SUKL x UZIS (Pearson Correlation r = 0.997), UZIS x OUH (r = 0.976) and

Table 4. The utilization of beta blocking agents in the Ostrava University Hospital in DDD/100BD in the period of 1985–1994

ATC code	ATC name	1985	1987	1988	1989	1990	1991	1992	1993	1994
C07AA	*Beta blocking agents, non-selective*	*20.2*	*21.4*	*23.0*	*57.7*	*25.0*	*17.5*	*14.5*	*13.7*	*11.3*
C07AA	metipranolol	19.9	20.7	22.8	56.7	23.2	16.6	14.0	13.0	10.2
C07AA03	pindolol	0.24	0.69	0.17	1.99	1.6	0.32	0.27	0.08	0.10
C07AA07	sotalol									0.06
C07AA17	bopindolol					0.22	0.53	0.31	0.64	1.01
C07 AB	*Beta blocking agents selective*	*0.25*		*0.67*	*6.7*	*1.8*	*1.3*	*0.64*	*3.1*	*5.9*
C07AB02	metoprolol	0.25		0.67	6.6	1.8	1.3	0.61	2.2	3.0
C07AB03	atenolol								0.55	1.6
C07AB04	acebutolol									
C07AB05	betaxolol								0.06	0.40
C07AB07	bisoprolol								0.24	0.84
C07AB08	celiprolol				0.06	0.01		0.03	0.02	
C07AG	*Alpha and beta blocking agents*			*0.05*	*0.01*	*0.02*	*0.34*			
C07AG01	labetalol			0.05	0.01	0.02	0.34			
C07A	*Beta blocking agents*	*20.4*	*21.4*	*23.7*	*64.4*	*26.8*	*19.1*	*15.2*	*16.8*	*17.2*
C07	*Beta blocking agents*	*20.4*	*23.1*	*26.0*	*69.7*	*31.2*	*21.6*	*17.0*	*18.7*	*18.8*

Table 5. The utilization of beta blocking agents in the Ostrava University Hospital in DDD/100BD in the period of 1995–2007

ATC code	ATC name	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
C07AA	*Beta blocking agents, non-selective*	*7.7*	*5.6*	*2.8*	*1.8*	*2.5*	*1.8*	*1.2*	*1.0*	*1.1*	*1.2*	*1.3*	*0.97*	*0.64*
C07AA	metipranolol	6.4	4.4	2.0	1.1	1.8	0.87	0.53	0.41	0.69	0.81	0.83	0.73	0.43
C07AA03	pindolol	0.06	0.07	0.01	0.05	0.02	0.02	0.01	0.03		0.02			
C07AA07	sotalol	0.16	0.17	0.12	0.06	0.13	0.29	0.37	0.25	0.17	0.27	0.23	0.24	0.22
C07AA17	bopindolol	1.06	0.96	0.59	0.58	0.59	0.66	0.28	0.34	0.27	0.09	0.27	0.17	0.13
C07AB	*Beta blocking agents, selective*	*6.6*	*6.9*	*4.9*	*5.6*	*10.7*	*12.0*	*8.8*	*9.6*	*10.2*	*10.5*	*13.5*	*15.5*	*15.6*
C07AB02	metoprolol	2.8	2.2	1.4	1.7	4.1	4.7	3.5	4.1	4.5	4.9	7.1	8.0	7.6
C07AB03	atenolol	1.7	1.7	1.4	1.6	2.4	2.5	1.1	1.0	1.1	1.2	1.5	1.4	1.4
C07AB04	acebutolol	0.16	0.33	0.47	0.96	1.4	1.6	2.0	1.7	1.8	1.4	1.5	1.6	1.5
C07AB05	betaxolol	0.95	1.6	1.2	0.97	2.3	2.9	1.9	2.2	2.5	2.4	2.6	3.4	4.0
C07AB07	bisoprolol	1.0	1.2	0.40	0.38	0.44	0.35	0.31	0.39	0.29	0.37	0.58	0.63	0.81
C07AB08	celiprolol	0.01				0.01		0.06	0.15	0.11	0.22	0.31	0.38	0.25
C07AB09	esmolol	<0.01	<0.01			<0.01				<0.01				
C07AG	*Alpha and beta blocking agents*	*0.02*	*0.04*	*0.00*	*0.2*	*0.32*	*0.31*	*0.24*	*0.36*	*0.23*	*0.32*	*0.35*	*0.65*	*0.53*
C07AG01	labetalol	0.02	0.04		0.02	0.04	0.10	0.02			0.01	0.005	0.01	0.01
C07AG02	carvedilol			0.00	0.18	0.28	0.21	0.22	0.36	0.23	0.31	0.35	0.64	0.52
C07A	*Beta blocking agents*	*14.2*	*12.5*	*7.6*	*7.6*	*13.6*	*14.2*	*10.2*	*11.0*	*11.6*	*12.0*	*15.2*	*17.1*	*16.8*
C07	*Beta blocking agents*	*14.9*	*13.3*	*8.2*	*7.8*	*13.8*	*14.3*	*10.2*	*11.2*	*11.7*	*12.2*	*15.4*	*17.3*	*17.0*

SUKL x OUH (r = 0.966) at the level of significance $P < 0.000$. The shift of the time series was zero for all three pairs of data. The T-Test shows a significantly higher utilization of this group in OUH in comparison to UZIS as well as to SUKL at the level of significance $P < 0.05$. That means that the differences between SUKL and OUH tended to be smaller during the last eight years in comparison to the whole period observed. No significant difference was further found between SUKL and UZIS.

DISCUSSION

The total utilization of beta-blocking agents in DDD/1000 inhabitants/day in the Czech Republic was significantly higher than in Australia and the Scandinavian countries [11–29]. A similar finding was described by Gorecka et al. [2], who compared the

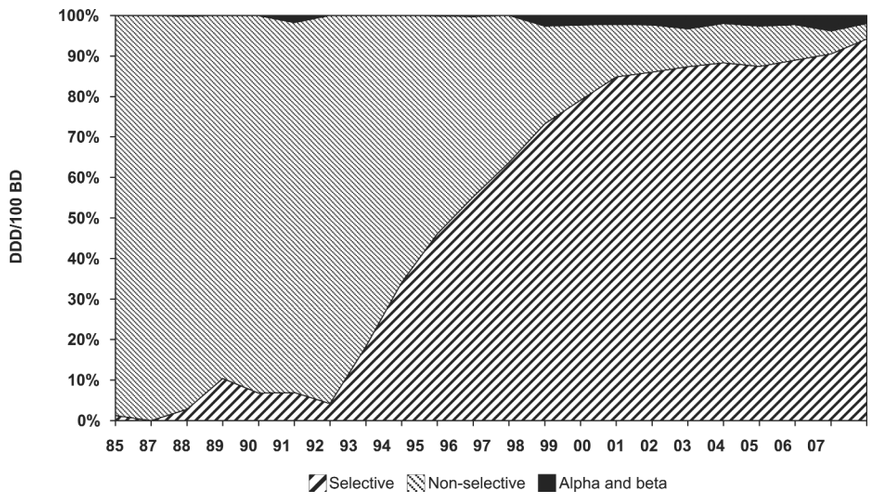

Fig. 2. The utilization of betablocking agents in the Ostrava University Hospital

Table 6. The utilization of beta blocking agents in the Czech Republic in DDD/TID in the period of 1998–2005 (UZIS data)

ATC code	ATC name	1998	1999	2001	2002	2003	2004	2005
C07AA	*Beta blocking agents, non-selective*	*17.1*	*14.8*	*11.6*	*10.2*	*8.9*	*7.8*	*6.6*
C07AA	metipranolol	12.3	10.2	7.4	6.2	5.2	4.4	3.7
C07AA03	pindolol	0.10	0.09	0.08	0.07	0.06	0.05	0.01
C07AA07	sotalol	0.42	0.49	0.63	0.68	0.74	0.82	0.85
C07AA17	bopindolol	4.3	4.0	3.5	3.2	2.3	2.6	2.1
C07AB	*Beta blocking agents, selective*	*32.3*	*37.7*	*49.4*	*54.9*	*59.4*	*64.5*	*67.4*
C07AB02	metoprolol	9.8	11.1	16.0	18.4	21.0	23.4	24.6
C07AB03	atenolol	9.0	9.8	11.0	11.0	10.5	9.7	8.9
C07AB04	acebutolol	2.6	3.7	4.7	4.9	5.0	5.4	5.6
C07AB05	betaxolol	10.3	12.4	15.8	17.3	18.4	20.5	22.4
C07AB07	bisoprolol	0.58	0.64	0.73	0.86	1.2	2.2	3.1
C07AB08	celiprolol	0.005	0.005	1.2	2.5	3.2	3.3	2.8
C07AG	*Alpha and beta blocking agents*	*0.17*	*0.31*	*0.44*	*0.57*	*0.70*	*1.0*	*1.4*
C07AG01	labetalol	0.017	0.020	< 0.001	< 0.001			
C07AG02	carvedilol	0.15	0.29	0.44	0.57	0.70	1.0	1.4
C07A	*Beta blocking agents*	*49.6*	*52.8*	*61.5*	*65.7*	*69.0*	*73.3*	*75.5*
C07	*Beta blocking agents*	*56.0*	*58.9*	*63.9*	*68.3*	*71.8*	*76.1*	*78.2*

cardiovascular drugs prescriptions in three districts in the Czech Republic and in three counties of Wales using health insurance companies' data. In this study the total utilization of antihypertensive agents was by 22.9% higher in the Czech districts compared to Wales in 2000. On the other hand, the utilization of beta-blocking agents in Wales oscillated between 27.8-35.6 DDD/TID in 1997 and 31.3-38.3 DDD/TID in 2000, i.e. similarly to the Scandinavian countries and Australia while in Czech districts it reached twofold higher levels. Authors also mentioned a lower amount of the selective compound observed in the Czech districts in comparison with Wales in the years 1997, 1999 and 2000.

The non-selective beta-blockers were dominant in CR up to 1997. However, according to statistical handbooks available, these were utilized in only approximately 15–30% in Australia, Norway or Sweden. In 1986–1987 only Finland reported a higher usage of these agents by about 40%. Generally the utilization of C07AA declined in all countries. Metipranolol, originally synthesized in the Czech Republic [30], was the major compound in Ostrava and probably also at the national level. On the other hand, the spectrum of non-selective compounds was broader in Australia and the Scandinavian countries, where the most widely utilized ones were propranolol and pindolol, in Finland and in Sweden also sotalol.

The utilization of non-selective agents in CR might be overestimated during the eighties and early nineties. Metipranolol has not the internationally defined DDD. Its equivalent was declared by SUKL as 10 mg [9] but the usual prescribed daily dose was 20 mg [31]. The overestimated utilization of metipranolol might distort the utilization of the C07AA group and consequently also the grand total. No such phenomenon appeared during the last decade as the usual doses of other beta-blocking agents recommended by the Czech Society for Hypertension [31] were not different from DDDs. The twofold utilization of beta-blockers in comparison with foreign countries hence must have another explanation. Twofold higher mortality on cardiovascular diseases in CR in comparison to the United Kingdom in 1998 mentioned by Gorecka et al. [2] might represent such a case.

The selective compounds appeared in the Czech Republic after 1991 and their utilization has been progressively increasing – doubled in every four years at the national level. The statistical analysis shows slightly higher usage of these compounds in OUH. The difference was yet not as large as, for example, in antiepileptic drugs that we studied previously [32]. In their study Gorecka et al. [33] found twofold differences in the utilization of beta-blocking agents in 20 randomly selected Czech districts in 1997 and 2000 (the district of Ostrava was not included). The values expressed in DDD/1000 inhabitants insured by General Health Insurance Company/day oscillated between 14.5–45.5 in 1997 and 39.5–80.5 in 2000. It is important to state that the mean population registered by this company represents 75% of the total population of the observed districts.

The OUH data were further in high correlation with the utilization in CR which allows a better insight into the utilization of single compounds as the information about the utilization of newer drugs is considered as confidential and therefore appears in the SUKL data after the introduction of generics. E.g. betaxolol, despite its utilization, has been high and has been the second most widely utilized beta-blocking agent in the Ostrava University Hospital as well as in the UZIS database since 1999, appeared in SUKL database in 2004. Statistical yearbooks apparently used a similar rule. The data of metoprolol and atenolol showed that these agents were the most widely utilized selective beta-blocking agents in all countries. In Finland this portfolio was broader by acebutolol, bisoprolol, celiprolol and betaxolol. However, their utilization could not be statistically evaluated from wholesale data as explained above. Interestingly, the utilization of C07AB was growing in CR, Finland and Norway, while in Australia it declined and oscillated in Sweden.

The utilization of beta-blocking agents was usually compared with other antihypertensive agents and plain substances were mentioned rarely. Long-term trends in the utilization of beta-blocking agents have not been reported yet with an exception for Jackevisius et al. [3]. They studied the trends in beta-blocking agents' utilization in Canada in the period between 1996–2001 using the number of prescriptions. They described increasing utilization of atenolol and metoprolol that doubled during the period. The utilization of acebutolol remained constant on a lower lever. Of interest was a relatively high utilization of non-selective propranolol and nadolol. Tiwari et al. [34] mentioned atenolol as the most common beta-blocker in outpatients in the Panjab University Health Centre in India in 2002/2003. Similarly Jassim Al Khaja et al. [35] shows that atenolol represents 97.7% of beta-blockers in 7 health centers in Bahrajn. On the other hand, Yusuff and Balogun [36] mentioned propranolol as the most common beta-blocker. Nevertheless only 1.9% hypertonic patients were treated with beta-blocking agents in Nigeria in 2002. The low utilization in this African country may result from the preference of inexpensive diuretics and formerly supposed lower efficacy of beta-blocking agents in black population in monotherapy.

We can conclude that the health care reform in the Czech Republic in 1992 led to the market enlargement that resulted in a wider spectrum of beta-blocking agents available and increase in the use of cardioselective compounds.

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Dedicated to the 90th birthday of Vaclav Trcka, Assoc. Prof., M.D., DrSc., the Father of metipranolol.