

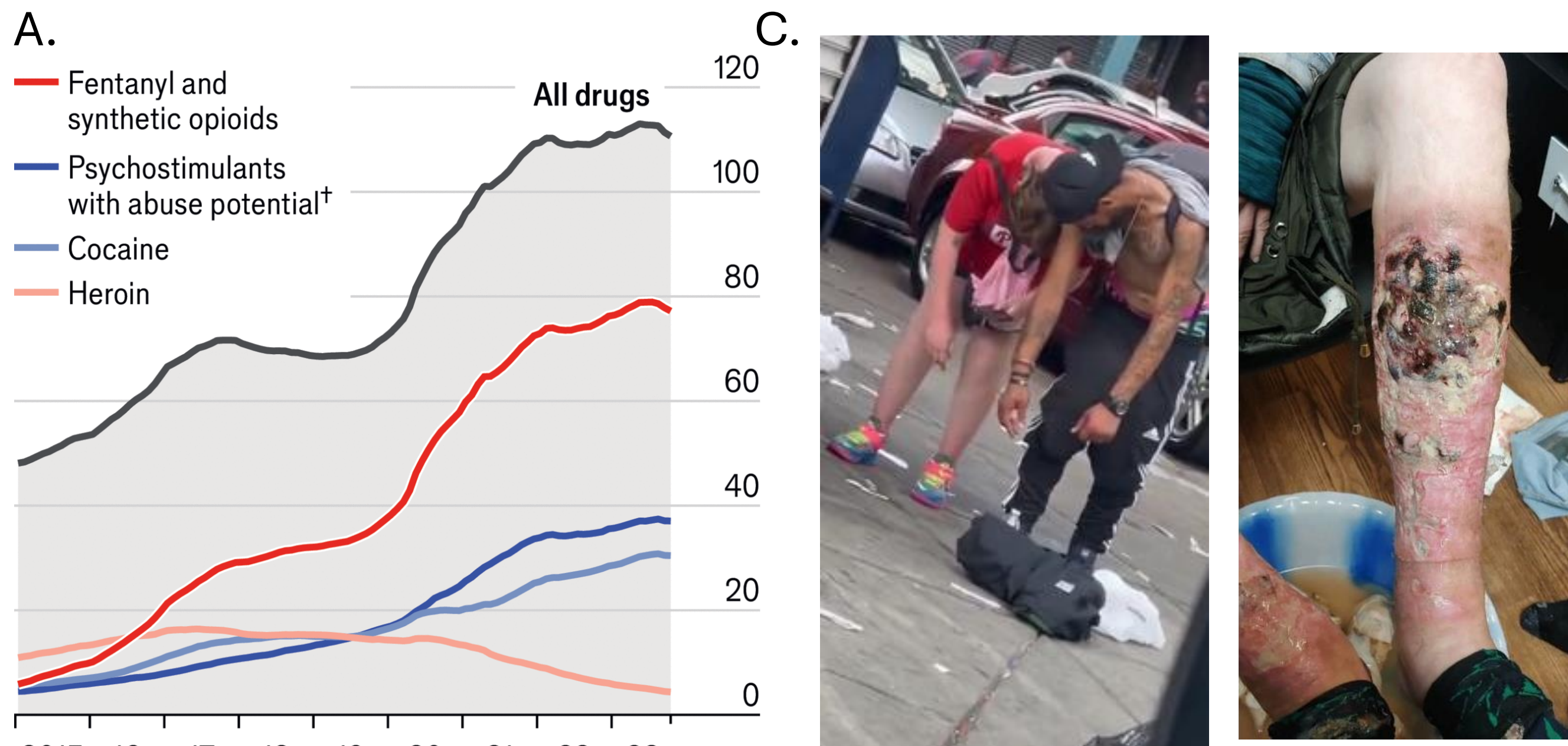
HUGS NOT DRUGS



If the drugs don't kill, the bugs will: insight to the opioid crisis

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INTRODUCTION



B. Drug Enforcement Administration Alert, 2022. “Xylazine is making the deadliest drug threat our country has ever faced, fentanyl, even deadlier.”

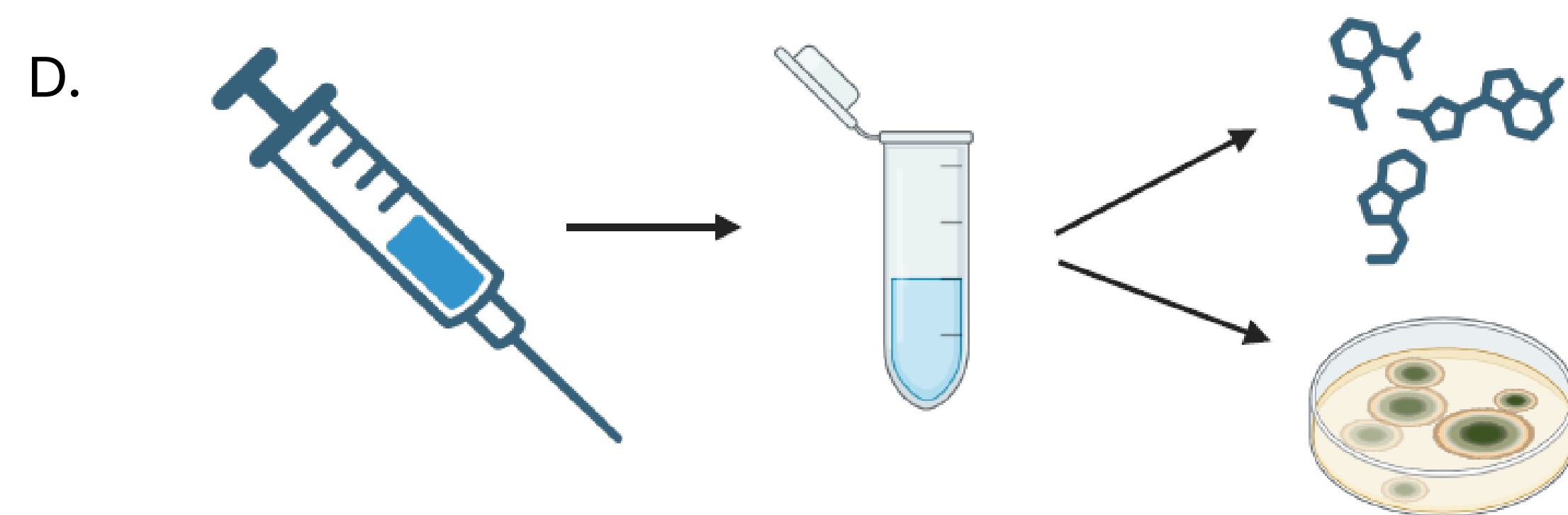


Figure 1. The opioid crisis. (A) U.S. drug overdoses from 2015-2023 as reported by the CDC. (B) In 2022, the DEA released an alert about xylazine being present in illicit drugs. (C) The effects of xylazine on people who inject drugs. (D) Our research plan.

RESULTS

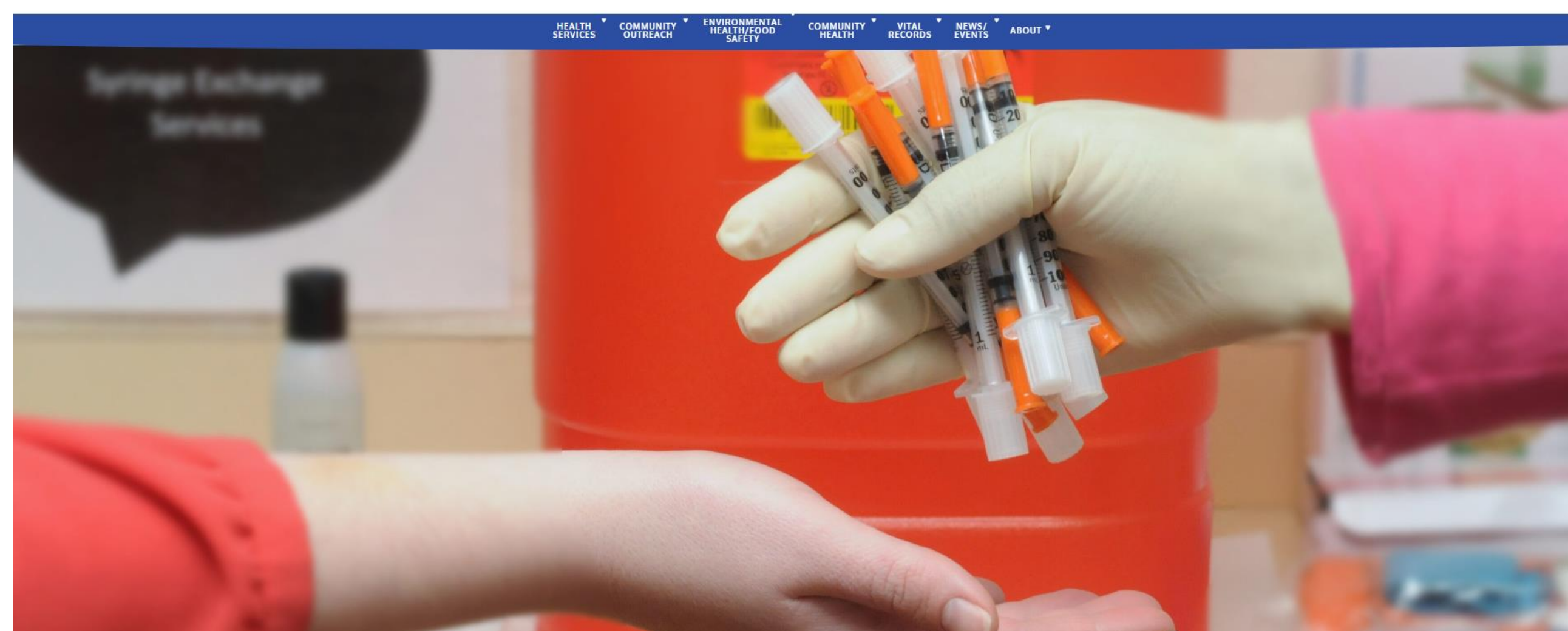


Table 1. Data from Northwest Ohio Syringe Services.

	2023	2022	2021	2020	2019	2018
New participants	493	306	267	168	152	162
Returning visits	2,347	1,949	1,139	503	572	550
Syringes in	30,645	32,906	29,768	47,916	23,003	1,889
Syringes out	245,832	255,905	185,918	116,764	49,105	3,744
Fentanyl strips	9,627	4,894	3,917	2,643	2,084	882
Xylazine strips	2,930	-	-	-	-	-



Figure 2. Used needles obtained from the Northwest Ohio Syringe Services program. (A) Different containers filled with used needles. (B) All needles are identical and 3 cc in size.

Table 2. Results of substances and parts contained in 50 analyzed drug-used syringes.

Substance Descriptives	μ substances in a syringe	Range of substances in a syringe
	7.800	1-15
Substance	In number of syringes	Parts Analysis
		μ Range
Fentanyl	98%	0.983 0.150 – 1.000
Cocaine	90%	0.754 0.020 – 8.810
Xylazine	86%	5.577 0.010 – 26.100
Acetyl Fentanyl	34%	0.013 0.010 – 0.030
Norfentanyl	32%	0.017 0.010 – 0.040
Caffeine	28%	0.126 0.010 – 0.330
Morphine	20%	0.133 0.010 – 0.510
Lidocaine	18%	0.068 0.010 – 0.230
Tramadol	16%	0.083 0.010 – 0.430
Acetaminophen	12%	0.017 0.010 – 0.020
Fluorofentanyl	6%	0.073 0.040 – 0.120
Medetomidine	6%	0.010 0.010 – 0.010
Acetylcodeine	4%	0.030 0.020 – 0.040
Heroin	4%	0.015 0.010 – 0.020

Drugs (Table 2) and bugs (Figure 3) identified in used syringes. (A) Fungi and (B) bacteria isolated from a syringe. (C) A 16S/18S phylogenetic tree of 150 microbes isolated from syringes. The 131 bacterial and 49 fungal strains were shaded blue and red, respectively. (D) Multiple strains of *Candida parapsilosis* were identified.

Table 2. World Health Organization fungal priority list to guide research, drug development, and public health action.

Critical group	High group	Medium group
<i>Cryptococcus neoformans</i>	<i>Nakaseomyces glabrata</i> (<i>Candida glabrata</i>)	<i>Scedosporium</i> spp.
<i>Candida auris</i>	<i>Histoplasma</i> spp.	<i>Lomentospora prolificans</i>
<i>Aspergillus fumigatus</i>	Eumycetozoa causative agents	<i>Coccidioides</i> spp.
<i>Candida albicans</i>	Mucorales	<i>Pichia kudriavzevii</i> (<i>Candida krusei</i>)
	<i>Fusarium</i> spp.	<i>Cryptococcus gattii</i>
	<i>Candida tropicalis</i>	<i>Talaromyces marneffei</i>
	<i>Candida parapsilosis</i>	<i>Pneumocystis jirovecii</i>
		<i>Paracoccidioides</i> spp.

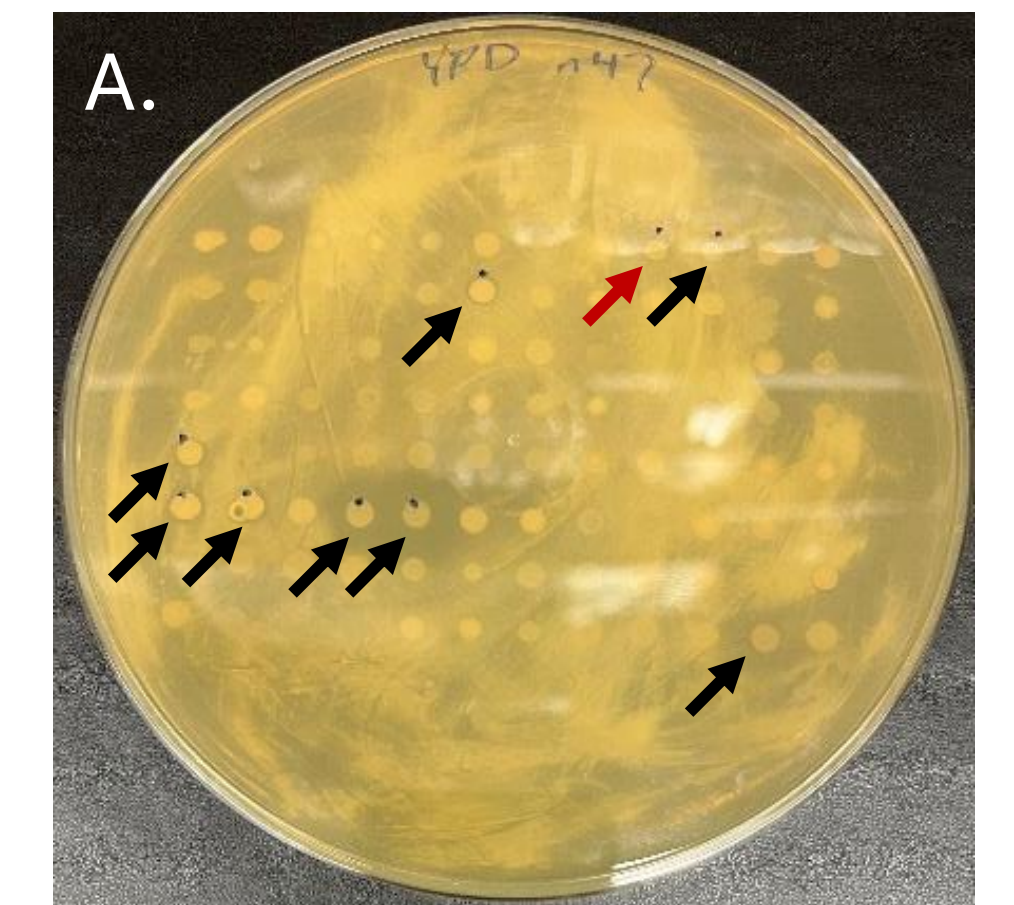
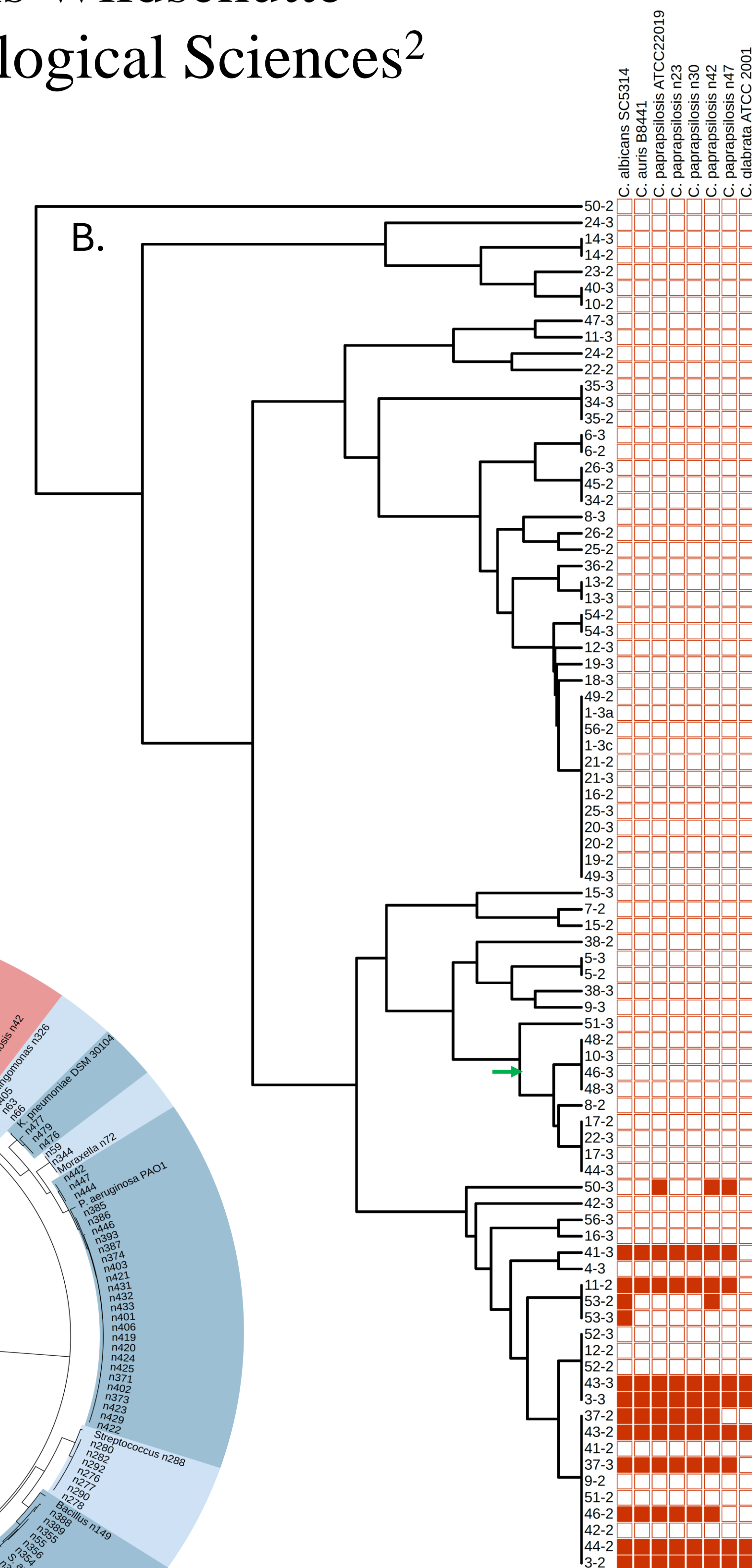


Figure 4. Antagonistic activity of *Pseudomonas* strains against *Candida* species. (A) Ninety-six environmental bacteria were stamped onto the spread plated *C. parapsilosis* n47 strain. A zone of clearing around a bacterial colony indicated inhibition (arrows). The red arrow indicates activity from *Pseudomonas* strain 3-3. (B) A 16S rRNA phylogenetic tree of the 96 *Pseudomonas* strains. *Pseudomonas* strains were depicted on the y-axis and *Candida* across the top x-axis. Red squares indicate specific inhibition against *Candida*.

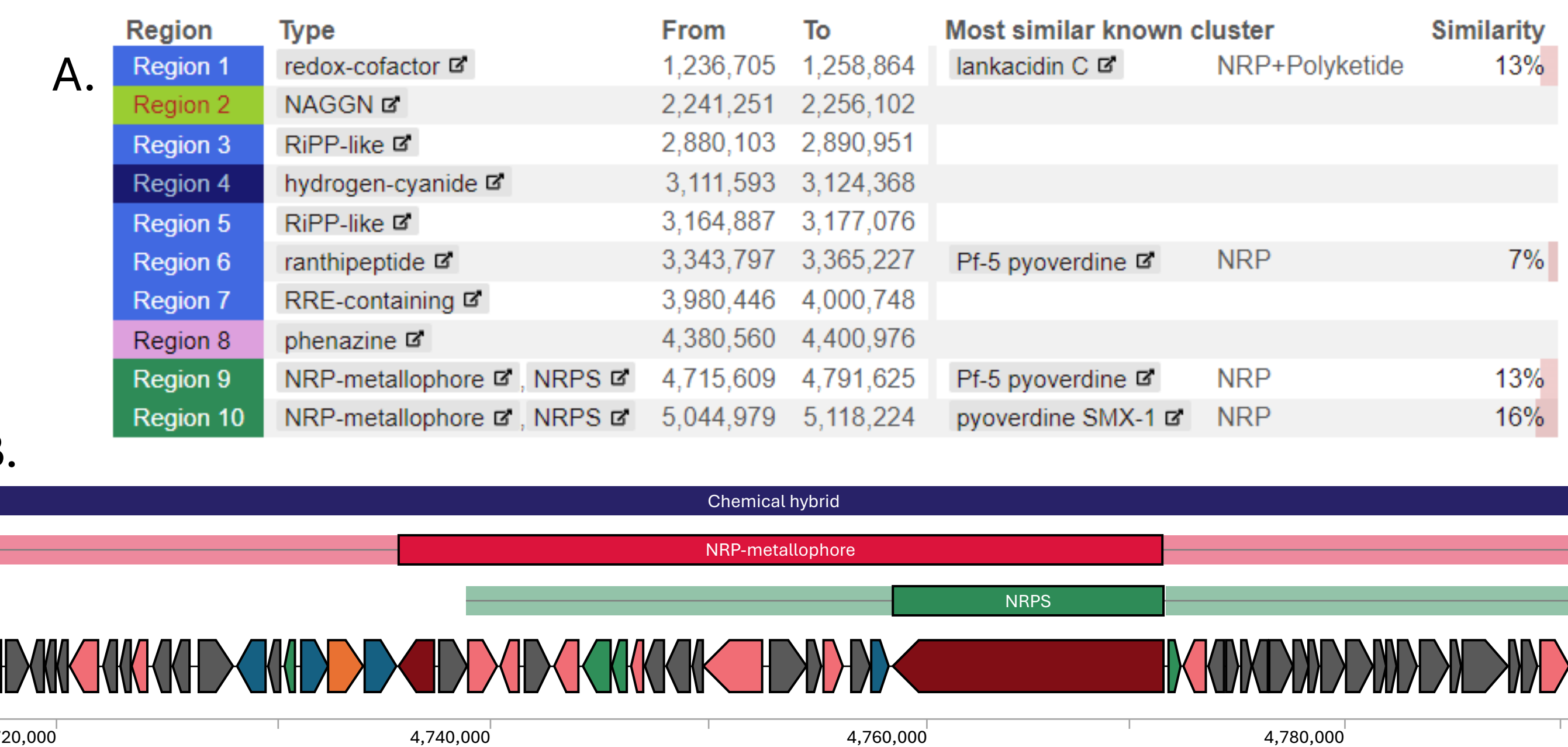
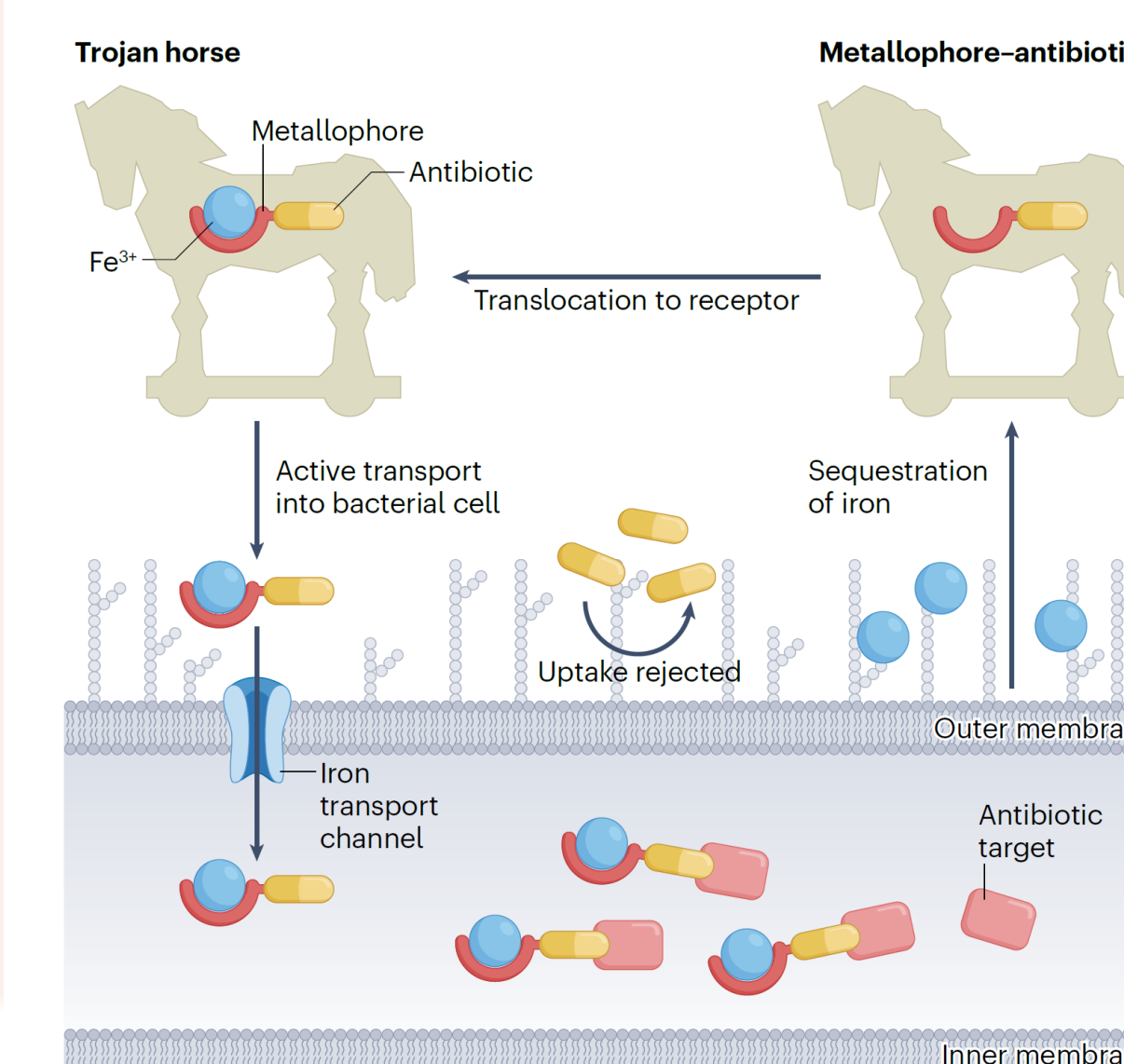


Figure 5. The gene cluster identified in the antagonistic *Pseudomonas* strain 3-3. (A) antiSMASH results of the 10 predicted biosynthetic gene clusters (BGC) in strain 3-3. (B) Region 9 was identified using transposon mutagenesis as the BGC involved in antagonistic activity. The gene cluster was 76 kb and predicted to encode a siderophore.



CONCLUSIONS

- Used needles contained a mixture of drugs and xylazine was present in most syringes and in the highest concentration.
- Our data and others suggest that xylazine is throughout the US.
- Needles contained opportunistic pathogens which can be life threatening especially when injected into the bloodstream.
- We identified environmental bacteria that inhibit *Candida* fungal pathogens.
- The identified BGC may encode a novel antifungal agent.