

National prescribing data for dabigatran

We agree with Auckland City Hospital (ACH) staff (10 February 2012)¹ for the need for caution in the prescribing of dabigatran anticoagulation in patient groups at increased risk of drug-induced bleeding.

It is difficult to tell to what extent the authors' concerns about the use of dabigatran seen in patients admitted to the hospital relates to the particular demographics of hospital admissions and to the prescribing of dabigatran in Auckland itself. The population in the ACH preliminary sample was representative of patients admitted to hospital and with complications (both who tend to be older), and not necessarily the whole population using dabigatran.

Our analysis of national dispensing (PharmWarehouse) data indicates that during July to December 2011, the same 6 months that the authors observed at ACH, there have been around 11,840 patients prescribed and dispensed dabigatran in New Zealand. This meant 3,500 person-years' exposure to dabigatran (with 23,673 prescriptions). The mean age was 73.0 years and median 75 years, similar to the RE-LY trial's mean of 71.5 years², and younger than the ACH preliminary series' 76 year mean age and 84 year median.¹

By domicile, we note there were 785 patients living in the Auckland District Health Board (DHB) catchment dispensed dabigatran, of whom 39% (309) were female, with a mean age of 72.8 years and median age of 75 years (being 3–9 years younger than the Auckland City Hospital preliminary series).

However, similar to the ACH series, nationally the proportion of women past/current users dispensed dabigatran was higher than in the RE-LY trial; nationally 60% were male and 40% female, compared with 36% female in RE-LY² and 42% female in the ACH preliminary series.¹ In addition, nationally women dabigatran users were older than men; men's mean age was 71.5 years, median 73; women's mean age was 75.3 years, median 77.

In the national dispensing data, of the 11,840 past/current users, 31% of patients (n=3,718) were aged 80 years and over (prevalence 1.3 per 1000 population aged 80+). This proportion was higher than the RE-LY trial's 17% being aged 80+ years.³ Half of all New Zealand's users were aged 75+ (see footnote 1). For those living in the Auckland DHB catchment, 276 users were aged 80+ years (398 aged 75+), being 35% of all ages of users there.

Of note, 171 users (1.4% of all users, 4.6% of users aged 80+) were both aged 80 and over and ended up using the 150 mg formulation, with higher proportions for those aged 75+ and for those in Auckland (see footnote 2).

The dabigatran datasheet⁴ and advice to prescribers^{5,6} in effect have recommended against using the 150mg dose for atrial fibrillation in the very elderly because of the risks of age-related reduced renal clearance-related toxicity. This is where they advise treating patients with atrial fibrillation aged 80+ years with the 110 mg formulation

(220mg/day as twice daily 110mg doses), and where the RE-LY trial showed a trend towards increased bleeding with the 150mg dose c.f. warfarin in those aged 75+.⁷

The national dispensing data currently do not provide information on weight nor renal function including creatinine clearance, hence the appropriateness of prescribing cannot be easily assessed on a national level. A great step forward will be when we can readily datamatch pharmaceutical use with laboratory data.

We note though varying evidence that some older patients starting on the 150mg dose have then down-titrated to the dose recommended for age. Nationally, 356 patients aged 80+ had been dispensed the 150 mg formulation at any time, hence 52% of patients had apparently reduced to the lower dose 110mg formulation (see footnote 3). Again we cannot tell what proportion of those aged 80+ years remaining on the 150mg dose did so with known adequate renal function, versus what proportion still had compromised renal function at risk of bleeding (needing to reduce their dose as per the blanket guidance for all of that age).

Further detail on dabigatran dispensings (including breakdowns by formulation, age/gender and DHB) can be seen in the tables and graphs below.

We agree with calls for all patients, especially those aged 80 years or older with impaired renal function or low body weight, being carefully evaluated for the risks and benefits of treatment before starting dabigatran,⁸ and then closely monitoring renal function (footnote 4).^{4,9} To this end we will continue to publicise these and other risk factors in both primary and secondary care.

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Footnotes:

1. All prevalence rates use 2006 Census denominators. In the national dispensing data, of the 11,840 users, 51% of patients (n=5,983) were aged 75 years and over (including the 3,718 aged 80+), with a prevalence of 29 per 1000 population aged 75+.
2. Nationally, 1,121 users were aged 75+ years and ended with the 150mg formulation, being 9.5% of all users and 19% of all users aged 75+. For those living in the Auckland DHB catchment, 276 users were aged 80+ years (398 aged 75+), being 35% of all ages of users. There were 21 patients in the Auckland DHB catchment aged 80 years who were last prescribed dabigatran 150mg (8% of users in Auckland aged 80+, 1.8 per 1000 Aucklanders aged 80+).
3. Nationally, 356 patients aged 80+ had been dispensed the 150 mg formulation at any time. As 171 patients of that age had the 150mg dose as their last dispensing of dabigatran, this suggests 52% of patients initially starting on the

150mg dose then reduced to the lower dose 110mg formulation (356 minus 171, divided into 356).

Likewise, nationally, 1,488 of those aged 75+ were dispensed the 150mg dose at any time, compared with the 1,125 of that age whose last dose dispensed was 150mg (thus 25% reducing to 110mg, i.e. 1488 minus 1125, divided into 1488).

Of Auckland patients aged 80+, 12 of the 33 patients reduced from 150mg to 110mg (36% reducing, the residual 21 apparently remaining on 150mg).

4. According to the updated datasheet for dabigatran (November 2011),^{4,9}
—renal function must be assessed in all patients before starting dabigatran;
—for patients taking dabigatran, renal function should be rechecked in any clinical situation where a decline in renal function is suspected, e.g. dehydration, hypovolaemia and with some medicines such as diuretics;
—renal function should be assessed at least annually in patients taking dabigatran aged over 75 years or with moderate renal impairment (creatinine clearance 30–50mL/min).

References:

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2. Connolly SJ, Ezekowitz MD, Yusuf S, Eikelboom J, Oldgren J, et al; RE-LY Steering Committee and Investigators. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009 Sep 17;361(12):1139-51. <http://www.nejm.org/doi/full/10.1056/NEJMoa0905561> Erratum in: N Engl J Med. 2010 Nov 4;363(19):1875-6. <http://www.nejm.org/doi/full/10.1056/NEJMc1007378>)
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6. The use of dabigatran in general practice: a cautious approach is recommended. Best Practice Journal 2011;39:10-21. <http://www.bpac.org.nz/magazine/2011/september/dabigatran.asp>
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9. Updated data sheet for dabigatran etexilate. Best Practice Journal 2011;41:50-51. <http://www.bpac.org.nz/magazine/2011/december/dabigatran.asp>

Tables and graphs

Table 1

	no.
all patients	11,840
patients, caps 150mg	6,227
scripts, caps 75mg	366
scripts, caps 75mg	11,662
scripts, caps 75mg	11,645
total scripts	23,673

Graph 1

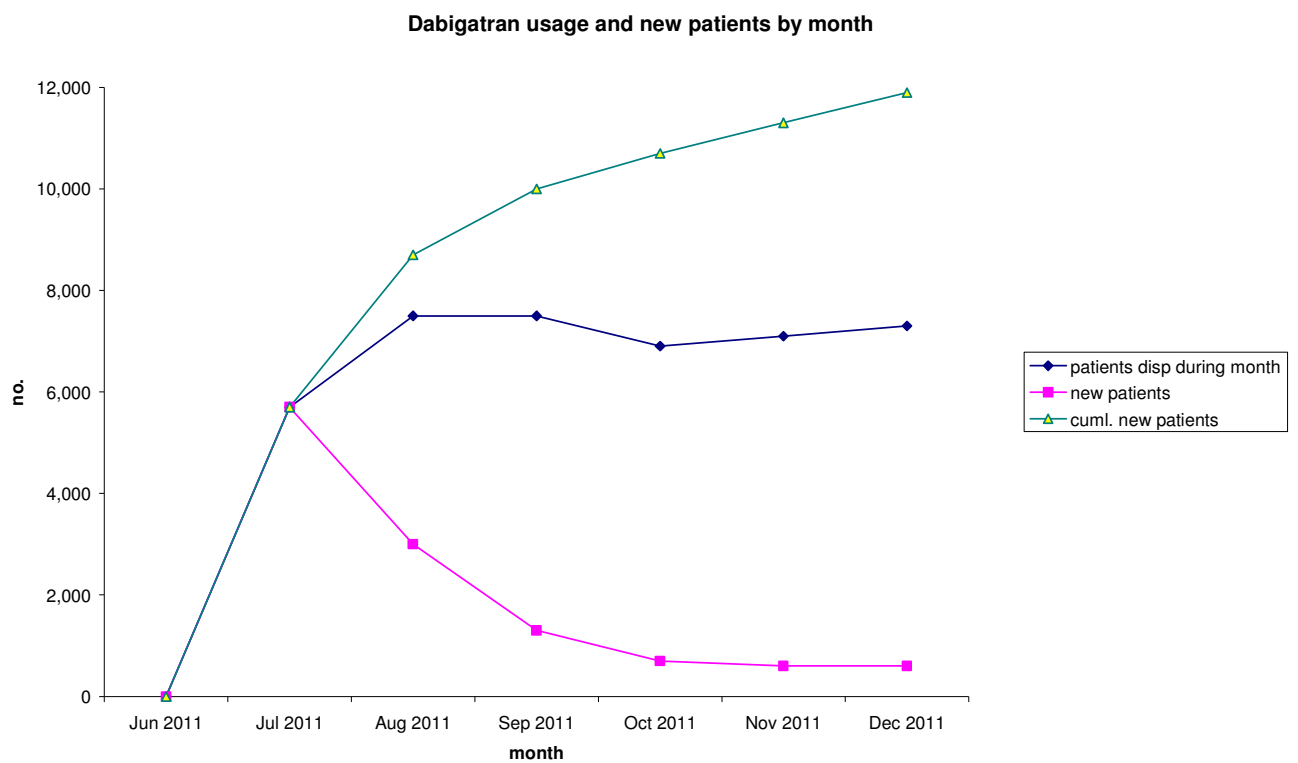


Table 2

5-year ageband	no. patients		
	male	female	total
10-14	2	0	2
15-19	7	1	8
20-24	5	3	8
25-29	11	1	12
30-34	13	9	22
35-39	28	11	39
40-44	71	25	96
45-49	145	49	194
50-54	260	97	357
55-59	415	164	579
60-64	708	329	1037
65-69	1026	475	1501
70-74	1233	769	2002
75-79	1317	948	2265
80-84	1107	1070	2177
85-89	589	633	1222
90-94	103	189	292
95-99	10	15	25
100+	0	2	2
total	7050	4790	11840
mean age	71.5	75.3	73.0
median age	73	77	75
% by gender	60%	40%	100%
aged 80+			3718
% [aged 80+] of all			31.4%
aged 75+			5983
% [aged 75+] of all			50.5%

Table 3

	older patients who use/d 150mg caps dabigatran				
	150mg at any time	last dose 150mg	change to 110	% change	% remaining
aged 75+	1488	1121	367	25%	75%
aged 80+	356	171	185	52%	48%

Table 4

5-year ageband no. patients by formulation of last dispensing of dabigatran

	Cap 75 mg	Cap 110 mg	Cap 150 mg	multiple	total
10-14	0	1	1	0	2
15-19	0	3	5	0	8
20-24	0	1	7	0	8
25-29	0	2	10	0	12
30-34	0	7	15	0	22
35-39	0	5	34	0	39
40-44	1	16	79	0	96
45-49	1	31	162	0	194
50-54	2	43	312	0	357
55-59	1	101	477	0	579
60-64	8	179	850	0	1037
65-69	13	298	1190	0	1501
70-74	16	630	1355	1	2002
75-79	30	1284	950	1	2265
80-84	51	1999	126	1	2177
85-89	38	1145	38	1	1222
90-94	14	271	7	0	292
95-99	4	21	0	0	25
100-104	0	2	0	0	2
total	179	6039	5618	4	11840
aged 80+, cap 150mg			171		
% [aged 80+, cap 150mg] of all			1.4%		
aged 75+, cap 150mg			1121		
% [aged 75+, cap 150mg] of all			9.5%		

Graph 2

Use of dabigatran by formulation by age

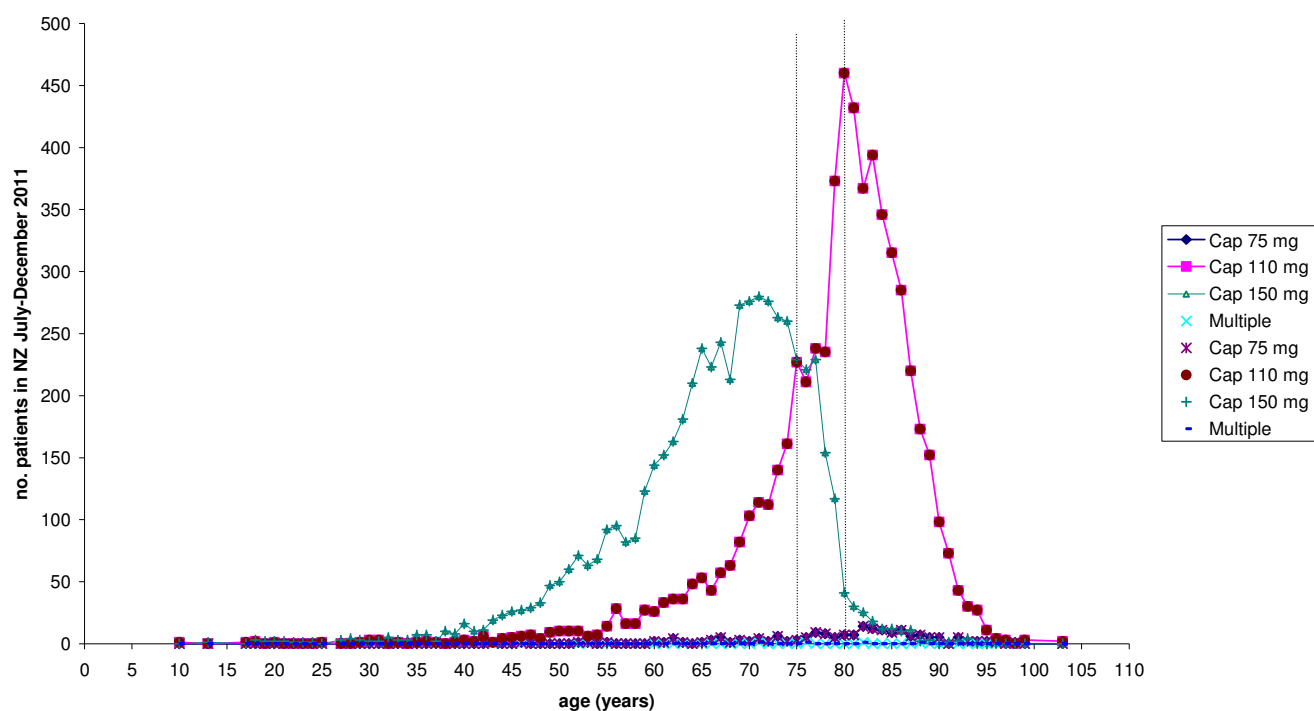


Table 5

no. prescriptions
no. patients

23673
11840

Count of NHI	Last_formulation gender												total
	Cap 75 mg		Cap 75 mg Total	Cap 110 mg		Cap 110 mg Total	Cap 150 mg		Cap 150 mg Total	Multiple		Multiple Total	
	male	female		male	female		male	female		male	female		
10-14				1		1	1		1				2
15-19				3		3	4	1	5				8
20-24				1		1	4	3	7				8
25-29				1	1	2	10		10				12
30-34				3	4	7	10	5	15				22
35-39				5		5	23	11	34				39
40-44		1	1	12	4	16	59	20	79				96
45-49		1	1	21	10	31	124	38	162				194
50-54		2	2	29	14	43	231	81	312				357
55-59		1	1	67	34	101	347	130	477				579
60-64		5	3	8	102	179	601	249	850				1037
65-69		8	5	13	171	298	847	343	1190				1501
70-74		9	7	16	350	630	873	482	1355	1		1	2002
75-79		20	10	30	708	1284	588	362	950	1		1	2265
80-84		27	24	51	1006	1999	74	52	126		1	1	2177
85-89		22	16	38	547	1145	20	18	38		1	1	1222
90-94		4	10	14	94	271	5	2	7				292
95-99		2	2	4	8	21							25
100-104						2							2
total	98	81	179	3129	2910	6039	3821	1797	5618	2	2	4	11840
% formulation x age / total	0.8%	0.7%	1.5%	26%	25%	51%	32%	15%	47%	0%	0%	0%	100%
mean age	79.3	79.8	79.6	78.0	79.8	78.9	66.0	67.8	66.6	73.5	85.0	79.3	73.0
median age	81	82	82	80	81	80	67	70	68	71	82	76	75
formulation x gender, aged 75+	75	62	137	2363	2359	4722	687	434	1121	1	2	3	5983
formulation x gender, aged 80+	55	52	107	1655	1783	3438	99	72	171	0	2	2	3718
% [formulation x gender, aged 75+] of all	0.6%	0.5%	1.2%	20.0%	19.9%	39.9%	5.8%	3.7%	9.5%				50.5%
% [formulation x gender, aged 80+] of all	0.5%	0.4%	0.9%	14.0%	15.1%	29.0%	0.8%	0.6%	1.4%				31.4%
% [formulation x gender, aged 75+] of all aged 75+	1.3%	1.0%	2.3%	39.5%	39.4%	78.9%	11.5%	7.3%	18.7%				100%
% [formulation x gender, aged 80+] of all aged 80+	1.5%	1.4%	2.9%	44.5%	48.0%	92.5%	2.7%	1.9%	4.6%				100%
% [formulation x gender, aged 80+] of that formulation/sex	56%	64%	60%	53%	61%	57%	2.6%	4.0%	3.0%				31%
formulation x gender, all ages	98	81	179	3129	2910	6039	3821	1797	5618	2	2	4	11840
% [formulation x gender, all ages] of all	0.8%	0.7%	1.5%	26.4%	24.6%	51.0%	32.3%	15.2%	47.4%	0.0%	0.0%	0.0%	100.0%

Table 6

DHB	no. patients			% female	mean age (years)			median age (years)			aged 80+ years		aged 75+ years	
	male	female	total		male	female	all	male	female	all	no.	% of all	no.	% of all
Northland	552	389	941	41%	72.8	75.9	74.1	74	78	75	330	35%	513	55%
Waitemata	633	445	1078	41%	72.7	76.4	74.2	74	78	75	366	34%	577	54%
Auckland	476	309	785	39%	71.1	75.5	72.8	72	78	75	276	35%	398	51%
Counties Manukau	522	349	871	40%	68.9	72.9	70.5	70	75	73	214	25%	371	43%
Waikato	718	564	1282	44%	71.1	75.0	72.8	72	77	74	380	30%	614	48%
Lakes	202	118	320	37%	70.0	72.9	71.0	72	74	73	70	22%	141	44%
Bay of Plenty	642	398	1040	38%	72.0	75.6	73.4	73	77	75	340	33%	538	52%
Tairāwhiti	112	80	192	42%	70.9	74.7	72.5	70	76	73	55	29%	88	46%
Taranaki	216	158	374	42%	71.7	76.9	73.9	73	78	75	126	34%	204	55%
Hawkes Bay	400	304	704	43%	73.0	77.5	74.9	75	78	77	256	36%	419	60%
Whanganui	94	84	178	47%	72.9	75.4	74.1	75	76	76	63	35%	100	56%
MidCentral	260	166	426	39%	72.4	74.9	73.4	74	76	75	134	31%	215	50%
Hutt Valley	124	114	238	48%	71.6	73.6	72.5	73	74	74	71	30%	113	47%
Capital and Coast	338	196	534	37%	69.4	74.8	71.3	71	77	73	161	30%	253	47%
Wairarapa	100	70	170	41%	72.9	76.1	74.2	73	79	76	60	35%	91	54%
Nelson Marlborough	189	118	307	38%	69.9	75.6	72.1	71	76	73	67	22%	134	44%
West Coast	38	22	60	37%	69.4	74.6	71.3	69	79	72	18	30%	25	42%
Canterbury	721	413	1134	36%	71.2	74.8	72.5	72	76	74	346	31%	548	48%
South Canterbury	156	117	273	43%	73.1	75.9	74.3	74	77	75	89	33%	146	53%
Otago	409	252	661	38%	71.9	75.6	73.3	74	78	76	219	33%	362	55%
Southland	136	119	255	47%	72.3	75.7	73.9	73	77	75	74	29%	130	51%
Overseas	11	6	17	35%							3	18%	3	18%
total	7049	4791	11840	40%	71.5	75.3	73.0	73	77	75	3718	31%	5983	51%

Table 7

DHB	no. patients aged 80+ years				all patients	prevalence 150mg per 1000 aged 80+	prevalence all doses, aged 80+	percentages	
	Cap 75 mg	Cap 110 mg	Cap 150 mg	all, 80+ years				%[80+,150mg] / all	%[80+,150mg] g/ 80+
Northland	7	316	7	330	941	1.5	68.6	0.7%	2.1%
Waitemata	9	342	13	366	1078	0.9	26.7	1.2%	3.6%
Auckland	11	244	21	276	785	1.8	23.8	2.7%	7.6%
Counties Manukau	2	205	7	214	871	0.8	24.9	0.8%	3.3%
Waikato	18	339	23	380	1282	2.2	36.2	1.8%	6.1%
Lakes	6	62	2	70	320	0.7	25.9	0.6%	2.9%
Bay of Plenty	4	316	20	340	1040	2.5	43.1	1.9%	5.9%
Tairāwhiti	1	51	3	55	192	2.3	42.0	1.6%	5.5%
Taranaki	3	115	8	126	374	1.9	30.1	2.1%	6.3%
Hawkes Bay	2	248	6	256	704	1.1	47.1	0.9%	2.3%
Whanganui	5	54	4	63	178	1.6	24.6	2.2%	6.3%
MidCentral	0	129	5	134	426	0.9	23.1	1.2%	3.7%
Hutt Valley	3	68	0	71	238	0.0	17.7	0.0%	0.0%
Capital and Coast	3	148	10	161	534	1.3	21.6	1.9%	6.2%
Wairarapa	2	55	3	60	170	1.9	37.3	1.8%	5.0%
Nelson Marlborough	0	62	5	67	307	1.0	13.0	1.6%	7.5%
West Coast	0	18	0	18	60	0.0	16.8	0.0%	0.0%
Canterbury	9	319	18	346	1134	1.0	19.8	1.6%	5.2%
South Canterbury	3	83	3	89	273	1.2	34.7	1.1%	3.4%
Otago	17	192	10	219	661	1.4	31.2	1.5%	4.6%
Southland	2	70	2	74	255	0.6	21.2	0.8%	2.7%
Overseas	0	2	1	3	17				
total	107	3438	171	3718	11840	1.3	28.8	1.4%	4.6%

Table 8**Patients aged 80+ who use/d 150mg caps dabigatran**

DHB	no. patients aged 80+			% change	% remaining
	150mg at any time	last dose 150mg	change to 110		
Northland	29	7	22	76%	24%
Waitemata	21	13	8	38%	62%
Auckland	33	21	12	36%	64%
Counties Manukau	18	7	11	61%	39%
Waikato	52	23	29	56%	44%
Lakes	8	2	6	75%	25%
Bay of Plenty	37	20	17	46%	54%
Tairāwhiti	6	3	3	50%	50%
Taranaki	9	8	1	11%	89%
Hawkes Bay	20	6	14	70%	30%
Whanganui	9	4	5	56%	44%
MidCentral	10	5	5	50%	50%
Hutt Valley	3	0	3	100%	0%
Capital and Coast	14	10	4	29%	71%
Wairarapa	4	3	1	25%	75%
Nelson Marlborough	6	5	1	17%	83%
West Coast	1	0	1	100%	0%
Canterbury	38	18	20	53%	47%
South Canterbury	6	3	3	50%	50%
Otago	26	10	16	62%	38%
Southland	5	2	3	60%	40%
Overseas	1	1			
total	356	171	185	52%	48%