

## Five years of non-prescription oseltamivir: effects on resistance, immunization and stockpiling

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**Objectives:** In 2007 New Zealand (NZ) became the first country to make oseltamivir (Tamiflu®) available off-prescription. This study investigated the extent of pharmacist supply of oseltamivir over 5 years, including during the influenza A(H1N1) pandemic, and the impact of pharmacist supply of oseltamivir on influenza virus oseltamivir susceptibility, personal stockpiling and influenza vaccine uptake.

**Methods:** Randomly selected community pharmacies in NZ reported oseltamivir provision by prescription and through pharmacist supply from 1 January 2007 to 15 September 2011. Oseltamivir resistance data on influenza viruses isolated during influenza surveillance from 2008 to 2011 were obtained, along with influenza vaccine uptake data from 2005 to 2011 and influenza detection data.

**Results:** Seventy of 85 eligible pharmacies completed the study (82% response rate). Most supplies of oseltamivir throughout the 5 years were dispensed against a prescription rather than pharmacist supplied, with pharmacist supply responsible for 11% of supplies during the pandemic years (2009–10) versus 27% and 31% during 2007 and 2008, respectively. Pharmacist-supplied oseltamivir did not appear to be associated with the development of resistance, with identified likely stockpiling or with a decline in influenza immunization. Pharmacist supplies largely matched the timing of influenza in the community and peaked in June 2009, as did prescription supplies.

**Conclusions:** Five years of non-prescription oseltamivir in NZ has resulted in no significant change in the development of resistance or rates of influenza immunization. Supplies remained modest and significant consumer stockpiling through pharmacist supply has not occurred, even during the influenza A(H1N1)pdm09 pandemic in 2009 and 2010. Pharmacists could be better utilized in ensuring fast distribution of antivirals to influenza sufferers during a pandemic.

**Keywords:** non-prescription drugs, pharmacists, self-medication, antiviral treatment, pandemic

### Introduction

The trend towards the reclassification of pharmaceuticals from prescription to non-prescription availability includes antimicrobials<sup>1</sup> such as chloramphenicol and azithromycin in the UK.<sup>2</sup> Reclassification is considered to have a number of advantages that include more timely access for consumers and increased utilization of pharmacists when the medical workforce and health budget are facing increasing pressures,<sup>1</sup> potentially freeing-up doctors for more serious conditions and reducing costs for the health system, as well as using the pharmacist's knowledge. As pharmacists are known to follow protocols with care, and

doctors tend to prescribe trimethoprim for longer than recommended, Reeves<sup>3</sup> speculated that the quality of supply may improve with reclassification of trimethoprim. However, the reclassification of antimicrobials remains controversial,<sup>4–6</sup> with the potential for increased resistance, misdiagnosis, adverse events and lost data post-reclassification.<sup>1</sup> In the UK, concerns about the potential for increased resistance<sup>7,8</sup> preceded the withdrawal of reclassification applications for both trimethoprim and nitrofurantoin.<sup>9</sup> In Australia, the reclassification of oseltamivir was rejected on the basis of the perceived potential for increased resistance, misdiagnosis, reduced vaccine uptake, pandemic stockpiling and a reduction of available supplies during a

pandemic.<sup>10–12</sup> In contrast, in New Zealand (NZ) similar concerns were addressed through strict criteria for supply,<sup>12</sup> allowing the reclassification of oseltamivir in 2007. The difference in approach between NZ and Australia may reflect the lack of data on usage patterns and resistance following the reclassification of antimicrobials.<sup>3</sup>

A 'Pharmacist Consultation and Supply' category, potentially with extra safeguards, has merit for newly reclassified medicines, to improve standards and scrutiny of these medicines.<sup>4</sup> NZ used such a model when oseltamivir became available for non-prescription supply only by a pharmacist between May and September (the influenza season in the Southern Hemisphere) to a persons  $\geq 12$  years of age presenting in the pharmacy with early symptoms of seasonal influenza.<sup>13</sup> In 2009 the requirement for the sufferer to present personally to the pharmacy to purchase oseltamivir was removed.<sup>14</sup> During the influenza A(H1N1)pdm09 pandemic, year-round pharmacist supply was allowed, along with supply from community-based assessment ('Flu') centres.<sup>14</sup> NZ has pharmacist-only medicines that legally require pharmacist involvement in supply. The exemption to prescription supply used for oseltamivir is similar, requiring pharmacist involvement, but only allows pharmacist supply in certain months of the year and where the other criteria are also met.

Comparison of the incidence of influenza resistance in countries with widespread and minimal use of oseltamivir, e.g. Japan, the USA and some European countries,<sup>15,16</sup> suggests that greater use is not associated with an increased incidence of resistance. However, there is no information on the impact of pharmacist supply of oseltamivir on resistance. Thus, our research sought to elucidate whether or not the above concerns, including increased viral resistance, were valid following reclassification of oseltamivir through pharmacist supply under strict criteria. Additionally, given the importance of antiviral usage in an influenza pandemic,<sup>17</sup> including their rapid distribution,<sup>18</sup> investigating pharmacist supply of oseltamivir in NZ during the pandemic could inform future pandemic planning.

The aims were to investigate: (i) the impact of pharmacist supply of oseltamivir on influenza virus antiviral susceptibility; (ii) the extent of pharmacist supply of oseltamivir, during inter-pandemic and pandemic periods; (iii) whether non-prescription availability of oseltamivir appeared to negatively affect influenza vaccination uptake rates; and (iv) whether private stockpiling from pharmacist supply appeared likely.

## Methods

The Multi-region Ethics Committee gave expedited approval (MEC/11/EXP/080) for this study. Pharmacies were randomly selected from the complete list of NZ community pharmacies held by the Pharmacy Guild of NZ using random numbers generated by C. Frampton. These pharmacies were telephoned then faxed a participant information sheet and instructions.

Seventy pharmacies were selected on the basis that there would be considerable variability between pharmacies.<sup>13</sup> In the absence of any data upon which to base a sample size estimation, we speculated that the SD between pharmacies in total monthly sales would be as large as 1.5 times the mean sales per pharmacy in terms of both the prescription and pharmacist supply sales of oseltamivir. On this basis the 95% CI for the total quantity supplied across the country would be approximately  $\pm 33\%$  of the estimate. Seventy pharmacies represent 7.8% of all NZ pharmacies.

Consenting pharmacists printed reports of supplies of oseltamivir for the period 1 January 2007 to 15 September 2011. The reports were annotated to indicate supply pursuant to a prescription or pharmacist supply and patient identifiers were removed. Characteristics of each pharmacy were also collected. Those pharmacies that declined to participate were asked for the characteristics of their pharmacy and replaced. Pharmacies that had opened after 1 January 2007 or could not access information back to 1 January 2007 were not included. Non-provision of reports prompted telephone and fax reminders. Pharmacies that withdrew or did not supply their data after consenting were replaced. Pharmacies were each reimbursed NZ\$80 (~UK£40) for their time.

Data relating to the supply of oseltamivir were extracted from the reports. This included the number of capsules supplied, the date and whether the supply was pursuant to a prescription (termed prescription supplies) or pharmacist supply without prescription (termed pharmacist supplies). A single course of oseltamivir is usually 10 capsules. The supply of suspension quantities was low (0.5% of courses supplied), thus only data on the capsules are presented.

Oseltamivir resistance data on influenza viruses isolated from throughout NZ from 2008 to November 2011 were obtained from reports produced by the Institute of Environment, Science and Research Ltd (ESR), NZ<sup>19,20</sup> and the WHO Collaborating Centre on Influenza & Research (WHOCC), Melbourne, Australia.<sup>21</sup> Viruses detected from most NZ regions are tested by ESR and then forwarded to the WHOCC. Influenza viruses from the Auckland region are sent to the WHOCC, while sets of viruses largely (but not solely) from the Canterbury/Westland region are forwarded to both the ESR and WHOCC. Thus, a proportion of the influenza viruses forwarded by the ESR to the WHOCC were retested by the WHOCC. The strategy for antiviral resistance testing at the ESR and WHOCC laboratories involves both genotypic and phenotypic (on viable virus) methods. Genotypic testing involves PCR followed by genomic sequencing to identify specific mutations known to be associated with neuraminidase inhibitor resistance, e.g. the H275Y amino acid substitution in the N1 neuraminidase protein. Phenotypic antiviral susceptibility was determined by the neuraminidase inhibition assay using a fluorescent substrate. Influenza viruses are considered to be resistant to oseltamivir when the concentration required to inhibit 50% of a viruses neuraminidase activity ( $IC_{50}$ ) is  $>150$  nM.<sup>19,21</sup>

The resistance data were presented as being oseltamivir susceptible/resistant for each year from 2008. Data on seasonal influenza A(H1N1) viruses carrying the naturally (non-drug selected) evolved H275Y resistance mutation<sup>22</sup> along with A(H3N2), B and influenza A(H1N1)pdm09 viruses are included.

The ESR runs the National Influenza Surveillance Programme, which contributes to the WHO's Global Influenza Surveillance & Response Programme.<sup>20,23</sup> About 85 selected sentinel general practices throughout NZ monitor consultations for influenza-like illness and take respiratory swabs from one patient (preferably the first) meeting this definition on all Mondays, Tuesdays and Wednesdays, which are then sent to a regional virus diagnostic laboratory, including ESR's National Influenza Centre, for viral detection, isolation and strain identification. The ESR surveillance data have been used to compare the timing of supplies through the pharmacy with the timing of positive influenza samples. National information on seasonal influenza vaccine uptake was accessed from Health Care Logistics and the Ministry of Health. It includes total supplies distributed and claims made for administration of funded vaccination to those eligible (people  $\geq 65$  years,  $<65$  years with specified chronic diseases or pregnant women).

Annual figures for 2007–11 pharmacist supply and prescription supply as a percentage of all supplies from pharmacies (doctor prescribed plus pharmacist supply) are provided for the sampled pharmacies. These data are used to estimate the total NZ figures, with the variation between individual pharmacies used to calculate 95% CIs for these estimates.

**Results**

Ninety-seven pharmacies were contacted. Of these, 11 pharmacies were excluded: 8 new pharmacies, 1 pharmacy no longer in business and 2 pharmacies that could not access data from 2007 due to software difficulties. Two pharmacies were not operational due to the Christchurch earthquake: one with accessible data was included; the second had no data available and was replaced with another randomly selected Christchurch pharmacy (included in the 97 contacted pharmacies). Thus, 85 pharmacies were eligible for entry into the study. Six pharmacies declined to participate (most also declined to provide pharmacy descriptors), five pharmacies withdrew and four did not provide a report. Seventy pharmacies (82% of those eligible) provided reports covering the period of 1 January 2007 to 15 September 2011 (or 22 February 2011 for the earthquake-affected pharmacy). This high response rate from the random sample of pharmacies gives us confidence that the respondent data are representative of the NZ supplies of oseltamivir through community pharmacies. One pharmacy had paper records for some pharmacist supplies of oseltamivir from 2009 and 2010. Exact supply dates were unavailable, so these supplies were incorporated within annual totals but not the monthly figures.

Participating pharmacies were self-described as suburban (51%), rural (21%), township (19%) or city business district (9%). Staff numbers averaged 6.9 per store (range 2–30). A minority (37%) belonged to a marketing group (branded pharmacies that are usually independently owned). Nearly half dispensed 100–250 prescriptions per day (45%), 34% dispensed >250 prescriptions per day, with the rest dispensing <100 prescriptions per day (4%) or declining to answer the question (16%). Pharmacies that withdrew or did not supply the report compared with the responding pharmacies were suburban 44% versus 51%, rural 22% versus 21%, or town 33% versus 19%; no city business district pharmacies dropped out. One-third belonged to a marketing group, compared with 37% for the responding pharmacies. In addition, those non-participating pharmacies were not profoundly different from participating pharmacies with regards to staff numbers or prescription rates.

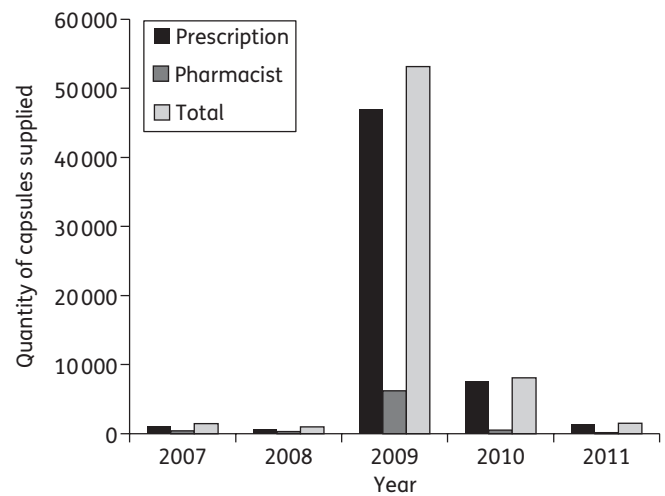
**Oseltamivir supplies**

Prescription supplies for the 70 pharmacies exceeded pharmacist supplies for oseltamivir throughout the 5 years (Figure 1). All supplies were low in the inter-pandemic years. Pharmacist supply as a percentage of total oseltamivir supplies was considerably higher pre-pandemic than in 2009–11 (Figure 2), but these are based on very low overall prescription levels.

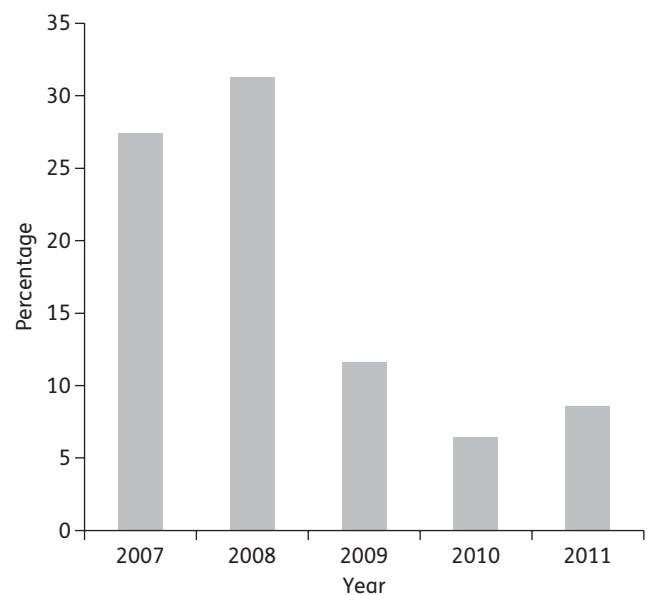
Both prescription supplies and pharmacist supplies varied considerably between pharmacies. Extrapolating the figures from our pharmacies to pharmacies throughout NZ ( $n=903$ ), the peak pharmacist supply occurred in June 2009, with an estimated 20086 capsules (about 2000 courses) supplied for all of NZ (95% CI 12 834–27 338), the same month as the prescription supplies peaked at 263 270 (95% CI 166 249–360 291).

**Influenza antiviral drug resistance**

Resistance data are presented for 2008–11 (sampling until November 2011; Table 1). All resistance testing is either performed



**Figure 1.** Pharmacist supply of oseltamivir compared with prescription supply (for the 70 pharmacies). Note: 2011 includes data to 15 September 2011.



**Figure 2.** Pharmacist supplies as a proportion of total community pharmacy supplies (pharmacist supplies plus prescription supplies for the 70 pharmacies). Note: 2011 includes data to 15 September 2011.

by the National Influenza Centre, ESR or WHOCC, Victorian Infectious Diseases Reference Laboratory (VIDRL), Melbourne, except during 2010–11 when Canterbury Health Laboratories (CHL) conducted an oseltamivir treatment trial.<sup>24</sup> A number of viruses underwent duplicate testing at these centres (estimated at 25% of ESR viruses) and these could not be identified.

**Oseltamivir supply timing**

Pharmacist supply peaks for the sampled pharmacies closely matched positive influenza test timing in the inter-pandemic

**Table 1.** Resistance findings 2008–11

Year	Lab	Influenza A	Number tested	Number resistant	Percentage resistant
2008	WHOCC	A(H1N1)	0		
		A(H3N2)	10	0	0
		B	4	0	0
	ESR	A(H1N1)	4	4	100
		A(H3N2)	107	0	0
	B	134	0	0	
2009	WHOCC	A(H1N1)pdm09	49	0	0
		A(H1N1)	42	42	100
		A(H3N2)	2	0	0
		B	0		
	ESR	A(H1N1)pdm09	483	0	0
		A(H1N1)	25	25	100
		A(H3N2)	0		
		B	0		
	CHL <sup>a</sup>	A(H1N1)pdm09	2	0	0
2010	WHOCC	A(H1N1)pdm09	434	0	0
		A(H3N2)	4	0	0
		B	3	0	0
	ESR	A(H1N1)pdm09	334	0	0
	CHL <sup>a</sup>	A(H1N1)pdm09	97	3*	3.1
2011	WHOCC	A(H1N1)pdm09	17	0	0
		A(H3N2)	46	0	0
		B	123	0	0
	ESR	A(H1N1)pdm09	12	0	0
		A(H3N2)	70	0	0
		B	179	0	0

<sup>a</sup>Three oseltamivir-resistant influenza A(H1N1)pdm09 viruses were recovered during an oseltamivir treatment trial. All were recovered from children on day 5 of treatment. Of 190 viruses (from multiple sampling in 97 patients) tested, 3 (1.6%) were phenotypically resistant: 2 with H275Y mutations and 1 with an unknown (non-H275Y) mutation.<sup>24</sup>

period of 2007 and 2008 (Figure 3). Prescription supplies were greater out of the peak season than pharmacist supplies. This graph was not rerun for the pandemic period because distribution changed, funding occurred partway through the period and influenza sampling varied.

More oseltamivir was supplied during 2009 than any other year, as seen in Figure 1, particularly for prescription supplies [some of which were government funded, costing most patients NZ\$3 (UK£1.50) plus a copayment for the doctor’s visit].

**Oseltamivir pharmacist supply and immunization**

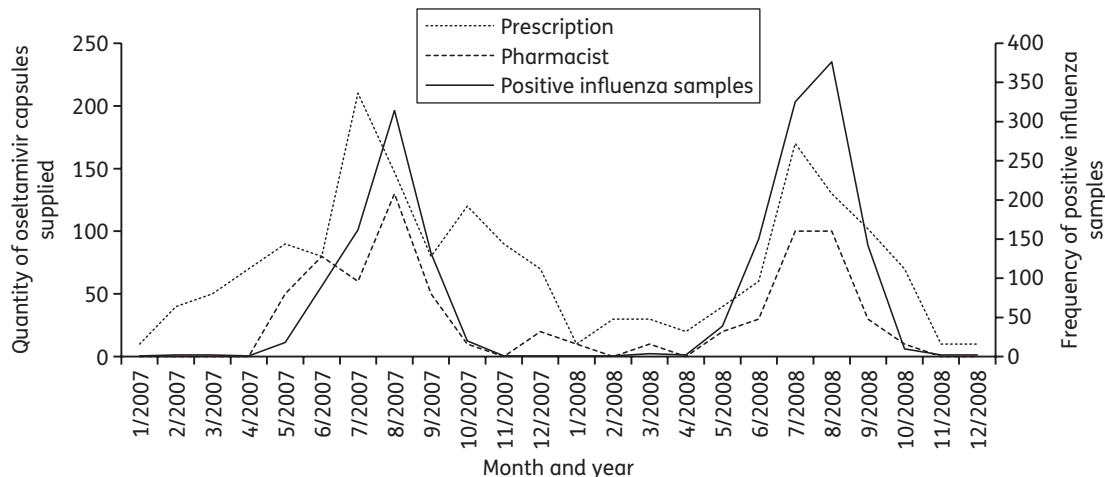
No apparent link was evident between the availability of oseltamivir from the pharmacist and influenza vaccine supplies (Figure 4).

**Supplies outside of the set time period**

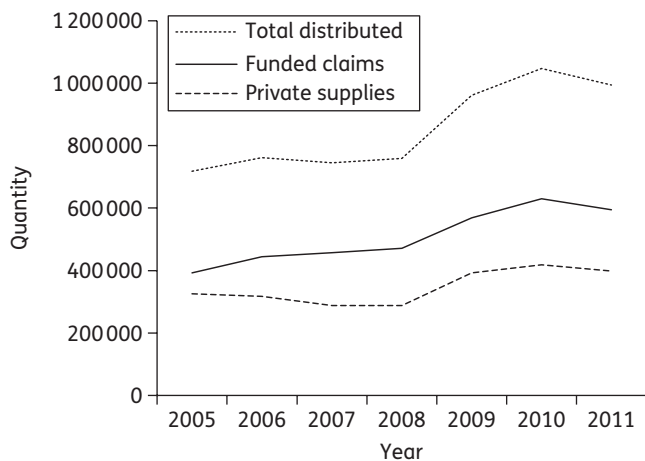
During inter-pandemic years, non-prescription oseltamivir was rarely supplied outside of the designated season, with 30 capsules (three courses) supplied in each of 2007 and 2008, and 20 capsules (two courses) supplied in 2011. In 2009, 450 capsules (45 courses) were pharmacist supplied from nine pharmacies outside of the time period (all late April 2009). This was 6.2% of total supplies from the 70 community pharmacies that month, with 93.8% prescription supplied.

**Discussion**

Data for nearly 5 years of pharmacist supply of oseltamivir in NZ in 2011 from the sampled pharmacies indicate the concerns raised about the reclassification of oseltamivir (increased resistance, stockpiling, overuse, misdiagnosis and reduced uptake of influenza immunization) were not realized. Pharmacist supply did not result in a large increase in overall usage. During this time the evolution and spread of the resistant seasonal A(H1N1) virus internationally in 2007–08 is believed to have been due to a mechanism unrelated to oseltamivir drug usage.<sup>16,22,25</sup> Following the emergence of influenza A(H1N1)pdm09, this virus rapidly



**Figure 3.** Pharmacist supplies and prescription supplies pre-pandemic compared with positive influenza samples reported in 2007 and 2008.



**Figure 4.** Seasonal influenza vaccine supplies by year, 2005–11. Note: 2011 includes data to 10 October 2011 for funded claims and to 31 July 2011 for vaccinations distributed. Oseltamivir first available May 2007.

became the predominant virus,<sup>26</sup> and resistance to oseltamivir has been low in Australasia, comparable to that seen in other countries (<1%).<sup>27,28</sup> The three cases of the oseltamivir-resistant influenza A(H1N1)pdm09 virus were isolated after 5 days of treatment following doctor supply of oseltamivir in a clinical trial. We believe that pharmacist supply in NZ under strict criteria has not resulted in the appearance of oseltamivir-resistant viruses in the community.

Similar to the qualitative research carried out following reclassification from 2007,<sup>13</sup> pharmacist supplies were modest and oversupply by pharmacists was not apparent. This is indicated both by the low volume supplied and the similarity of the temporal patterns of pharmacist supply and influenza virus circulation in NZ in the inter-pandemic years. In contrast, supply of chloramphenicol significantly increased in England and Wales following reclassification.<sup>29</sup> Restrictions to supply and a strict protocol for supply may have assisted in reducing the risk of inappropriate usage, as intended. Multiple barriers to pharmacist supply of oseltamivir include a mind-set of treating symptoms rather than using a neuraminidase inhibitor, lack of awareness by consumers, lack of recommendation by pharmacists and cost (F. Kelly, N. J. Gauld and J. Shaw, unpublished data from the oseltamivir qualitative study in 2007<sup>13</sup>). Modelling in 2000–01 found cost is an important barrier for over-the-counter (OTC) purchase of a neuraminidase inhibitor.<sup>30</sup> Therefore, we believe that cost, restrictions on supply, agent and indications will all affect the likelihood of an increase in usage (or not) following reclassification. Similarly the development of resistance may also be affected.

Pharmacist supplies of oseltamivir increased during the pandemic, but were minimal by comparison with prescription supplies. Supplies in April through doctor prescription or pharmacist supply occurred at a very early stage in the pandemic and would almost entirely represent personal stockpiling, of which the vast majority occurred on prescription. The low level of pharmacist supplies, the lack of pharmacist supplies in April 2009 at the beginning of the pandemic and the similarity

between the pharmacist supply and influenza incidence in the community suggests personal stockpiling was probably minimal, in line with the intent of the criteria for supply. Unlike pharmacist supplies, doctors could prescribe oseltamivir in advance of need. Additionally, doctor prescriptions were government funded for acute illness where a higher risk of severe outcomes existed. Pharmacist supply or unfunded prescriptions cost consumers NZ\$75–80 (around UK£40) per 10 capsules versus NZ\$3 (UK£1.50) for funded prescriptions. Thus, symptomatic patients were financially incentivized to visit the doctor for treatment, even with a patient copayment for the doctor's visit and likely delay in treatment. In some areas government funding of oseltamivir continued during 2011.

In Norway, oseltamivir (and zanamivir for pregnant women) were pharmacist supplied for 8 months during the pandemic (5 November 2009 to 1 July 2010), peaking at 75% of all supplies being pharmacist supplies.<sup>31</sup> Unlike NZ, pharmacist supply in Norway was funded, and saved the patient a doctor visit charge of 136 Norwegian krone (UK£15) (T. Reinholdt, Norwegian Pharmacy Association, 18 November 2011, personal communication).

Early antiviral usage was uncommon in pandemic fatalities in NZ.<sup>32</sup> Given the protective effects seen with oseltamivir,<sup>33,34</sup> the advantages of early administration<sup>35</sup> and the effects on intensive care units and hospital admissions from the pandemic,<sup>32,36</sup> provision of oseltamivir through funded pharmacist supply may have been prudent, as was suggested before the pandemic.<sup>18</sup> Of the 49 pandemic deaths in NZ in 2009, 25 cases had used an antiviral (a median of 6 days from the onset of illness). One of these cases had self-medicated with oseltamivir without medical review, although whether the supply was through pharmacist supply or from a personal stockpile from a previous prescription is unspecified. The first contact with a health professional was with a doctor or in a hospital in 37 cases (75%) and maternity services for 1 case, but was unknown for 5 cases. Six cases did not see any health professional in the course of their illness. Non-prescription availability did not appear to contribute particularly to the death rate in influenza cases in the pandemic in NZ.

In the UK, to reduce pressure on primary care doctors during the pandemic, many antiviral courses were supplied via call centre operators with no clinical background and 1 day of training.<sup>37</sup> Pharmacists are accessible health professionals already working in a triage role and may be more appropriate suppliers of advice and antivirals than call centre staff. In a pandemic, active deployment of antivirals,<sup>38</sup> including the reduction of barriers to accessing antivirals, is recommended to support early treatment for people with symptoms of influenza.<sup>32</sup> Research comparing antiviral usage between different countries, including the funded pharmacist-supplied antivirals in Norway, may suggest preferred models to increase early patient access and limit pressure on doctors and hospitals. Such research may also help to resolve the July 2009 criticism of the UK and other countries for a lack of detail around antiviral delivery in pandemic planning.<sup>39</sup>

The 2007 qualitative research exploring pharmacists' experiences and opinions on non-prescription availability of oseltamivir in NZ found low supply by most interviewees and a reticence for recommendation.<sup>13</sup> Although pharmacists became more familiar with oseltamivir supply, particularly given the pandemic,

pharmacist supplies in 2011 were lower than in the pre-pandemic years. Possible reasons include continued funding for prescribed oseltamivir in some areas and substantially lower influenza activity than in 2009 and 2010, coupled with lower public health messaging activity and media attention. Pharmacists may have simply reverted to being less proactive in looking for influenza and suggesting oseltamivir. This supports the view from 2007 that despite a potential sale of NZ\$75–80 (UK£37–40), commercial imperatives for pharmacies did not appear to drive sales. Removal of the requirement for the influenza sufferer to come into the pharmacy in person and extension of the supply period (from May 2009 until November 2010, and since then with April to November availability) has apparently had little impact on post-pandemic supplies.

Pharmacist supply outside of the allowable dates was rare in the inter-pandemic years. These supplies may be due to confusion about dates of supply (which changed several times), as was found previously.<sup>13</sup> The supplies at the start of the pandemic (April 2009) indicate possible supply in advance of need. Some of these may be supplies to a doctor (anecdotal information from one pharmacy indicated this occurrence) or on doctor recommendation, or may reflect ignorance or flouting of the criteria for supply. Given the infrequent pharmacist supplies prior to the pandemic, confusion by some is likely, so a reminder of the criteria for supply at the start of each season or a pandemic may be useful.

A particular strength of this research was the supply of computer-generated reports detailing each supply (patient-identifying details removed). In situations where these reports gave computer coding specific to prescription or pharmacist supply, this produced confidence in the accuracy of the dataset in addition to the pharmacists' annotations. A further strength is the high proportion of randomly selected pharmacies that consented and supplied the reports. The retrospective data collection ensured pharmacist behaviour was not affected by their participation in the study. The availability of data showing inappropriate (outside the allowable season) supplies as well as appropriate supplies helps confirm the veracity of the dataset.

We were unable to break our prescription figures down by funding. An estimated 55 000 funded courses of oseltamivir were used from the National Reserve, treating 1.3% of the NZ population (Charles Blanch, Ministry of Health, 19 October 2011, personal communication). Many of these would have been captured in our data. However, in Christchurch in 2009, which included ~9% of the NZ population, 'Flu' centres dispensed oseltamivir that is not captured in our data.<sup>36</sup> In the Auckland region (~33% of the NZ population) selected pharmacies dispensed funded oseltamivir during 2009 and 2010. Our sample included 2 of the 26 selected Auckland region pharmacies, which may not have been representative of supplies throughout these pharmacies. Supply through public health nurses early in the pandemic and inpatient hospital use were not captured in our data. Thus, the pharmacist supply figures are accurate, but prescription supply may be underestimated in 2009 and possibly 2010.

We could not assess the suitability of supply time for one pharmacy because some of their pharmacist supply records did not include dates. The information was provided during a visit by the lead author to the pharmacy and came from a mixture of computer records (which were seen and were all in the

correct date range) and paper-based consultation records (which were not seen individually but were totalled by the pharmacist at the pharmacy, by year).

A further limitation is the reliance on resistance and susceptibility data from samples that were collected for surveillance or diagnostic purposes. Further, a relatively small proportion of the virus-positive samples were actually tested for oseltamivir susceptibility. Use of oseltamivir in NZ is relatively low and our findings may have less relevance to countries where the use of antivirals is high. Vaccine data include claims data for those eligible for vaccination (representing vaccinations) and total vaccine supplies. Thus, the private market may be overstated, as some of the vaccines distributed may not have been administered. As medical practices pay for vaccines prior to being claimed or patients charged, there is a financial incentive not to overorder. Our research cannot comment on the appropriateness of individual supplies by pharmacists, apart from the temporal relationship between supply and positive influenza results. Research at the consumer level is warranted, including testing for influenza in consumers deemed eligible by pharmacists for oseltamivir.

## Conclusions

Nearly 5 years of pharmacist supply of oseltamivir was not associated with increased resistance, reduced influenza vaccination or significant levels of personal stockpiling, and largely matched the timing of influenza activity in the community. Supplies remained modest, even during the A(H1N1) pandemic waves in 2009 and 2010. Funding oseltamivir provision from pharmacists during a pandemic may improve access and could be considered (along with influenza immunizations from pharmacy) for future pandemics.

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## Transparency declarations

N. J. G., L. C. J. and C. F. have received unrestricted research funding from F. Hoffmann–La Roche. N. J. G. was a member of the Medicines Classification Committee in NZ in 2006 during the consideration of oseltamivir and has received conference support (2008) from F. Hoffmann–La Roche. N. J. G. has received funding from Pharmacybrands Ltd for work on reclassifications. L. C. J. has received unrestricted research funding from F. Hoffmann–La Roche and honoraria and travel assistance from F. Hoffmann–La Roche and GlaxoSmithKline for participating on advisory groups or in scientific meetings. Q. S. H. receives funding from the NZ Ministry of Health to conduct national sentinel GP-based influenza surveillance.

### Author contributions

N. J. G., L. J. and C. F. designed the research and were all involved in analysis and reporting. N. J. G. was responsible for data collection of pharmacy data. Q. S. H. collected and provided resistance data and influenza detection data. All authors provided input to the article with the first draft written by N. J. G.

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