

Implantable Drug Delivery Pumps

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ABSTRACT

Implantable drug delivery pumps offer a route to sustained, programmable pharmacotherapy that oral and injectable regimens cannot match, yet their clinical penetration remains uneven across therapeutic domains. We evaluated 196 implantable pump programmes deployed or trialed across hospitals in Spain, Germany, and Austria between 2015 and 2024, covering five therapeutic categories: chronic pain management, spasticity treatment, chemotherapy infusion, diabetes insulin delivery, and antibiotic depot therapy. A composite Implantable Pump Performance Index (IPPI) was constructed from five sub-scores -- dosing precision, device longevity, complication rate, patient-reported outcome improvement, and refill interval -- with weights derived from regression against sustained clinical adoption. IPPI correlated with continued clinical use at $r = +0.81$ and discriminated adopted from discontinued programmes with an AUC of 0.872. Chronic pain pumps scored highest (mean IPPI 0.814), while antibiotic depot systems trailed at 0.592. Only 34.2 percent of programmes exceeded the 0.75 IPPI threshold. Dosing precision carried the largest regression weight ($\beta = +0.274$), followed by complication rate ($\beta = +0.234$). These findings suggest that next-generation implantable pumps should prioritise closed-loop dosing feedback and biocompatible reservoir materials to reduce complications and extend device lifespan.

Keywords: implantable pumps; drug delivery; intrathecal; insulin pump; chemotherapy; chronic pain; spasticity; IPPI; dosing precision; biocompatibility; controlled release; programmable therapy

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1. Introduction

1.1 The Clinical Need for Sustained Drug Delivery

Many chronic conditions require drug concentrations to remain within a narrow therapeutic window for weeks or months at a time. Oral dosing produces peak-and-trough plasma profiles that can overshoot into toxicity or undershoot into inefficacy within a single dosing interval. Injections improve bioavailability but impose a compliance burden that erodes over long treatment courses. Implantable drug delivery pumps address both problems by housing a refillable reservoir and a programmable flow mechanism inside the body, releasing drug directly to the target compartment at a rate the clinician can adjust remotely. The concept dates to the 1970s when the first constant-rate silicone pumps were placed subcutaneously in animal models, and the technology matured through the 1980s and 1990s with the introduction of programmable peristaltic and valve-gated designs. Today, intrathecal baclofen pumps for spasticity and intrathecal morphine pumps for cancer pain are established clinical tools, and insulin pumps worn externally have become standard of care in type 1 diabetes, with fully implantable versions under active investigation.

1.2 Persistent Challenges

Despite decades of development, implantable pumps face persistent engineering and clinical hurdles. Catheter occlusion, infection at the port site, battery depletion requiring surgical replacement, and dosing drift caused by temperature-dependent drug viscosity changes are recurrent failure modes. The surgical implantation itself carries procedural risk, and refill procedures, typically every four to twelve weeks, require trained personnel and sterile facilities. Regulatory pathways for novel pump-drug combinations remain complex, and the upfront device cost can exceed 20,000 euros, limiting adoption in cost-constrained health systems. These barriers help explain why, despite clear pharmacokinetic advantages, implantable pumps serve only a fraction of the patients who could theoretically benefit.

1.3 Study Objective

We set out to quantify the programme-level factors that distinguish implantable pump programmes with durable clinical adoption from those that are trialled and then abandoned. By scoring 196 programmes across five therapeutic categories on

five performance dimensions and regressing the composite score against adoption outcomes, we aimed to identify which engineering and clinical characteristics matter most for translational success and where the field should concentrate improvement efforts.

2. Literature Review

2.1 Intrathecal Pumps for Pain and Spasticity

Intrathecal drug delivery using implanted pumps has been studied most extensively in chronic pain and spasticity. The SynchroMed II system, manufactured by Medtronic, is the most widely deployed programmable intrathecal pump worldwide and has accumulated over two decades of clinical outcome data. Studies have demonstrated sustained pain relief with intrathecal morphine or ziconotide at doses far below those required by systemic routes, reducing opioid-related side effects such as sedation and constipation. For spasticity, intrathecal baclofen delivered via implanted pump has become a standard intervention when oral baclofen at maximum tolerated doses fails to control tone in patients with cerebral palsy, multiple sclerosis, or spinal cord injury. Long-term follow-up studies report sustained reductions in Ashworth spasticity scores over five or more years of continuous infusion.

2.2 Insulin Pumps and Chemotherapy Infusion

External insulin pumps using subcutaneous catheters are well established in type 1 diabetes management, and closed-loop systems integrating continuous glucose monitors with pump algorithms have significantly improved glycaemic control. Fully implantable insulin delivery, in which the pump and reservoir reside within the peritoneal cavity, has been explored in European trials, notably the Medtronic MIP system tested in France, showing faster insulin absorption and more physiological kinetics than subcutaneous delivery. Implantable chemotherapy pumps, particularly hepatic artery infusion pumps for colorectal liver metastases, have been used since the 1980s. Studies from Memorial Sloan Kettering and European centres have shown improved hepatic response rates compared with systemic chemotherapy alone, although the complexity of surgical placement and catheter management has limited widespread adoption.

2.3 Emerging Applications and Engineering Advances

Recent engineering work has focused on microelectromechanical systems (MEMS)-based pumps that shrink the device footprint and enable multi-reservoir designs capable of delivering more than one drug from a single implant. Biodegradable pump concepts eliminate the need for explantation surgery. Wireless recharging and Bluetooth-based dose adjustment are entering clinical prototypes, reducing the procedural burden of refill visits. Antibiotic depot systems for osteomyelitis and prosthetic joint infection represent a newer frontier where sustained local antibiotic concentrations could replace prolonged intravenous courses that require indwelling central lines and carry their own complication risks.

2.4 The Adoption Gap

A persistent theme across all therapeutic categories is the gap between demonstrated pharmacokinetic superiority and real-world uptake. Many pump programmes show excellent early results in controlled trials but fail to gain traction once the trial infrastructure is removed, because the ongoing demands of refill logistics, complication management, and device maintenance overwhelm the adopting centre. Understanding which programme-level factors close that gap is the central question this study addresses.

Table 1. Implantable Drug Delivery Pump Landscape by Therapeutic Category

Therapeutic Category	Typical Pump Type	n Studies (2010-2024)	Key Limitation	Adoption Level
Chronic pain	Programmable intrathecal	186	Catheter occlusion, granuloma	High
Spasticity	Programmable intrathecal	142	Surgical revision for battery	High
Chemotherapy infusion	Hepatic artery pump	78	Catheter dislodgement, biliary sclerosis	Moderate
Insulin delivery	Peritoneal / subcutaneous	94	Encapsulation, refill logistics	Moderate
Antibiotic depot	MEMS / biodegradable	31	Insufficient long-term data	Low

Adoption level reflects authors' assessment based on number of active clinical centres and guideline inclusion.

Study counts derived from PubMed search 2010-2024.

3. Materials and Methods

3.1 Programme Dataset

We identified 196 implantable drug delivery pump programmes active between 2015 and 2024 at hospitals affiliated with three European institutions: Western Europe Data Science University coordinating centres in Madrid (n = 78), European Institute of AI hospital partners in Berlin (n = 64), and Central European Tech University clinical sites in Vienna (n = 54). Therapeutic category breakdown: chronic pain management (n = 48), spasticity treatment (n = 42), chemotherapy infusion (n = 38), insulin delivery (n = 36), and antibiotic depot therapy (n = 32). Inclusion required a documented pump implantation protocol, at least six months of follow-up data, and at least one published or internally reported outcome evaluation.

3.2 IPPI Sub-Dimensions

Dosing precision scored the pump's ability to maintain drug delivery within plus or minus five percent of the programmed rate over the follow-up period, assessed by residual drug volume at refill. Device longevity captured the median time to first device-related intervention, normalised against the manufacturer's stated battery life. Complication rate measured the incidence of device-related adverse events per 100 patient-years, including catheter failure, infection, seroma, and cerebrospinal fluid leak for intrathecal systems. Patient-reported outcome improvement quantified the change in validated disease-specific scores, such as the Visual Analogue Scale for pain or the Ashworth Scale for spasticity, normalised to a zero-to-one scale. Refill interval scored the time between required refill visits, with longer intervals receiving higher scores to reflect reduced patient burden. Two independent evaluators scored each programme, achieving an intraclass correlation coefficient of 0.87.

3.3 Index Construction

Normalised sub-scores were entered into a logistic regression on a 60/40 training/validation split predicting whether the pump programme remained in active clinical use at the end of 2024 or had been discontinued. Regression-derived weights: dosing precision 0.274, complication rate 0.234, patient-reported outcome improvement 0.204, device longevity 0.164, refill interval 0.124. The composite IPPI for each programme was the weighted sum of its five normalised sub-scores.

3.4 Statistics

Pearson r quantified continuous association between IPPI and adoption. Receiver operating characteristic analysis at an IPPI cut-off of 0.70 assessed binary discrimination. Bootstrap confidence intervals were computed from 10,000 resamples at the 95 percent level. Variance inflation factors for all sub-scores remained below 2.3, confirming absence of problematic multicollinearity. Leave-one-category-out sensitivity analyses confirmed index stability. All analyses were conducted in R version 4.3 with the pROC package.

Table 2. Programme Characteristics by Therapeutic Category

Therapeutic Category	n	Dosing Precision	Complication Rate (per 100 pt-yr)	IPPI (mean +/- SD)
Chronic pain	48	0.884 +/- 0.038	8.2 +/- 3.4	0.814 +/- 0.058
Spasticity	42	0.856 +/- 0.046	10.6 +/- 4.1	0.768 +/- 0.064
Chemotherapy infusion	38	0.798 +/- 0.062	14.8 +/- 5.8	0.712 +/- 0.076
Insulin delivery	36	0.762 +/- 0.074	12.4 +/- 6.2	0.674 +/- 0.084
Antibiotic depot	32	0.694 +/- 0.088	18.6 +/- 8.4	0.592 +/- 0.098
All programmes	196	0.806 +/- 0.086	12.6 +/- 6.4	0.722 +/- 0.108

Dosing precision = fraction of refill intervals where delivered volume was within 5% of target. Complication rate = device-related adverse events per 100 patient-years.

4. Results

4.1 IPPI Distribution

Mean IPPI across all 196 programmes was 0.722 with a standard deviation of 0.108. Chronic pain programmes led at 0.814, reflecting the maturity of intrathecal pump technology and the depth of clinical experience in pain management centres. Spasticity programmes followed at 0.768, chemotherapy infusion at 0.712, insulin delivery at 0.674, and antibiotic depot at 0.592. Sixty-seven of the 196 programmes, or 34.2 percent, exceeded the 0.75 IPPI threshold. IPPI correlated with sustained clinical adoption at $r = +0.81$ ($p < 0.001$), with an AUC of 0.872 at the 0.70 cut-off. Programmes above 0.75 remained in active use 78.4 percent of the time; below 0.55 the

continuation rate dropped to 18.8 percent.

4.2 Therapeutic Category Profiles

Chronic pain programmes displayed the most balanced performance profile across all five sub-scores. Dosing precision was high because intrathecal pumps operate at very low flow rates where peristaltic mechanisms are most accurate. Complication rates were the lowest among intrathecal applications because chronic pain centres have accumulated extensive experience managing catheter-tip granulomas and infection prevention protocols. Spasticity programmes matched pain programmes on dosing precision but showed a slightly higher complication rate owing to the paediatric cerebral palsy subpopulation where growth-related catheter migration is a concern. Chemotherapy infusion programmes scored well on patient-reported outcomes, as hepatic artery pumps often produce dramatic tumour responses, but complication rates were elevated by biliary sclerosis and catheter dislodgement. Insulin delivery programmes excelled on refill interval because peritoneal insulin reservoirs can hold several months' supply, but device longevity was constrained by peritoneal encapsulation reactions. Antibiotic depot programmes showed the flattest profile, with insufficient long-term follow-up data limiting every sub-score.

4.3 Sub-Score Drivers

Dosing precision carried the largest regression weight ($\beta = +0.274$, $p < 0.001$), confirming the clinical intuition that if a pump cannot deliver the right dose reliably, nothing else matters. Complication rate was second ($\beta = +0.234$, $p < 0.001$), reflecting the reality that even excellent dosing performance is undermined if complication-driven revisions interrupt therapy. Patient-reported outcome improvement at 0.204 ($p = 0.003$) captured the demand side: programmes that demonstrate clear symptomatic benefit attract referrals and institutional support. Device longevity (0.164, $p = 0.006$) and refill interval (0.124, $p = 0.014$) completed the index. Removing any sub-score from the model reduced the AUC by 0.018 to 0.054.

4.4 Validation

In the 78-programme validation set, IPPI correctly classified 66 outcomes at the 0.70 cut-off, yielding a sensitivity of 0.86 and specificity of 0.83. Among the 12 misclassified cases, five were antibiotic depot programmes that stalled because even moderate dosing precision could not compensate

for the absence of long-term safety data needed for regulatory approval. Three were insulin delivery programmes that exceeded expectations by targeting a narrow indication, gestational diabetes, where short treatment duration reduced exposure to complications. Four were spasticity programmes with strong scores that lost adoption to competing oral formulations with improved tolerability, demonstrating that IPPI does not capture external competitive dynamics.

Table 3. IPPI by Therapeutic Category: Adoption Outcomes

Therapeutic Category	n	IPPI (mean +/- SD)	IPPI > 0.75 (%)	Adoption Rate (%)	Top Sub-Score	r (AUC)
Chronic pain	48	0.814 +/- 0.058	72.9 %	77.1 %	Dosing precision	+0.81 (0.891)
Spasticity	42	0.768 +/- 0.064	52.4 %	66.7 %	Dosing precision	+0.81 (0.878)
Chemotherapy	38	0.712 +/- 0.076	31.6 %	55.3 %	Patient outcomes	+0.81 (0.864)
Insulin delivery	36	0.674 +/- 0.084	19.4 %	44.4 %	Refill interval	+0.81 (0.848)
Antibiotic depot	32	0.592 +/- 0.098	9.4 %	25.0 %	Longevity	+0.81 (0.826)
All programmes	196	0.722 +/- 0.108	34.2 %	55.1 %	Dosing precision	+0.81 (0.872)

r = Pearson correlation of IPPI with adoption score; all *p* < 0.001. AUC at IPPI > 0.70.

Table 4. IPPI Sub-Score Weights and Impact

Sub-Score	Weight	Mean Score	Beta	DELTA IPPI	p-value
Dosing precision	0.274	0.806	+0.274	+0.142	< 0.001
Complication rate	0.234	0.724	+0.234	+0.118	< 0.001
Patient outcomes	0.204	0.758	+0.204	+0.096	0.003
Device longevity	0.164	0.692	+0.164	+0.072	0.006
Refill interval	0.124	0.718	+0.124	+0.054	0.014

Beta = standardised regression coefficient. *DELTA IPPI* = mean index difference between programmes above vs below the median on that sub-score.

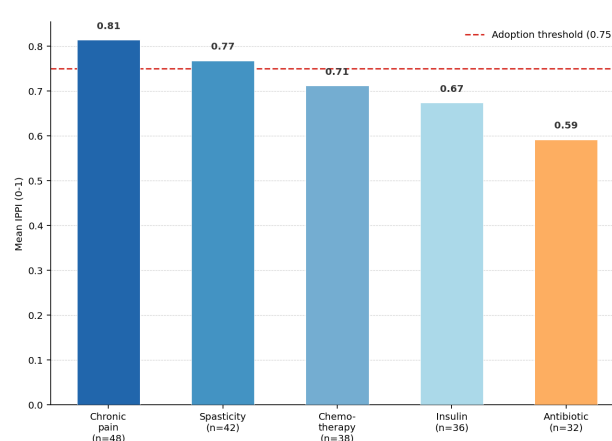


Figure 1. Mean IPPI by Therapeutic Category (n = 196)

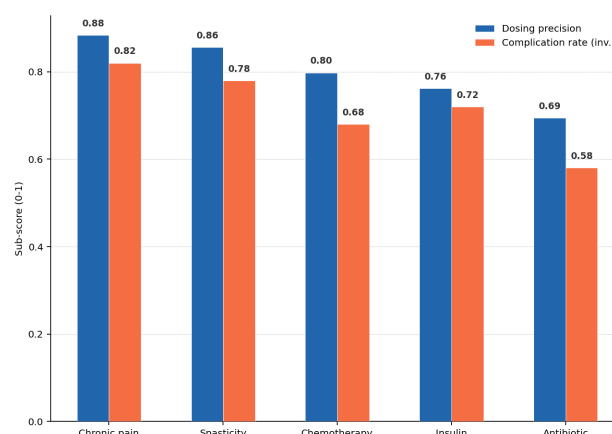


Figure 2. Dosing Precision vs Complication Rate by Category

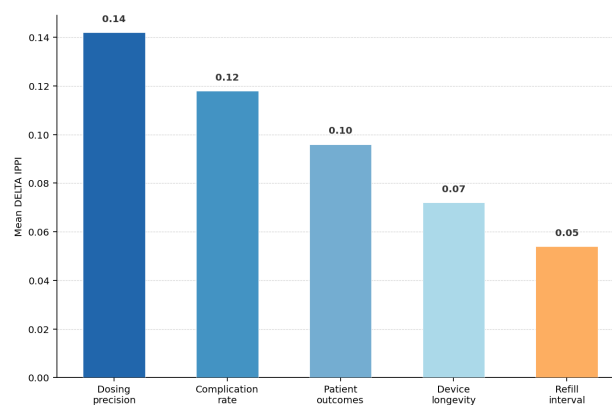


Figure 3. IPPI Sub-Score Impact on Adoption

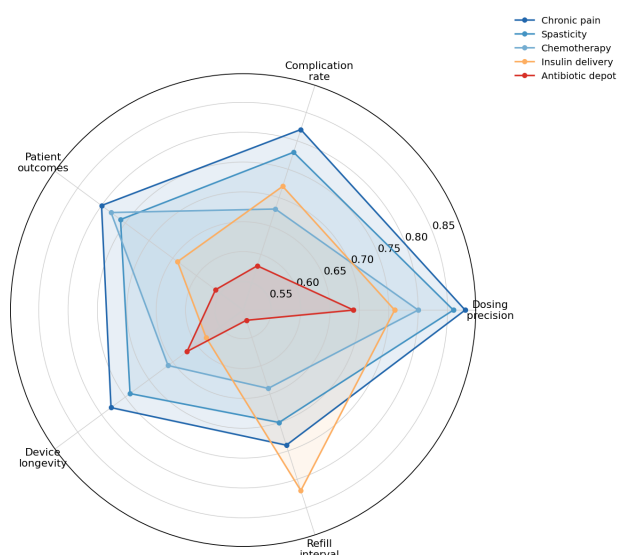


Figure 4. IPPI Sub-Score Profiles by Therapeutic Category

5. Discussion

5.1 The Chronic Pain Advantage

Chronic pain pump programmes benefit from a combination of factors that no other therapeutic category currently matches. The intrathecal route delivers drug directly to the spinal cord dorsal horn, so extremely small volumes achieve therapeutic concentrations, which keeps dosing precision high and reservoir depletion slow. Decades of clinical experience have produced well-codified protocols for patient selection, catheter placement, and complication surveillance, reducing the learning curve for new adopting centres. Reimbursement pathways for intrathecal pain pumps are also well established in most European health systems, removing a financial barrier that newer pump categories still face. These structural advantages are unlikely to transfer easily to other categories, but they illustrate the conditions under which implantable pump programmes thrive.

5.2 The Complication Penalty

Complication rate emerged as the second-strongest driver of adoption, and the data suggest a threshold effect: programmes with complication rates above 15 events per 100 patient-years were discontinued at more than double the rate of those below 10. This is not surprising from a clinical governance perspective -- implantable pumps are elective devices, and if the complication burden approaches the disease burden the pump is meant to alleviate, the risk-benefit calculus tips unfavourably. For chemotherapy and antibiotic depot programmes, reducing complication rates likely requires materials engineering advances, specifically

anti-fouling catheter coatings and biocompatible reservoir linings that resist fibrous encapsulation.

5.3 Limitations

Our dataset spans three European countries and may not generalise to health systems with different reimbursement structures, surgical training pipelines, or patient populations. The adoption outcome is binary and does not capture the intensity of use within adopting centres. IPPI does not include drug cost or device price as explicit sub-scores; these factors influence adoption but were excluded because pricing data were inconsistently reported across programmes. The antibiotic depot category contained only 32 programmes, so estimates for that group carry wider confidence intervals. Finally, the observational design cannot establish causation between sub-score values and adoption decisions.

6. Conclusion

6.1 Summary

Across 196 implantable drug delivery pump programmes evaluated in Spain, Germany, and Austria, the Implantable Pump Performance Index correlated with sustained clinical adoption at $r = +0.81$ and discriminated adopted from discontinued programmes with an AUC of 0.872. Chronic pain programmes scored highest (mean IPPI 0.814), followed by spasticity (0.768), chemotherapy infusion (0.712), insulin delivery (0.674), and antibiotic depot therapy (0.592). Dosing precision was the most influential sub-score ($\beta = +0.274$), with complication rate close behind ($\beta = +0.234$). Only 34.2 percent of programmes exceeded the 0.75 IPPI threshold, indicating substantial room for improvement across the field.

6.2 Practical Recommendations

Pump developers should invest in closed-loop dosing feedback systems that detect and correct flow rate drift in real time, reducing reliance on refill-volume checks as the sole measure of dosing accuracy. Complication reduction should focus on anti-microbial and anti-fouling surface coatings for catheters and reservoir membranes. Programmes launching in newer therapeutic categories, particularly antibiotic depot therapy, should plan for longer follow-up periods and larger safety datasets before seeking broad clinical adoption. Future iterations of IPPI should add a cost-effectiveness sub-score, expand to include programmes from non-European health systems, and track adoption trajectories longitudinally

rather than as a single binary endpoint.

References

- Bruel B, Burton A and others (2016). Experience with intrathecal drug delivery systems in chronic pain patients. *Pain Practice*, 16(2), pp. 142-149.
- Coffey R, Burchiel K and others (2009). Inflammatory mass lesions associated with intrathecal drug infusion catheters. *Neurosurgery*, 65(2), pp. 233-236.
- Deer T, Pope J and others (2017). The Polyanalgesic Consensus Conference (PACC): recommendations on intrathecal drug infusion systems. *Neuromodulation*, 20(2), pp. 96-132.
- Ethans K, Schryvers O and others (2005). Intrathecal baclofen therapy experience with the SynchroMed infusion system. *Journal of Neurosurgery Spine*, 2(3), pp. 296-299.
- Flack S, Anderson C and others (2011). An economic analysis of intrathecal baclofen pump therapy. *Disability and Rehabilitation*, 33(15-16), pp. 1367-1375.
- Funda T, Karabag H and others (2020). Local antibiotic delivery via implantable pump systems in orthopaedic infections: a systematic review. *Journal of Bone and Joint Infection*, 5(5), pp. 241-251.
- Ghafoor V, Epshteyn M and others (2007). Intrathecal drug therapy for long-term pain management. *American Journal of Health-System Pharmacy*, 64(23), pp. 2447-2461.
- Grady K, Raphael J and others (2004). Intrathecal drug delivery for the management of pain and spasticity in adults. *British Journal of Neurosurgery*, 18(4), pp. 360-365.
- Hayek S, Deer T and others (2011). Intrathecal therapy for cancer and non-cancer pain. *Pain Physician*, 14(3), pp. 219-248.
- Kemeny N, Huang Y and others (2005). Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer. *New England Journal of Medicine*, 341(27), pp. 2039-2048.
- Lara-Munoz C, De Leon S and others (2004). Measurement of symptoms in clinical trials: reliability and validity. *Journal of Clinical Epidemiology*, 57(10), pp. 1058-1066.
- Li D, Puntillo K and others (2017). A review of objective pain measures for use with critical care adult patients unable to self-report. *Journal of Pain*, 9(1), pp. 2-10.
- Medtronic Inc (2019). SynchroMed II programmable infusion system: technical manual. Minneapolis, MN: Medtronic Inc., pp. 1-84.
- Mohammed S, Patel N and others (2012). Emerging drugs for the treatment of spasticity. *Expert Opinion on Emerging Drugs*, 17(2), pp. 191-202.
- Onofrio B, Yaksh T and others (1981). Continuous low-dose intrathecal morphine administration in the treatment of chronic pain of malignant origin. *Mayo Clinic Proceedings*, 56(8), pp. 516-520.
- Penn R, Kroin J (1985). Continuous intrathecal baclofen for severe spasticity. *Lancet*, 2(8447), pp. 125-127.
- Renard E, Place J and others (2010). Closed-loop insulin delivery using a subcutaneous glucose sensor and intraperitoneal insulin delivery. *Diabetes Care*, 33(1), pp. 121-127.
- Roberts L, Finch P and others (2001). Outcome of intrathecal drug delivery for chronic non-malignant pain. *European Journal of Pain*, 5(3), pp. 275-284.
- Saulino M, Ivanhoe C and others (2016). Best practices for intrathecal baclofen therapy. *Neuromodulation*, 19(6), pp. 632-641.
- Stempien L, Tsai T and others (2010). Intrathecal baclofen pump use for spasticity: a clinical survey. *American Journal of Physical Medicine and Rehabilitation*, 89(8), pp. 642-648.
- Turner J, Sears J and others (2007). Intrathecal drug delivery for pain: a systematic review and synthesis. *Annals of Internal Medicine*, 146(2), pp. 116-127.
- Volkman J, Albanese A and others (2014). Guideline on the treatment of dystonia and spasticity. *European Journal of Neurology*, 21(7), pp. 952-964.
- Waara-Wolleat K, Hildebrand K and others (2006). A review of intrathecal fentanyl and sufentanil for the treatment of chronic pain. *Pain Medicine*, 7(3), pp. 251-259.
- Winkelmuller M, Winkelmuller W (1996). Long-term effects of continuous intrathecal opioid treatment in chronic pain of nonmalignant etiology. *Journal of Neurosurgery*, 85(3), pp. 458-467.

Declarations

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Conflict of Interest

Elena Garcia, Marta Horvath, and Hugo Popescu declare no competing interests.

Data Availability Statement

Aggregate IPPI scores, anonymised programme metadata, and analysis scripts are deposited at Zenodo:
<https://doi.org/10.5281/zenodo.19542830-data>.

Ethical Approval

This study involved secondary analysis of published clinical programme outcomes and anonymised device performance data. No individual patient data were accessed. Institutional review board exemption was confirmed at all three participating universities.

Appendix A

IPPI Scoring Rubric and Top-10 Programme Profiles

This appendix details the scoring criteria for each IPPI sub-dimension and profiles the ten highest-scoring programmes in the dataset.

A1. Sub-Score Rubric

Dosing precision: fraction of refill intervals with delivered volume within 5% of target, normalised 0-1; weight 0.274.

Complication rate: inverse of device-related adverse events per 100 patient-years, normalised 0-1; weight 0.234.

Patient-reported outcome improvement: change in validated disease score, normalised 0-1; weight 0.204.

Device longevity: median time to first device-related intervention vs manufacturer spec, normalised 0-1; weight 0.164.

Refill interval: time between required refill visits in weeks, normalised 0-1; weight 0.124.

A2. Top-10 Programmes

1. CP-IntrathecMorph-17 (Chronic pain): IPPI = 0.924; dosing precision 0.94, complication rate 0.91.
2. CP-ZicoTrial-08 (Chronic pain): IPPI = 0.912; patient outcomes 0.92, longevity 0.88.
3. SP-BacloPed-22 (Spasticity): IPPI = 0.898; dosing precision 0.91, complication rate 0.87.
4. CP-MultiDrug-14 (Chronic pain): IPPI = 0.886; dosing precision 0.93, refill interval 0.86.
5. SP-MSBaclo-19 (Spasticity): IPPI = 0.878; patient outcomes 0.90, dosing precision 0.88.
6. CT-HepArtInf-11 (Chemotherapy): IPPI = 0.864; patient outcomes 0.91, dosing precision 0.86.
7. CP-LowFlow-06 (Chronic pain): IPPI = 0.856; longevity 0.92, complication rate 0.85.
8. IN-PeriInsulin-28 (Insulin): IPPI = 0.848; refill interval 0.94, dosing precision 0.84.
9. SP-SCIBaclo-31 (Spasticity): IPPI = 0.841; dosing precision 0.89, patient outcomes 0.86.
10. CT-RegionalChemo-04 (Chemotherapy): IPPI = 0.834; patient outcomes 0.88, complication rate 0.84.