PREDICTING PATIENT INTEREST AND PARTICIPATION IN CLINICAL TRIALS

WHAT REALLY MATTERS?

SURVEY DATA META-ANALYSIS OF PATIENTS WITH CHRONIC CONDITIONS

HEALTH UNION

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inspires people to live better with challenging health conditions - combining new, original content every day with digital, social and mobile technologies to cultivate active, engaged online communities. Health Union platforms are unique ecosystems dedicated to illuminating the voices and experiences of people with migraine, multiple sclerosis, rheumatoid arthritis, hepatitis C, and more. By leveraging these communities, Health Union services support a patient-centric approach to clinical trials throughout study planning, start-up, recruitment programs and ongoing activities.

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INTRODUCTION

Today, clinical development of new therapies – especially patient recruitment into clinical trials – has never been more challenging. It takes longer to recruit patients; trial complexity is increasing; and fewer patients are willing to volunteer,[1] despite the fact that **most patients report interest in clinical trials**. So what patient characteristics *really* influence interest - and more importantly, participation - in clinical research? To help answer this question, Health Union compiled data from more than 21,000 respondents across six surveys conducted in 2014 and 2015 to examine factors involved in patients' interest and participation in clinical research. Each survey focused on gathering insights from patients with a chronic condition, such as COPD, migraine, multiple sclerosis, rheumatoid arthritis, and hepatitis C, about their disease journey, as well as its impact on quality of life and treatment experiences, including clinical trials.

WHAT PATIENT CHARACTERISTICS REALLY INFLUENCE INTEREST AND PARTICIPATION IN CLINICAL RESEARCH?

When asked, most patients report interest in participating in a clinical trial for their condition. They hope to benefit from the new treatment and help others with the condition to benefit as well. And not surprisingly, patients who have participated in a clinical trial are **more likely to be willing to do so again**. A 2012 meta-analysis of patient feasibility and recruitment studies published in *Applied Clinical Trials* found that health condition, age and patient dissatisfaction with current treatment plan are significant drivers of interest in clinical trials.[2] The meta-analysis of Health Union data confirms these findings and also suggests that **gender, patient-physician engagement, concerns about financial aspects of treatment and awareness of new medications in development** may be significant factors in predicting patient interest in clinical trials.

Unlike the 2012 meta-analysis, Health Union survey data also provided a profile of patients who had previously participated in clinical trials (generally a clinical trial for their specific health condition) and the significant factors that may predict not just interest, but actual participation in clinical research. These findings have important implications for biopharmaceutical companies and clinical research organizations to optimize their patient recruitment programs and engage patients who are more likely to participate in clinical studies (if eligible).

METHODOLOGY

Health Union created a dataset from six proprietary *[Condition] In America* surveys conducted across 2014 and 2015 among patients with symptomatic chronic conditions, including **chronic obstructive pulmonary disease (COPD), migraine, multiple sclerosis, rheumatoid arthritis and hepatitis C**. Questions regarding treatment journey, as well as clinical trial interest and participation were included in the dataset. Steps were taken to consolidate and unify data across the various surveys and conditions to facilitate analysis. Data analysis used a $p<0.05$ for determining statistical significance.

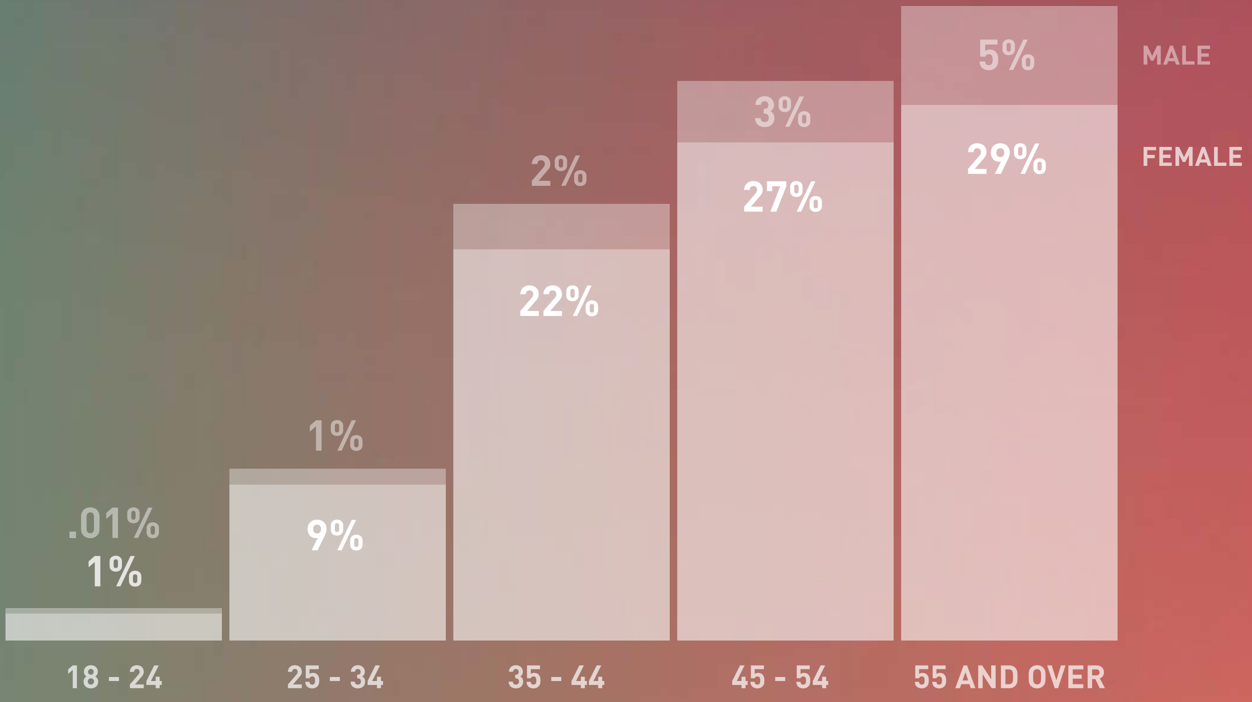
Where applicable, satisfaction ratings on a 5-point scale were collapsed into levels of satisfaction for comparison purposes. Those indicating the top-2 box satisfaction ratings were thought to be “satisfied” and those indicating neutral and the bottom-2 satisfaction ratings were considered “not satisfied.”

It is important to note that Health Union *[Condition] In America* patient surveys were self-reported questionnaires and were **not specifically focused on clinical trials**, nor was this data collected within the context of actual clinical trial recruitment, screening or enrollment. During actual clinical study enrollment, there are other factors that influence patients’ interest and participation, such as travel distances to study locations, potential reimbursement, study facility and/or study physician reputation, as well as the specific requirements of the study protocol and procedures.

In total, **data from 21,627 respondents were included in this analysis**. All respondents were residents of the U.S. (99%) or U.S. citizens living abroad (1%) recruited from Health Union online patient communities, including email subscribers, website visitors and Facebook fans, as well as other social media users. 89% of respondents were female and 11% were male, with most being over the age of 45.

MOST RESPONDENTS WERE WOMEN, OVER AGE 45

Distribution of respondents by age and gender (N = 21,627)



RESPONDENTS HAD BEEN DIAGNOSED WITH SYMPTOMATIC CHRONIC CONDITIONS

Respondents' primary health condition (N = 21,627)

COPD	1,009	5%
HEPATITIS C	403	2%
MIGRAINE	5,723	26%
MULTIPLE SCLEROSIS	10,931	51%
RHEUMATOID ARTHRITIS	3,561	16%

Respondents reported they had been diagnosed with one of five specific health conditions. 87% of respondents were seeing a healthcare professional (HCP) for that health condition at the time of the survey.

RESPONDENTS AT A GLANCE

TREATMENT EXPERIENCE

- **51%** of respondents reported being **satisfied with their current treatment plan**, which may or may not have included taking a prescription medication *(N = 21,141)*
- Medication cost played a role in treatment experience, with **35% of respondents having avoided a medication due to cost** at some point in their journey *(N = 21,462)*
- **21% were aware of new treatments in development** to treat their health condition *(N = 21,627)*

SOCIAL-ECONOMIC PROFILE

- **40%** of respondents were **currently employed** *(N = 15,904)*
  Among those who were unemployed, 49% were on disability, 17% were retired and 10% were Homemakers (N = 9,546)
- **62%** of respondents were **commercially insured** and **31%** had **subsidized health insurance**, most of which was Medicare/Medicaid *(N = 21,161)*

CLINICAL TRIAL INTEREST & PARTICIPATION

Across all health conditions, a majority of respondents (69%) were interested in participating in clinical trials for their condition *(N = 21,627)*. Most commonly, patients' interests were motivated by the potential to benefit from the treatment being studied (89%), along with the potential for others to benefit as well.

PATIENTS INTERESTED IN CLINICAL TRIALS HOPE TO BENEFIT FROM TREATMENT(S) BEING STUDIED

Motivations for participation in a clinical trial (N = 11,526)

89%	I might benefit from the treatment(s) being studied
71%	Others will benefit from the study of the treatment(s) being studied
23%	I feel like the doctors would pay more attention to helping me treat my condition
22%	I have already tried everything and have no other options
18%	It's the only way for me to get access to the treatment(s) being tested
6%	Other

Among those not interested in clinical trials, the main barrier was fear of the unknown / untested treatments (55%) *(N = 5,097)*.

Among survey respondents interested in clinical research, **12% had previously participated in a clinical trial** *(N = 16,623)*, most of which were related to their primary health condition (71%) *(N = 1,924)*. 82% of those clinical trial participants completed their trial *(N = 1,923)*; the most common reasons for exiting the trial early were side effects or tolerability of the study treatment.

PATIENTS WHO HAD PREVIOUSLY PARTICIPATED IN CLINICAL TRIALS WERE SIGNIFICANTLY MORE LIKELY TO BE INTERESTED IN FUTURE CLINICAL RESEARCH STUDIES

Those who had previously participated in clinical trials were significantly more likely to be interested in future clinical trial participation (77%) than their counterparts who had never participated (66%) *(N = 16,623)*. Patients who had previously participated in clinical trials but were no longer interested cited reasons such as fear of unknown / untested treatments (34%) and that their health condition was currently well controlled (31%).

This analysis compared a number of different variables among patients interested in clinical trials and those who were not, and again examined those same variables among respondents who had participated in a clinical trial and those who had not.

The findings revealed significant differences that may be used to predict interest and participation in clinical trials based on:

AGE & GENDER

HEALTH CONDITION

TREATMENT EXPERIENCES

PATIENT-PHYSICIAN ENGAGEMENT

SOCIAL-ECONOMIC STATUS

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AGE AND GENDER

Gender played a significant role in respondents' level of interest in clinical trials, with males being significantly more interested than females (73% as compared to 69%) *(N = 21,627)*. Linear regression confirmed gender had a significant effect on interest ($R^2 = 0.001$). **Similarly, males were significantly more likely to have participated in clinical trials than females** (13% to 11%) *(N =16,623)*.

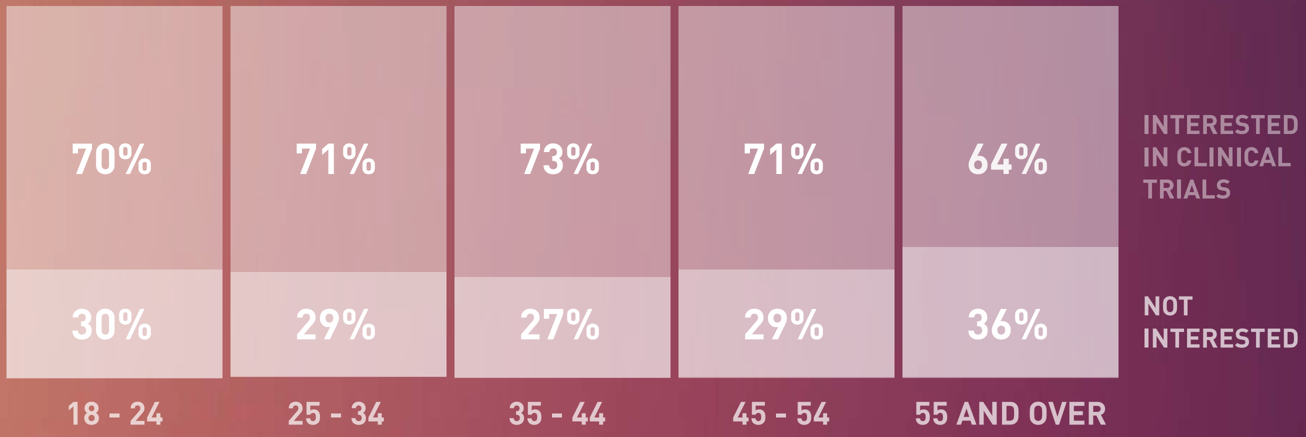
MEN ARE MORE LIKELY TO BE INTERESTED AND TO PARTICIPATE IN CLINICAL TRIALS

Why don't more women participate? While these data don't provide insight into reasons behind this gender divide, the hypothesis (based on extensive experience with these patient communities) is that women are often managing children, household responsibilities and careers - in addition to a chronic health condition. They may lack a support system that would enable them to commit to a research study, as well as have more concerns about the potential impact of new treatments on fertility and childbearing. Certainly more research and insights in this area are needed.

Age was also a significant factor in determining interest, with **those aged 55 and over significantly less interested in clinical trials** than their younger cohorts. Regression analysis supported the negative impact of age ($R^2 = 0.004$).

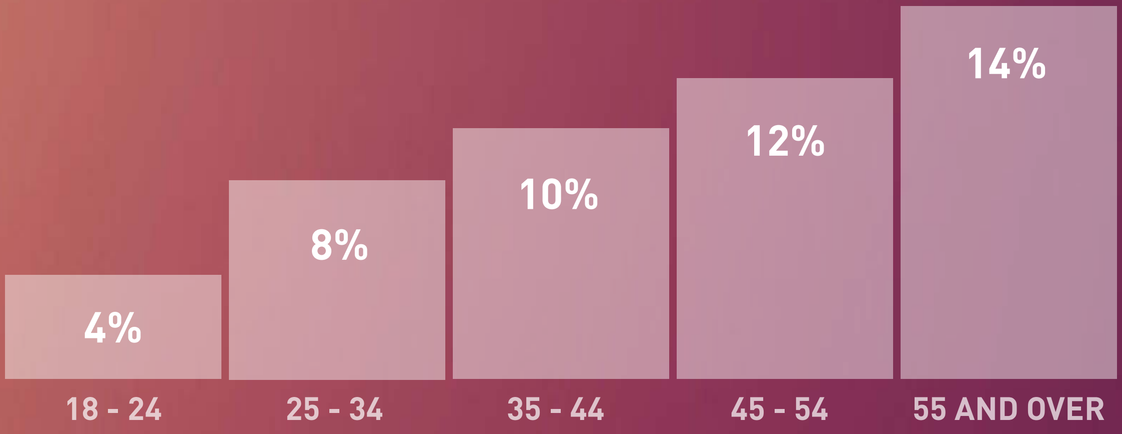
YOUNGER PEOPLE SHOW MORE INTEREST IN CLINICAL TRIALS

Clinical trial interest by age (N = 21,627)



EXPERIENCE INCREASED WITH AGE

Proportion of respondents that have previously participated in a clinical trial (N = 16,623)



While most respondents who had participated in clinical trials were over the age of 45, this may be related to the fact that these individuals have had more years (ie, opportunity) to participate.

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HEALTH CONDITION

Among the patients with symptomatic chronic conditions in these surveys, those with migraine and hepatitis C were significantly more likely to be interested in participating in clinical trials for their conditions; whereas Hepatitis C and MS patients were significantly more likely to have participated in a previous clinical trial. Clinical trial completion varied across health conditions, with patients suffering Hepatitis C having a significantly higher dropout rate.

> *Patients with Hepatitis C were most likely to be interested and to participate in clinical trials*

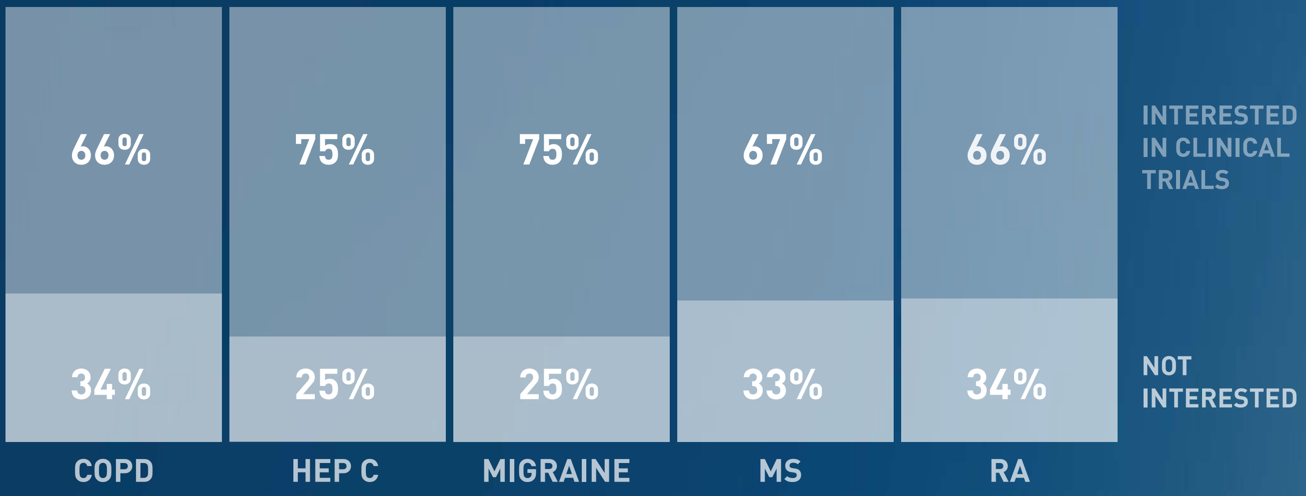
What do Hepatitis C and MS have in common? Why are these patients more likely to participate in clinical trials? Health Union's experience suggests this effect may be related to three things:

- Hepatitis C and MS are progressive, debilitating conditions that are also potentially life-threatening (high perceived severity)
- Current treatments for Hepatitis C* and MS are not always effective, and many patients experience problems tolerating side effects (low satisfaction)
- Industry has invested heavily in developing new compounds to treat these conditions – in other words, study sponsors are recruiting lots of patients with these conditions for clinical trials (increased opportunity)

**Until recently, treatments for Hepatitis C achieved sustained virologic response (SVR) for less than 50% of patients*

MIGRAINE, HEP C PATIENTS MORE INTERESTED IN CLINICAL RESEARCH

Clinical trial interest by health condition (N = 21,627)



HEP C, MS PATIENTS MORE LIKELY TO PARTICIPATE

Participation in clinical trial by health condition (N = 21,627)

	CLINICAL TRIAL PARTICIPATION	PARTICIPATION IN TRIAL FOR HEALTH CONDITION
COPD	8%	4%
HEPATITIS C	14%	10%
MIGRAINE	9%	5%
MULTIPLE SCLEROSIS	16%	14%
RHEUMATOID ARTHRITIS	9%	6%

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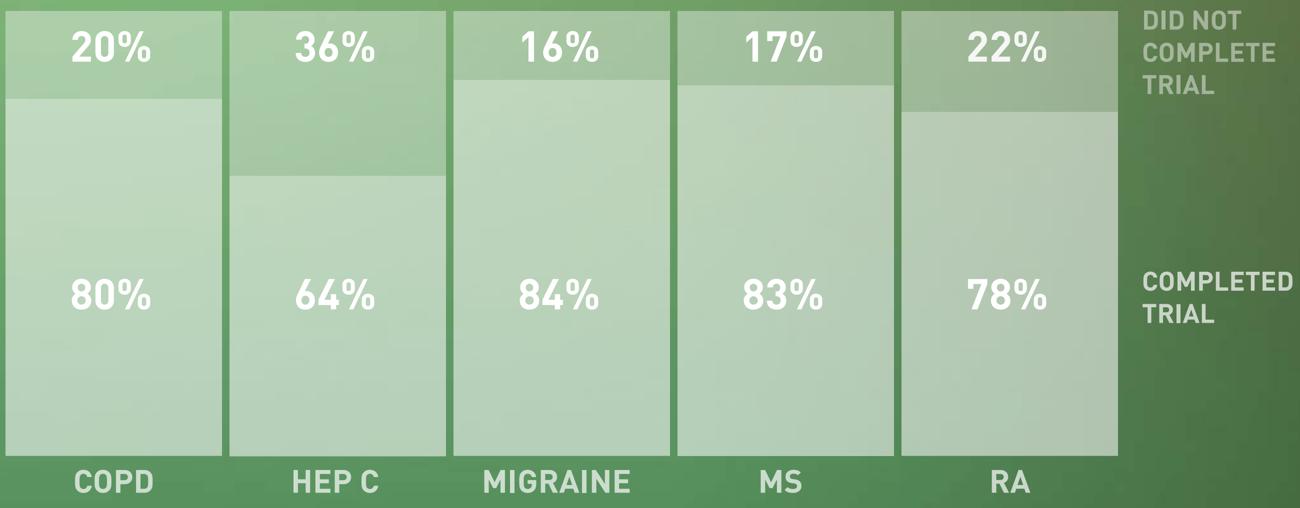
PATIENTS WITH HEP C LESS LIKELY TO COMPLETE TRIALS

Clinical trial completion by health condition (N = 1,923)



TREATMENT EXPERIENCE

Similar to the 2012 meta-analysis in *Applied Clinical Trials,* regression analysis of this data found **a significant effect between patients' satisfaction with current treatment plan and interest in clinical trials**, with lower satisfaction associated with higher interest ($R^2 = 0.023$). The level of interest in clinical trials was overwhelmingly different between satisfied patients (62%) and dissatisfied patients (76%) *(N = 21,141)*. And, this finding supports the earlier discussion of patient motivations for interest in clinical trials – that they might benefit from the treatment(s) being studied - as well as a lack of interest in clinical research among previous clinical trial participants who indicate their condition is well-controlled.

Interestingly, there were a significantly higher proportion of individuals satisfied with their current treatment plan among those who had participated in clinical trials (54% compared to 47% of non-participants) *(N = 16,137)*.

Why would dissatisfaction be related to interest in clinical trials while satisfaction is related to actual participation? Although these data do not indicate causation, the hypothesis is that those who participate in a clinical trial have access to better healthcare (in general) and hence, are more satisfied with their treatment. It is also possible that patients who participated in a clinical trial are more satisfied with their current treatment because they participated in a trial. Previous research has shown patients who participate in clinical trials are highly satisfied with medical aspects of treatment within a clinical trial, including perceived personal benefit or improvement in health.[3]

> *As patients learn more about new treatments and how those treatments are developed, they become more interested and are more likely to participate in the process via clinical trials*

Awareness of new medications in development for their health condition also went hand-in-hand with significantly higher interest in clinical trials ($R^2 = 0.002$). Respondents that were aware reported significantly more interest (73%)

than those that were not (68%) *(N = 21,627)*. Awareness of new medications in the pipeline was also a differentiating factor for clinical trial participation – 23% of those who had previously participated in a clinical trial were aware; significantly more than those who had not (19%) *(N = 16,623)*.

It is important to note that financial concerns about treatment are factors influencing both interest and participation in clinical research. Patients reporting they have avoided taking medication due to cost were significantly more likely to be interested in clinical trials *(regression yielded* $R^2 = 0.010$*)*, with 75% of those that had avoided medication due to cost indicating interest (compared to 66% among those who had not) *(N = 21,462)*. This association continued for respondents who had participated in clinical trials, with 38% of clinical trial participants reporting avoiding a medicine due to cost (compared to 34% among non-participants) *(N = 16,458)*.

PATIENT-PHYSICIAN ENGAGEMENT

As expected, whether or not respondents currently see an HCP for their condition played a role in their interest surrounding clinical trials, with regression finding a significant effect *(*$R^2 = 0.001$*)*. **Those seeing an HCP were significantly more interested in clinical research** (70%), compared those not seeing an HCP (66%) *(N = 21,627)*. And this trend continued among individuals who had participated in clinical trials; 90% of previous trial participants reported they currently see an HCP (compared to 86% of respondents who had not participated in a trial) *($N = 16,623$)*.

76% of respondents that were dissatisfied with their current HCP were interested in clinical trials

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However, there were a significantly higher proportion of individuals interested in clinical trials among those not satisfied with their current HCP (76% as compared to 67%) *($N = 18,899$)*, and regression analysis identified the negative relationship between HCP satisfaction and clinical trial interest (dissatisfaction resulted in more interest) *($R^2 = 0.007$)*.

These findings, considered together with the previous discussion of respondents' dissatisfaction with their current treatment plan, seem to indicate that **less satisfied patients are more willing to consider clinical trials** as a care option.

Also similar to the treatment experience findings, significantly **more clinical trial participants were satisfied with their current HCP** (78% compared to 73%) *($N = 14,313$)*. Again, this data does not show causation; however, the hypothesis is that respondents were more satisfied with their current HCP because they participated in a trial. Most patients who participate in clinical trials are satisfied with the experience, particularly in their interactions with the study clinician;[4] patients' satisfaction with their clinical trial experience may carry over to their current HCP that recommended the trial as a treatment option or continued their care after the trial.

Both dissatisfaction with current HCP and dissatisfaction with current treatment plan were each significantly connected to greater interest in clinical trials, while previous participation in clinical trials was related to greater satisfaction in both of those areas.

SOCIAL-ECONOMIC STATUS

This analysis found no notable difference in clinical trial interest between those that were employed and those that were not (68% to 67%, regression analysis was insignificant). However, **unemployed respondents were significantly more likely to have participated in clinical trials** than those that were employed (14% to 11%) *(N =10,900)*. Among those that reported previous clinical trial participation, 64% were unemployed at the time of the survey *(N = 1,392)*. Unemployed individuals may not be working due to their condition (even if not on disability) and may be more likely to seek out new/

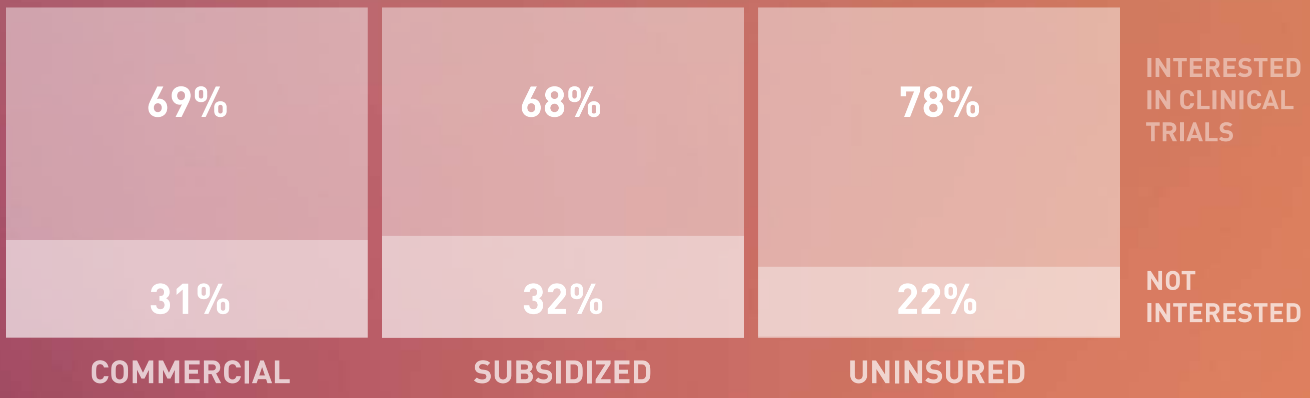
different treatments. Additionally, those who are unemployed may have more time to participate in a clinical trial or be attracted by the potential to receive "free treatment" in a clinical study.

Unemployment and subsidized health insurance were more common among clinical trial participants

Similar to the relationships with employment status, **those respondents who had subsidized health insurance were significantly more likely to have participated in a clinical trial** (15%) as compared to their commercially insured (10%) and uninsured (11%) counterparts.

UNINSURED PATIENTS ARE MORE INTERESTED IN CLINICAL TRIALS

Clinical trial interest by health insurance status (N = 21,161)



Respondents that were uninsured (at the time of the survey) were **significantly more likely to be interested in participating in clinical trials** than those that were commercially insured or had subsidized insurance *(regression yielded $R^2 = 0.001$).*

These findings continue a theme of financial concerns about healthcare – avoiding medication due to cost, lack of health insurance – that may drive interest in clinical trials among patients with chronic disease.

CONCLUSIONS & IMPLICATIONS

Patient-centric trial design continues to gain traction as a key element for success in clinical development initiatives. **Relevant insights and deep understanding of patients' experiences, motivations and barriers are important to provide the foundation for patient-centricity**. This meta-analysis offers a unique window into drivers of patients' interest and participation in clinical trials that study sponsors and clinical research organizations can use to optimize recruitment programs and engage those patients who are most likely to participate (if eligible).

ADDRESS UNCONSCIOUS MOTIVATIONS (AND BARRIERS)

These findings demonstrate that while patients with chronic, symptomatic conditions may self-report motivations of personal benefit and altruism as reasons for their interests in clinical trials, there are other significant factors influencing that interest – most notably dissatisfaction with current treatment plans or healthcare professionals and concerns about the cost of treatment. Patient recruitment materials should seek to address these factors (directly and indirectly) through key messages, imagery and FAQs. Alternately, considering these factors when designing outreach and recruitment strategies may help address practical barriers inhibiting patients from acting on their interest in clinical research. For example, patients who are dissatisfied with their HCP may be more interested in clinical trials but less likely to discuss this with their physician – making it more difficult for these patients to refer into trials through traditional HCP-focused patient identification methods. Offering easy pathways for patients to self-refer may encourage dissatisfied patients to act on their interest in clinical trials.

CONNECT WITH ONLINE PATIENT COMMUNITIES

Supplemental recruitment programs – those that pre-qualify community-based patients and refer them to clinical trial sites for study screening[5] – are becoming more and more important as the competition for patients willing to participate in clinical trials increases. Study sponsors and CROs often foster partnerships with patient groups and advocates to help with community outreach for trials; however, online patient communities remain under-utilized partners for patient screening and recruitment. More than simply platforms for web advertising, patient communities offer unique opportunities to connect with active, engaged patients who are interested to learn about clinical research, to share their opinions and experiences, and to screen to participate in trials. These communities are often havens for the patients that this analysis demonstrated to be most interested and most likely to participate in research – patients that are dissatisfied with current options, that are suffering conditions with high perceived severity, and that are aware of (and seeking out) new treatments in development. Online patient communities may also provide researchers with avenues to engage more women and special patient populations in clinical studies, as well as offer insight about patient preferences, needs and values that can inform all phases of clinical development – from study planning and feasibility to screening and recruitment.

EXPAND AND ENHANCE AWARENESS (AND EDUCATION) OF CLINICAL TRIALS

Awareness of new medications in development was an important factor related to both interest and participation in clinical research, indicating that as patients learn more about new treatments and how those treatments are developed, they become more interested and more likely to participate in the process via clinical trials. Moreover, patients often cite a lack of awareness and understanding of clinical trials as key barriers to participation, along with concerns about unknown/untested treatments and receiving placebo treatments.[6] Together, these data present a strong case for ongoing investment in patient education efforts about how clinical trials work, patient protections and safety, as well as patient rights and responsibilities if/when they enroll.

[1] CliniPace Worldwide. (2014) *Infographic – Trends in Clinical Trial Site Selection and Patient Recruitment*. Accessed from: https://www.clinipace.com/wp-content/uploads/2014/12/final_sitepatienttrends_infographic.pdf

[2] Burgess, A., Nixon, M., and Cascade, E. (2012) Drivers of Patient Interest In Referral. *Applied Clinical Trials,* Volume 21. Issue 7.

[3] Verheggen, F.W., Nieman, F.H., Reerink, E., and Kok, G.J. (1998) Patient Satisfaction With Clinical Trial Participation. *International Journal for Quality in Health Care.* Volume 10. Issue 4. pp. 319-330. Accessed from: http://intqhc.oxfordjournals.org/content/intqhc/10/4/319.full.pdf

[4] *Ibid.*

[5] Burgess, A., Nixon, M., and Cascade, E. (2012) Drivers of Patient Interest In Referral. *Applied Clinical Trials,* Volume 21. Issue 7.

[6] Health Union, LLC. (2015) Clinical Trial Viewpoints Patient Survey. Data on file.