Mode of injection and treatment adherence: results of a survey characterizing the perspectives of health care providers and US women 18–45 years old

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Purpose: A market research study was conducted to characterize perceptions of intramuscular (IM) and subcutaneous (SC) routes of injection, including use of autoinjectors, and how these perceptions affect adherence to injection regimens. The perspectives were from women of childbearing age (18–45 years old; consumers) and health care providers (HCPs) involved in women’s health care.

Methods: Two telephone surveys, one of HCPs and the other of consumers, were conducted by KRC Research (New York, NY, USA) between May and July 2017. HCPs were recruited across the US; the consumer survey was administered to a nationally representative sample. Survey questions identified potential challenges of IM and SC administration, their impact on treatment adherence, and perceptions of autoinjectors. Results are reported using descriptive statistics and reflect an unweighted sample; margin of error is ±3% for the consumer survey.

Results: HCP respondents included 100 generalist OB/GYNs, 101 maternal-fetal medicine specialists, and 519 nurses; there were 1,012 female consumer respondents. Nurses reported more experience than physicians in administering injections, including with autoinjectors. Consumers reported having received treatments via both IM and SC injections; 26% had received treatment with injections at regular intervals. Most HCPs (58%) said they preferred to administer SC injections, which was also the preference for receiving injections among consumers, who reported needle size as a concern regardless of administration mode. Other major concerns were perceptions of pain and fear/anxiety, and seeing the needle, all of which were greater for IM than for SC injections. HCPs and consumers both reported greater likelihood of adherence to therapy administered SC using an autoinjector because they believe that this method provides substantial HCP and patient benefits.

Conclusion: HCPs and consumers identified similar challenges with adherence to injections. However, there was consistently higher preference for SC relative to IM. HCPs and consumers believe that autoinjectors may increase adherence.

Keywords: women’s health care, intramuscular, subcutaneous, injection, patient preference, adherence

Introduction
In the clinical setting, injections provide a method of drug administration that serves several purposes including therapeutic care, immunization, and preventive care. Consequently, injections have become one of the most common medical procedures administered by health care providers (HCPs), sometimes requiring that injections be given at regular intervals over a specified time period.
The intramuscular (IM) and subcutaneous (SC) routes are the most frequent types of injections in routine clinical practice, although occasionally intravenous (IV) administration may be necessary due to the formulation or pharmacokinetics of a drug or based on the clinical situation. Unless specifically dictated by the drug or disease, optimal choice of injection route is often guided by a variety of factors including available options, efficacy and safety profiles, convenience, and economic benefits. These factors are also recognized by the World Health Organization as components of five interrelated dimensions that contribute to treatment adherence. However, when multiple modes of administration are available that provide equivalent safety and efficacy, patient preference may be a key factor that is likely to improve treatment acceptance, adherence, and thus potentially effectiveness, especially if a regimen of multiple injections is required. For example, among patients with rheumatoid arthritis, route of administration was the most important factor cited by patients when choosing a biologic therapy, with SC administration the first choice relative to IV and IM. Consequently, it is important to characterize the factors most likely to increase patient acceptance and adherence to therapy. Understanding perceptions regarding preferences for mode of injection from both the HCP and patient perspectives, which may not necessarily be in agreement, can potentially inform treatment decisions.

Autoinjector devices have been developed for administration of some medications, with use of these devices by either the patient or clinician, although some devices require administration only by HCPs. These preloaded devices avoid the need for drawing up medication and handling vials and needles, which ensures accurate dosing. The self-contained autoinjector needle is generally small, especially in SC autoinjectors, and is deployed only during the injection, remaining hidden from view both before and after administration. With these devices, the needle generally has a needle guard to protect it in such a way as to avoid inadvertent needle-stick injuries.

Women are often recipients of injections that provide a range of therapeutic benefits, including pharmacologic treatment of chronic conditions (eg, chronic pain, musculoskeletal and metabolic disorders), as well as management of reproductive health issues, for which injections are available to treat infections, provide contraception, and for ovulation/fertility treatments, preterm birth prevention, and Rh isoimmunization. As reviewed by Jin et al, many of the studies that have comparatively evaluated injection routes have done so within a setting of optimizing treatment for a chronic disease. However, few data are available on perceptions and preferences of injection routes from a general population that may be applicable to women’s reproductive care.

This market research study was sponsored by AMAG Pharmaceuticals (Waltham, MA, USA) to better understand injection preferences. AMAG Pharmaceuticals is the marketer of Makena® (hydroxyprogesterone caproate injection), which has recently become available as an autoinjector via SC injection, and is also preparing for potential approval by the US Food and Drug Administration of another autoinjector for SC injection in the women’s health space. Given the paucity of data on injection route preferences among women of childbearing age, the purpose of this survey was to characterize the perceptions of this population with regard to the IM and SC modes of injection, as well as the use of an SC autoinjector, and how these devices may impact treatment adherence. Furthermore, because treatment is a mutual collaboration between patients and their HCPs, on whom patients often rely for advice and recommendations, the perspective of HCPs was also queried.

Methods

Two telephone surveys, one directed toward HCPs and the other to consumers, were fielded by KRC Research (New York, NY, USA). The surveys, provided as Supplementary material, were developed by KRC Research with input from the survey sponsor (AMAG Pharmaceuticals Inc.) and were conducted from May 25 to July 5, 2017 (HCP survey) and May 22 to June 16, 2017 (consumer survey). This research was not subject to institutional review board review. KRC Research, the principal investigator, adheres to all ethical principles and guidelines for the protection of human subjects established by the Office for Human Research Protections, and complies with all federal regulations for human subjects research and the Code of Standards established by the Insights Association.

Both surveys were designed to provide information on experience with and perceptions of IM and SC injections including autoinjectors, and how these experiences and perceptions are likely to affect adherence to treatments requiring such injection regimens. While the terms “intramuscular” and “subcutaneous” were used in the HCP survey, the consumer survey used simpler, plain language terminology. The consumer survey questions provided a description with examples, and consistently referred to injection administration as “deeper into a muscle, such as the buttock” (for IM) and “just below the surface of the skin, such as in the arm”
(for SC); however, for the purposes of this analysis, IM and SC are used when referring to results based on these questions.

To qualify for participation in the survey, physicians were required to be licensed OB/GYNs or maternal-fetal medicine specialists, spending at least half of their time in direct patient care. Nurses qualified if they were certified nurse midwives, nurse practitioners, and administering nurses (including advanced practice registered nurses). Consumers qualified if they were a woman of childbearing age, defined as being between 18 and 45 years old. HCPs were recruited across the US from a Masterfile drawn from proprietary and public databases of physicians. Screening questions were included to identify the specialties of those who qualified for the survey. The survey was administered via telephone, and the response time was approximately 16 minutes. The consumer survey was administered by telephone to a nationally representative sample randomly selected from comprehensive lists of US consumers; response time was approximately 13 minutes. Sample sizes were 720 HCPs and 1,012 consumers. HCPs were offered compensation for completing the survey.

Results are reported using descriptive statistics. All results reflect an unweighted sample. The margin of error for a probability sample of 1,012 is ±3 percentage points for the consumer survey. Results were also stratified in the HCP sample by physicians and nurses, and post hoc statistical analyses were conducted using Z-tests to explore differences in perceptions between physicians and nurses. In additional post hoc analyses, sign tests determined the significance of HCP perceptions for the likelihood of patient preferences for IM vs SC and autoinjector vs traditional injection, and differences between physicians and nurses for perceptions of these patient preferences were evaluated using two-sample t-tests.

**Results**

**Respondent populations**

The 720 HCP respondents included 201 physicians (101 maternal-fetal medicine specialists and 100 obstetricians/gynecologists) and 519 nurses, of whom 101 were certified nurse midwives, 100 were nurse practitioners, and 318 were administering nurses. The characteristics of these HCPs are presented in Table 1, and show that while most physicians were male (56%), 84% of the nurses were female, with both groups of HCPs primarily in the age range of 35–64 years; most of the physicians had been in practice for 3–15 years (61%). All geographic regions of the US were represented, with the highest representation from the South.

| Table 1 Characteristics of health care practitioner respondents |
|---------------------------------------------------------------|
| **Variable** | Physicians (n=201) | Nurses (n=519) |
| Sex | | |
| Male | 56 | 16 |
| Female | 44 | 84 |
| Age distribution | | |
| 18–34 years | 7 | 19 |
| 35–64 years | 79 | 69 |
| ≥65 years | 2 | 6 |
| Geographic region | | |
| Northeast | 20 | 18 |
| South | 35 | 45 |
| Midwest | 18 | 19 |
| West | 26 | 17 |
| Years in practice | | |
| 3–15 | 61 | — |
| 16–40 | 39 | — |
| Practice setting | | |
| Small private practice | 26 | 17 |
| Group private practice | 37 | 22 |
| Community or clinic-based practice | 12 | 28 |
| Hospital-based practice | 24 | 33 |
| Community type | | |
| Urban/suburban | 76 | 73 |
| Small city | 22 | 20 |
| Rural | 2 | 7 |
| Proportion of Medicaid patients or managed Medicaid | | |
| <25% | 52 | 27 |
| 25%–49% | 31 | 44 |
| ≥50% | 17 | 29 |

Among the consumer respondents (n=1,012), the sampling frame was women aged 18–45 years. The majority were between 25 and 45 years old (76%), white (59%), and with at least some college education (71%) (Table 2); all geographic regions were represented. While 68% of the respondents had already given birth, 46% stated that they did not plan to have a child in the future, and 17% were not sure (Table 2). Health status was reported as “excellent” or “very good” by 52% of the women, and most reported visiting a physician either one to two times (40%) or three to five times (36%); 6% reported no physician visits in the past year.

**Injection experience**

Experience with SC and IM injections was nearly universal among HCPs; fewer than 1% of physicians (3 OB/GYNs)
reported “never” having administered an SC injection. However, nurses reported a higher frequency of administering injections relative to physicians: 49% of nurses compared to 35% of physicians said they administer IM injections “very often,” and 44% of nurses compared to 33% of physicians administer SC injections “very often.”

Experience with autoinjectors was overall somewhat lower than with traditional injection administration. Nurses reported more frequent administration using an autoinjector device; 53% of nurses vs 46% of physicians reported having administered injections using an autoinjector device “somewhat often” or “very often,” and this rate was even lower (36%) among physicians who had been in practice for ≥16 years, and among HCPs from small town or rural settings (38%).

The consumer respondents also reported substantial experience with injections, which was greater for SC (84%) than for IM injections (61%) (Figure 1A). This experience included current or previous treatment via injections at regular intervals, and approximately one-quarter of women (26%) reported such treatment including daily, weekly, or monthly injections (Figure 1B). However, 25% of women overall reported that they avoided or declined an injection at some point, and the percentage who avoided or declined an injection varied based on injection experience (Figure 1C).

HCP preferences and perceptions of SC vs IM

Most HCPs (58%) said they preferred to administer SC injections relative to IM injections (22%), with similar proportions preferring SC among both physicians (55%) and nurses (59%). While 15% of physicians and 22% of nurses expressed no preference of one administration route over the other, more physicians than nurses stated that they preferred the IM route (28% vs 19%). Consistent with their preference of injection route, 50% of physicians and 61% of nurses considered SC easier to manage and administer; no difference in ease of administration was expressed by 24% and 21% of physicians and nurses, respectively.

HCPs were queried regarding their perceptions of the two routes of administration. More HCPs reported that IM injections cause patients high levels of discomfort (21%) than SC injections (4%), even when stratified by HCP type; 18% and 23% of physicians and nurses, respectively, associated IM with high levels of discomfort relative to 4% of each group for SC. HCPs were also asked to rate a selection of potential challenges of administering IM injections relative to SC as “major,” “minor,” or “no difference.” The primary challenges, as indicated by the proportions of physicians and nurses rating the items as a “major” challenge, were patient fear/anxiety and degree of patient willingness to accept therapy, followed by concerns regarding needle-stick injuries to HCPs (Figure 2A). The proportion of nurses who rated each item as a “major” challenge was consistently higher than that of physicians and was statistically significant (P<0.05) for most of these challenges.

Overall, HCPs thought that IM administration was a greater challenge to patient adherence with therapy than SC

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Table 2 Characteristics of consumer respondents (n=1,012)

| Variable                              | Percent of respondents |
|---------------------------------------|------------------------|
| Female                                | 100                    |
| Age distribution, years               |                        |
| 18–24                                 | 24                     |
| 25–34                                 | 43                     |
| 35–45                                 | 33                     |
| Race/ethnicity                        |                        |
| White                                 | 59                     |
| Hispanic/Latino                       | 19                     |
| Black/African-American                | 12                     |
| Other                                 | 10                     |
| Geographic region                     |                        |
| Northeast                             | 21                     |
| South                                 | 41                     |
| Midwest                               | 20                     |
| West                                  | 18                     |
| Community type                        |                        |
| Urban/suburban                        | 62                     |
| Small city                            | 25                     |
| Rural                                 | 13                     |
| Education                             |                        |
| Some high school or less              | 4                      |
| High school graduate or equivalent    | 24                     |
| Some college                          | 30                     |
| Associate degree or trade-school grade| 9                      |
| Bachelor’s degree                     | 21                     |
| Master’s degree or more               | 11                     |
| Household income                      |                        |
| <$50 k                                | 48                     |
| $50–$100 k                            | 32                     |
| >$100 k                               | 16                     |
| Given birth                           | 68                     |
| Plan to have a child in the future    |                        |
| Yes                                   | 38                     |
| No                                    | 46                     |
| Not sure                              | 17                     |
| Have health insurance                 | 89                     |
administration; 86% of all HCPs reported that IM injections represent a challenge relative to 78% for SC. Stratification by HCP type showed that while physicians found both routes equally challenging (90% IM, 89% SC), more nurses considered IM challenging (84%) relative to SC (74%). When specific barriers to patient adherence with injections were rated by the HCPs as having “major,” “minor,” or “no” impact, patient fear/anxiety and patient perceptions of pain associated with injections were considered major barriers to patient adherence (Figure 2B). However, needle size and patient ability to see the needle were also rated as barriers by substantial proportions of HCPs, and these represented greater barriers for IM than for SC, as with other issues addressed.

Between the two routes of administration, a higher proportion of HCPs overall thought that patients would be more willing to accept therapy and remain adherent to treatment with SC injections (80%) than with IM (13%). Post hoc analysis showed a significant effect such that physicians and nurses both indicated a higher preference for SC than for IM ($P<0.05$), although the preference for SC relative to IM was stronger among nurses than among physicians ($P<0.05$) (Figure 3A). The major benefits of SC injection included less perceived patient pain, smaller needle, and less fear/anxiety. Issues related to privacy, such as not needing to undress or having a private room for the injection, were also considered major benefits by 37% and 30% of HCPs, respectively. Across all items, significantly higher proportions of nurses perceived these as major benefits relative to physicians ($P<0.05$) (Figure 3B).

### Consumer preferences and perceptions of SC vs IM

If regular treatment by injection is needed, most women (79%) expressed a preference for SC injections. Among women

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**Figure 1** Injection experience among women of childbearing age with regard to (A) type of injection, (B) regimens of regular injections and frequency of injections, and (C) avoidance of injections.

**Abbreviations:** IM, intramuscular; SC, subcutaneous.
who had experience with both SC and IM injections, 75% reported that they preferred SC, while 25% preferred IM.

Consumers were presented with a list of potential concerns associated with the two routes of injection administration and were asked to rate them as “major,” “minor,” or “no concern.” All concerns were more frequently ranked as major for IM than for SC (Figure 4A), with the most important issues being pain and needle size, followed by fear/anxiety and seeing the needle (Figure 4A). Although privacy issues with both routes of administration were also considered concerns, “needing a private room” showed a large difference between IM (31%) and SC (17%).

Overall, 90% of women reported that they would be “very likely” or “somewhat likely” to remain adherent to a series of injections given SC, while 72% reported that they would be likely to remain adherent to an IM regimen. However, when given a choice between the two routes of administration, 71% of women said that they were more likely to be adherent to treatment when the injections could be administered SC vs 17% for IM. The most commonly perceived major benefits of SC administration reflected the women’s concerns, and included less perceived pain (63%), smaller needle size (56%), and the privacy issue of not needing to undress (53%) (Figure 4B).

**Autoinjector perceptions**

More than two-thirds (69%) of all HCPs reported that when injections are needed, their preference is for use of an autoinjector rather than a traditional syringe and needle; this preference was directionally higher among nurses (71%) than among physicians (64%). Furthermore, 71% of all HCPs (67% of physicians and 72% of nurses) reported that they thought patients would also prefer injections by autoinjectors relative to a traditional syringe and needle. Post hoc analysis
showed that these perceptions for autoinjector preference were significant relative to traditional injection ($P<0.001$). However, preference patterns were similar between physicians and nurses.

HCPs identified multiple major HCP benefits in administering SC injections via autoinjector relative to IM injections (Figure 5A), including ease of use, fewer needle-stick injuries, more consistent dosing, and faster administration. HCPs also thought that use of an autoinjector would provide major benefits to patients (Figure 5B). These perceptions of HCP- and patient-related benefits were consistently greater among nurses than among physicians.

Nearly all HCPs (90%) thought that patients would likely be more adherent with therapy using an SC autoinjector relative to IM administration (Figure 6A), and this proportion was similar to the proportion of women who reported that they were more likely to adhere to such therapy (86%) (Figure 6B).

**Discussion**

This survey of women of childbearing age and HCPs provides insight into perceptions and preferences regarding injection administration that may facilitate patient adherence with therapy while reducing the burden that HCPs associate with administering injections. Given the choice between IM and SC, the results show that SC is the preferred route of injection among most respondents. The perceived challenges associated with IM as well as the benefits of SC were generally consistent between HCPs and women of childbearing age, with use of an autoinjector reported to likely further promote adherence with injection therapy.

All nurses and nearly all physicians reported at least some experience with administering both IM and SC injections, although three OB/GYNs reported not administering SC injections in their practice. Experience with autoinjectors was lower than that with traditional needles and syringes, most likely because autoinjectors are more frequently used for self-injection by patients in the management of chronic diseases. Nurses tended to administer injections with a greater frequency than physicians regardless of route (SC or IM) or whether by autoinjector or the traditional needle and syringe method. This higher frequency of injections by nurses may be consistent with how health care is provided in the clinical setting, with nurses performing many of the
routine procedures required in daily practice, and may also account for the significant differences in perceptions relative to physicians.

Women of childbearing age reported exposure to both SC and IM injections, and among those with exposure, approximately one-quarter had previously undergone treatment administered by injection at regular intervals. Thus, perceptions reflect real-life experiences, although one out of four women also indicated that they had avoided or declined an injection, and this proportion was higher among those who have had regular injections, emphasizing the impact on treatment adherence.

There was concordance between HCPs and women of childbearing age that the IM route represents a challenge to treatment adherence, with general agreement also regarding other concerns associated with IM injections. While women reported concerns about both methods of injection, more women reported concerns with IM than with SC. HCPs and women both cited pain and fear/anxiety as major concerns with IM, with reduction in these factors considered major potential benefits of SC. However, consumers cited needle size as a major concern regardless of route of administration, as was needle visibility. Women and HCPs both reported needle size as a major concern, especially for IM. However, there was some discordance between the two groups regarding their perceptions of needle size with SC administration. While women recognized that smaller needle size is a benefit of SC compared with IM, a high proportion (45%) still expressed major concerns about SC needle size. These concerns with needle size and visibility are especially relevant because the prevalence of some degree of needle fear in adults has been reported to range from 14% to 38%. In particular, needle phobia, which is more common in women than in men, and may result in vasovagal syncope, is included as a Specific Phobia (Blood-Injection-Injury Type Phobia) that is recognized in the Diagnostic and Statistical Manual of Mental Disorders and has been estimated to be present in 7–22% of the general population. While the prevalence of needle phobia was not determined in the current study, the concerns expressed by women and also recognized by HCPs indicate a need to decrease administration anxiety further even when using the SC route.

Figure 4 Perceptions of women of childbearing age regarding (A) major concerns about injections and (B) perceived benefits of subcutaneous administration.

Notes: Percentages in panel (A) reflect the proportions of women who rated the item as a “major” concern. The consumer survey referred to injection administration as “just below the surface of the skin, such as in the arm” and “deeper into a muscle, such as the buttock” for subcutaneous and intramuscular administration, respectively.
An ongoing regimen of injections is especially challenging for maintaining adherence, and while some women stated a preference for IM injections, more than three-quarters of women (79%) reported a preference for SC if regular treatment was needed. The proportion of women who reported that they would likely be adherent to treatment was even higher (86%), when SC treatment would be administered using an autoinjector, with almost half (47%) reporting that they would be “very likely” to continue therapy. HCPs not only had similar perceptions of patient adherence, but also expressed a preference for using an autoinjector. This preference was a result of perceptions that an autoinjector provides HCP benefits including greater convenience and safety from needle-stick injuries, as well as patient benefits, such as a smaller needle that is not visible, which directly addresses patient concerns about receiving an injection. While these HCP perceptions of patient benefits may also account for why women reported that they would likely be adherent with autoinjector therapy, the specific reasons that women would be adherent to such therapy were not determined. However, in the real-world clinical setting, adherence to treatment may also be a function of drug-related factors such as safety and efficacy. Preferences and adherence reported in the current survey assumed availability of therapeutic options that would provide comparable safety and efficacy.

Limitations
As with all surveys, the results should be interpreted within the context of the study limitations, which include limited generalizability outside of the populations surveyed in this study. While both landlines and cell phones were used for the consumer survey, lack of stratification of results based on

![Figure 5](https://www.dovepress.com/)

**Figure 5** Perceptions of HCPs regarding (A) major benefits to HCPs and (B) patients, of subcutaneous injection using an autoinjector relative to a traditional intramuscular injection.

**Notes:** Percentages reflect the proportions of HCPs who rated the item as a “major” benefit. *P < 0.05 vs physicians (post hoc Z-test).

**Abbreviation:** HCP, health care provider.
these methods may be potentially criticized, because landline responders may have characteristics and perceptions different from individuals using an alternative communication technology. Selection bias may represent another limitation, because respondents who agreed to participate may have perceptions different from those who refused to participate. Additionally, while social desirability bias is often a limitation of surveys, it may have been minimized in the current study because survey language maintained neutrality with regard to administration routes and study objectives. In this regard, it should also be noted that some language and terminology may have affected responses among consumers. For example, because the plain language terminology consistently referred to injection sites with the examples of “arm” (for SC) and “buttocks” (for IM), it is possible that mention of other anatomical sites for each of the routes of administration would have resulted in different responses and perceptions.

Similarly, the survey did not specify who would administer the drug by autoinjector, and the frequency of administration was not specifically stated. As more frequent administration may reduce adherence, responses regarding adherence should be judiciously interpreted.

**Conclusion**

Adherence to prescribed therapy is key to clinical outcomes, and the effect is particularly critical for treatments that require regular injections. Potential barriers to maintaining adherence with an injection regimen were generally similar from the perspectives of HCPs and women of childbearing age, with needle size and needle visibility, fear/anxiety, and perceptions of pain among the major concerns identified. Despite these concerns, the SC route was consistently preferred relative to the IM route, because of perceived SC benefits including less pain, less fear/anxiety, and greater convenience. HCPs also reported that an autoinjector for SC administration would provide additional benefits to the HCPs themselves (convenience of administration and reductions in needle-stick injury risk), and would likely enhance patient adherence with therapy. These HCP perceptions of increased adherence were paralleled by the consumer perspective, with women also endorsing a greater likelihood of adherence with therapy when administered SC by autoinjector. When different routes of administration provide comparable safety and efficacy, HCPs may select the route based upon patient preference and likelihood to accept and be adherent to therapy. The results of this survey suggest that SC is overwhelmingly preferred to IM by consumers, with SC also perceived by HCPs as conveying greater benefits than IM. The use of an autoinjector is additionally perceived by HCPs to be easier and safer to use, and is likely to further reduce the barriers to medication acceptance and adherence among women of childbearing age who require a regimen of regularly scheduled injections.

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**Disclosure**

David L Gandell, MD, is a consultant to AMAG Pharmaceuticals and has served on its speakers’ bureau and advisory board. E Jay Bienen, PhD, is an employee of the Curry...
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