Descriptive Study of Users of Depo-Medroxyprogesterone Acetate (DMPA) in the MHRA GPRD

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Background

Depot-medroxyprogesterone acetate (DMPA) is a progestogen-only injectable contraceptive that inhibits secretion of pituitary gonadotropins and causes anovulation, amenorrhea, and decreased serum estradiol. The recommended DMPA dose for contraception is 150 mg/mL every 3 months.

In the UK, the British National Formulary (BNF) advises that a reduction in bone mineral density (BMD) is associated with a prolonged use of DMPA. The UK Medicines and Health Care Products Regulatory Agency (MHRA) requested to have a better understanding of DMPA use in the UK and to evaluate the clinical impact of the reduction in BMD among DMPA users.

Objectives

- To estimate the number of women younger than 50 years of age using DMPA in the General Practice Research Database (GPRD) population and to describe their baseline demographic and fracture risk profile characteristics.
- To describe the patterns of DMPA use (frequency and duration).
- To examine the feasibility of evaluating the risk of fractures in women taking DMPA using GPRD as the source population.

Methods

We used the population of GPRD[1] to describe demographic characteristics, fracture risk factor profiles, and use of DMPA in women before age 50. For each woman, we defined an individual baseline history period and a subsequent follow-up period for assessment of fracture risk. The time at risk of fracture started at the first DMPA prescription and ended at the earliest of a woman's first fracture date, her last GPRD utilization record, or the study end date of 31 December 2004. We used Read/OXMIS drug, procedure, and diagnosis codes to classify women according to baseline characteristics and to ascertain the first fracture event (if any) per woman during time at risk. Prevalence of baseline factors was estimated per 100 women.

We counted the first fracture code per woman to estimate incidence rates of fracture per 1,000 woman-years of follow-up. We stratified rates by age group, site and short or long-term DMPA use (< or ≥ 8 prescriptions corresponding to a duration of < or ≥ 2 years, respectively). This study was conducted according to the Guidelines for Good Pharmacoepidemiology Practices.[2]

Results

In the GPRD population, 68,971 women younger than 50 years of age (0.7% of the population) initiated use of DMPA. Using Multilex drug codes, we obtained a sample of 49,999 women with at least one DMPA prescription from Jan 1987 to Dec 2004.

From this sample, we identified a total of 42,808 women ≤ 50 years of age who met all study eligibility criteria. Twenty-one percent of women had less than 20 years of age and approximately 50% were between 20 and 29 years of age at the time DMPA was first prescribed (Table 1). There were 160,579 woman-years at risk and the median follow-up time was 2.9 years per woman, most of which occurred during the 2000-2004 period.

Table 1. Number of Women by Age at Index Prescription of DMPA

Age Group (years)	Study Women N	%
<20	8,886	20.8
20-24	10,921	25.5
25-29	9,231	21.6
30-34	7,058	16.5
35-39	4,476	10.5
40-44	1,718	4.0
45-49	518	1.2
Total	42,808	100.0

At baseline, twelve percent of the women had a history of any fracture. Of conditions predisposing to lower BMD, only history of alcohol abuse had a prevalence as high as 1%. Prevalence of a positive history of a neoplasm (less than 1%) increased with age. Few women had used oral steroids or other immunosuppressants. Baseline evaluations of BMD or diagnosis of osteoporosis were rare (under 1%).

The results for patterns of DMPA use showed that more than half (56.7%) of the women had ≤ 3 prescriptions, while 43.4% had ≥4, and 22% had ≥8 prescriptions (Figure 1). The median number of prescriptions per woman was three. Seventy-five percent of prescriptions showed an interval between prescriptions of 61 to 90 days.

A total of 1,530 codes for incident fractures at any bone site were ascertained in the study population. For all ages up to 50 years, the incidence of codes for "any fracture" was 9.5 per 1,000 DMPA woman-years with the highest rates observed in women of ≤20 years of age and among women 40 to 49 years of age (Table 2).

Among women with ≥8 DMPA prescriptions the incidence of codes for any type of fracture was 5.9/1,000 DMPA woman-years. During the 1993 to 2004 period when the majority of data were accumulated, the incidence of any fracture appeared stable over time.

Figure 1. Percentage of Women by Number of DMPA Prescriptions, GPRD 1987-2004
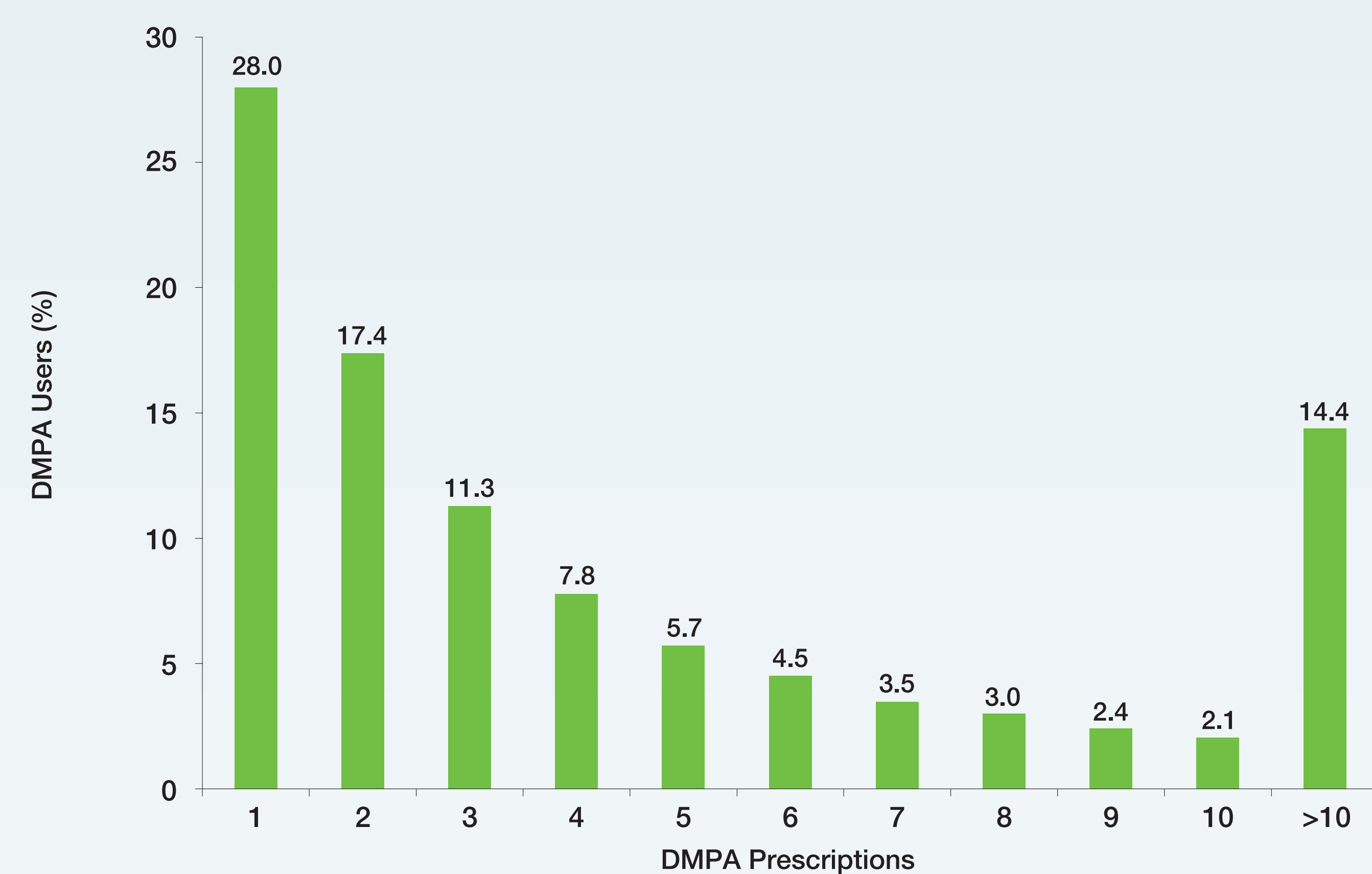

Table 2. Number of Fractures and Incidence Rates by Age

Number of Fracture Events	Age Group				All Ages
	<20	20-29	30-39	40-49	
Arm	32	64	46	17	159
Hip	0	1	0	1	2
Vertebra	2	10	6	1	19
Arm or Hip or Vertebra	34	75	52	19	180
All Other*	259	649	363	79	1,350
Total, any	293	724	415	98	1,530
Woman-Years at Risk	28,529	77,993	45,707	8,349	160,579
Rate per 1,000 Woman-Years					
Arm	1.1	0.8	1.0	2.0	1.0
Hip	0.0	0.0	0.0	0.1	0.0
Vertebra	0.1	0.1	0.1	0.1	0.1
Arm or Hip or Vertebra	1.2	1.0	1.1	2.3	1.1
All Other*	9.1	8.3	7.9	9.5	8.4
Total, any	10.3	9.3	9.1	11.7	9.5

* All other includes pelvis, leg, and all other specified or unspecified bone sites.

Conclusions

- The MHRA GPRD is an adequate data source to study the demographic/fracture risk profile characteristics and the patterns of use of women taking DMPA in the UK.
- Incidence rates based on codes for any type of fracture have been reported. Further work would be needed to validate that the codes accurately ascertain fractures. A decrease in the total number of fractures is expected after such validation.
- Based on this feasibility study and other published studies, the GPRD population provides a reasonable setting for a study of medication exposure and fracture risk.[3-5]
- A full evaluation on the risk of fractures among DMPA users would require the selection of the appropriate comparison groups of women to put into context the fracture findings.

References

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