Supplementary Material: A validated model to predict placebo response using patients' discourse

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Table 1. Demographic, baseline pain, and pain duration data for study 1 and study 2 (mean ± SD)

	Study 1		Study 2			
	Placebo (N = 42)		Placebo (N = 20)		Naproxen (N = 22)	
	Resp. N = 23	Non-Resp N = 19	Resp. N = 8	Non-Resp. N = 12	Resp. N = 15	Non-Resp. N = 7
Age (years)	46.9 ± 11.4	45.4 ± 14.7	56.7 ± 9.1	57.7 ± 11.9	51.3 ± 13.7	62.7 ± 4.9
Sex (M/F)	14/9	12/7	2/6	5/7	10/5	5/2
Pain duration (weeks)	204 ± 215	271 ± 469	306 ± 382	414 ± 680	439 ± 450	345 ± 221
Pain at baseline (NRS)	5.5 ± 2.5	5.8 ± 2.5	5.1 ±1.1	5.9 ± 1.3	6.4 ± 1.5	6.4 ± 1.1

Supplementary Figures

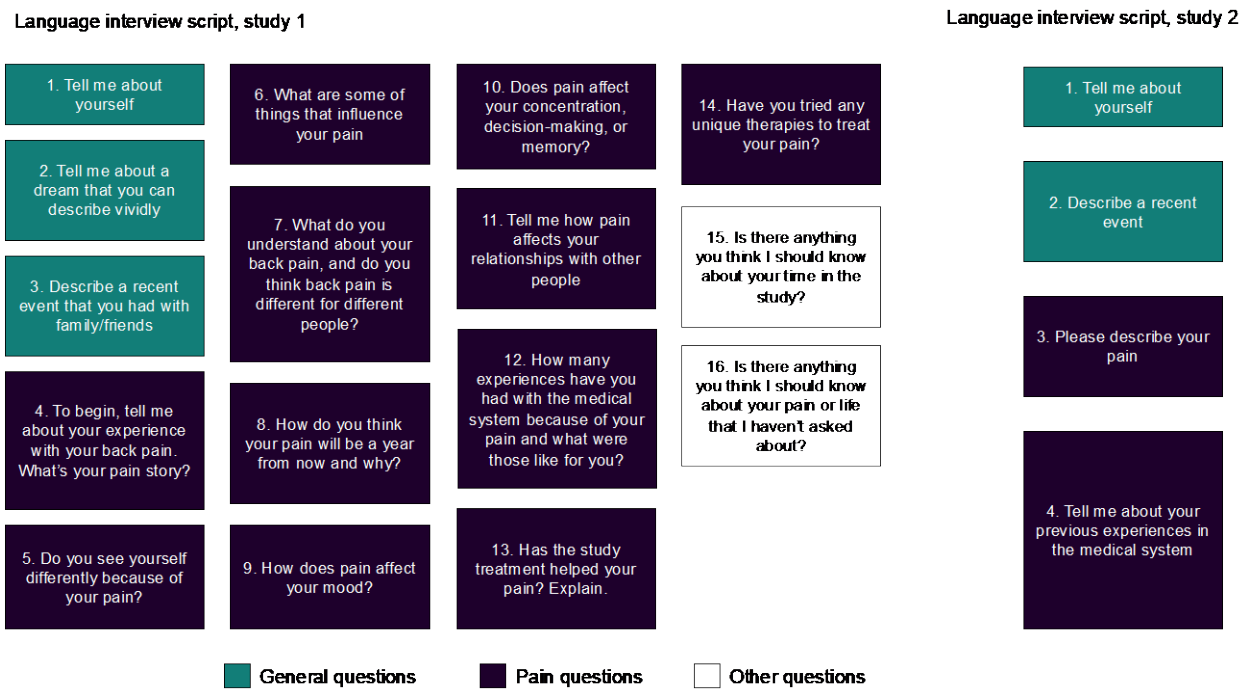

Fig S1. Language interview script for study 1 and study 2. Study 1 interview was composed of 16 questions, 3 of which were general (green), 11 were pain-related questions (blue), and 2 general questions (white). Additional information regarding the interview, experimental set-up, and follow-up questions can be seen in [1]. Study 2 was composed of four questions, two of which were general and two pain-related questions.

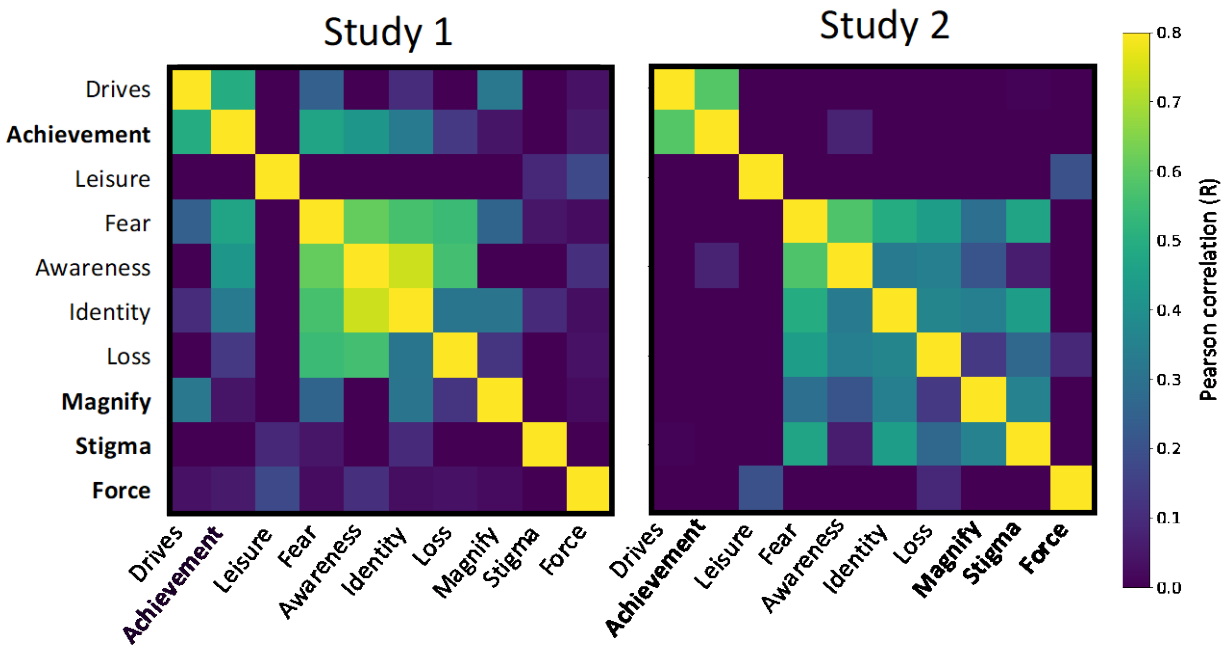

Fig S2. Correlation matrix between the 11 pre-selected features. Covariance matrix between the 11 features pre-selected based on a nested cross-validation published previously[1]. There is evidence for collinearity across features although the structure of the data remains relatively similar across studies. Stepwise regression selected *Achievement*, *Magnify*, *Stigma*, and *Force*, highlighted in bold. Stigma and Force are orthogonal to the remaining features. Magnify is moderately associated with Fear, Awareness, Identity and Loss, and hence it's a good representation of the underlying semantic topic. Achievement is strongly correlated with Drives, again representing another semantic dimension. Leisure was not correlated with any feature for both studies.

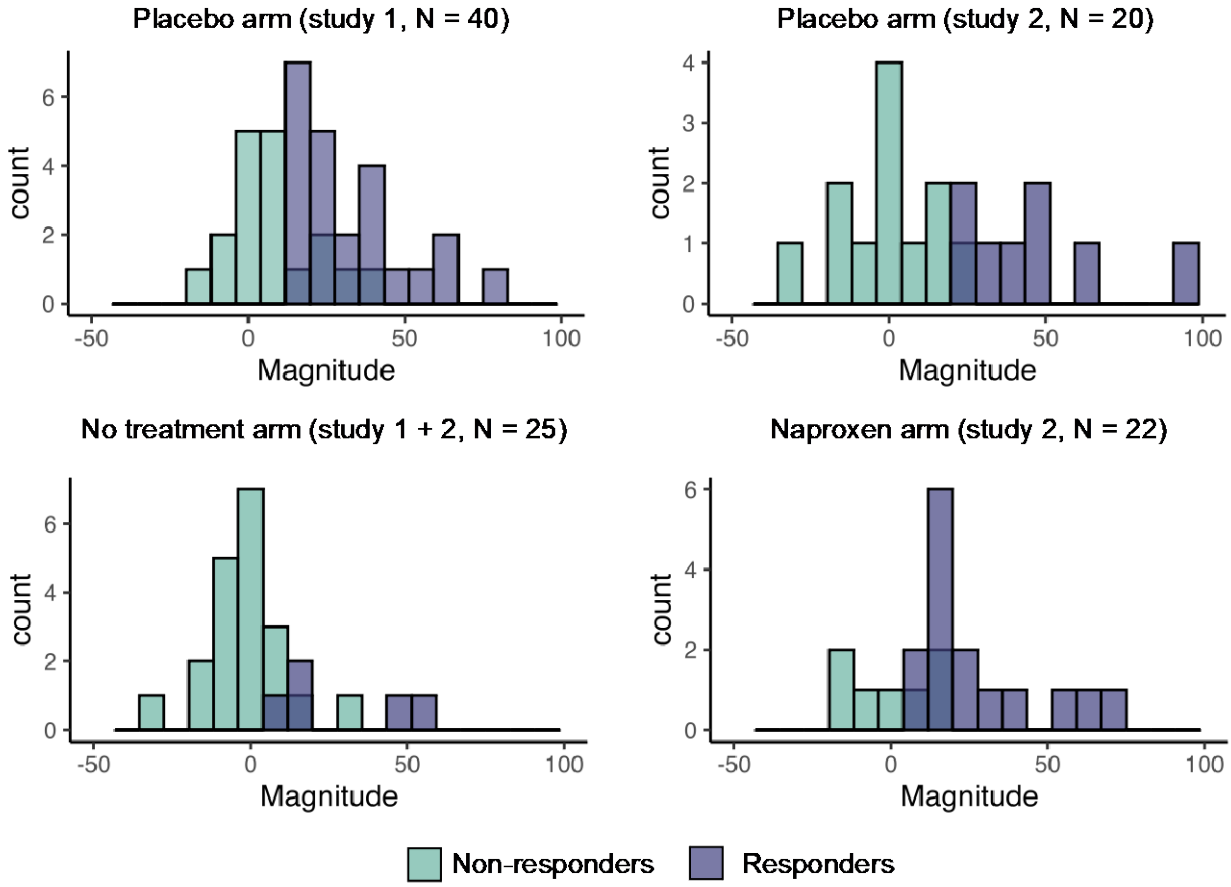

Fig. S3. Distribution overlap between magnitude of analgesia and outcome. Histograms quantifying the magnitude of analgesia for placebo study 1 and 2 (upper left, upper right, respectively), no-treatment arm (bottom left) and naproxen arm (bottom right), color-coded by whether their pain was significantly lower at the study treatment phase through a permutation analyses (see Methods). No-treatment arm shows largely unchanged pain ratings; placebo arms show two clear distributions, again highlighting the idea that some people respond to placebos and others do not. Naproxen arm shows overall significant changes in pain for a large majority of patients.

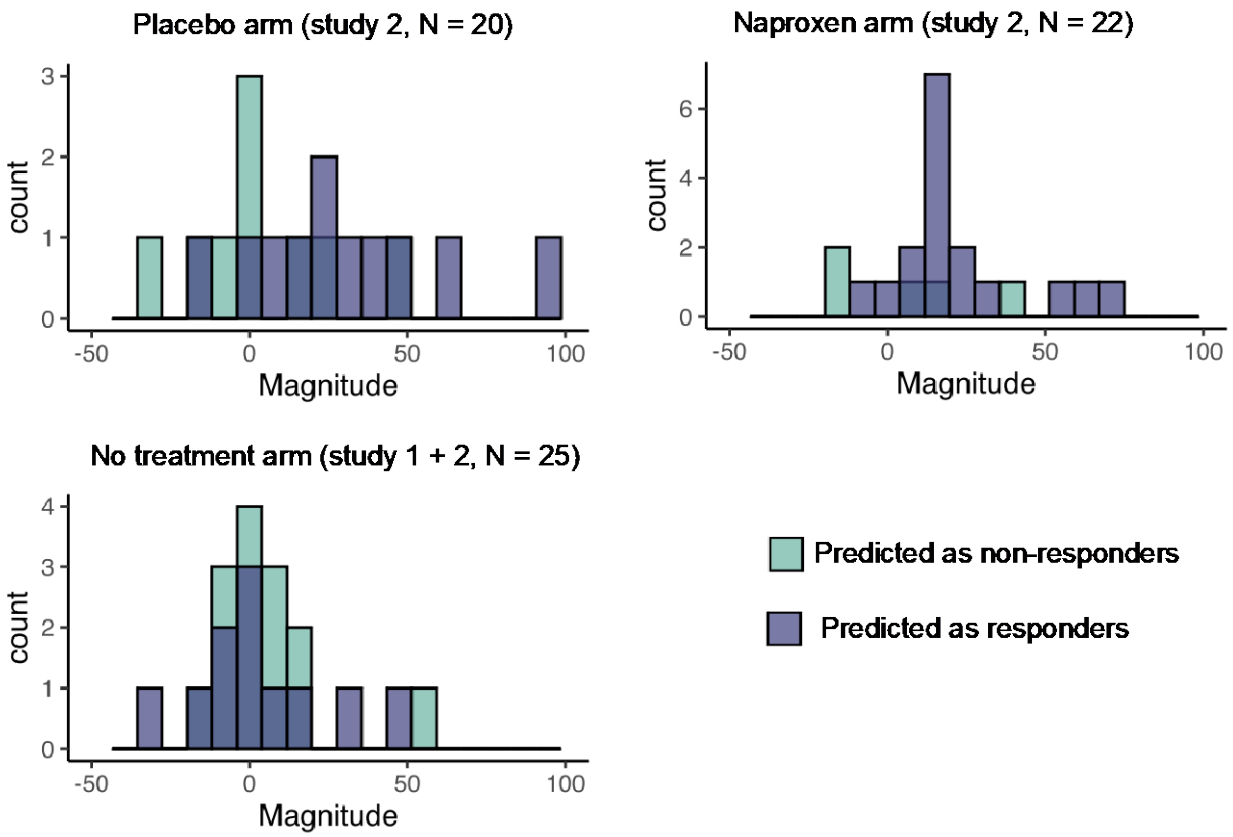

Fig. S4. Distribution overlap between magnitude of analgesia and model prediction.

Histograms quantifying the magnitude of analgesia for the placebo and drug treatment arm for the validation study (study 2), color-coded by whether they were classified as placebo responder or not based on language parameters derived from study 1. While for the placebo arm (left panel) the placebo responders show larger magnitudes of analgesia, this was not observed for the drug (naproxen) arm. On the bottom panel, the same histogram for the no-treatment arm (study 1 + study 2) shows that regardless of model predictions, the magnitudes of analgesia are similar.

[1] Berger SE, Branco P, Vachon-Presseau E, Abdullah TB, Cecchi G, Apkarian AV. Quantitative language features identify placebo responders in chronic back pain. PAIN 2021;162:1692–1704.