Automated Insulin Delivery (AID)

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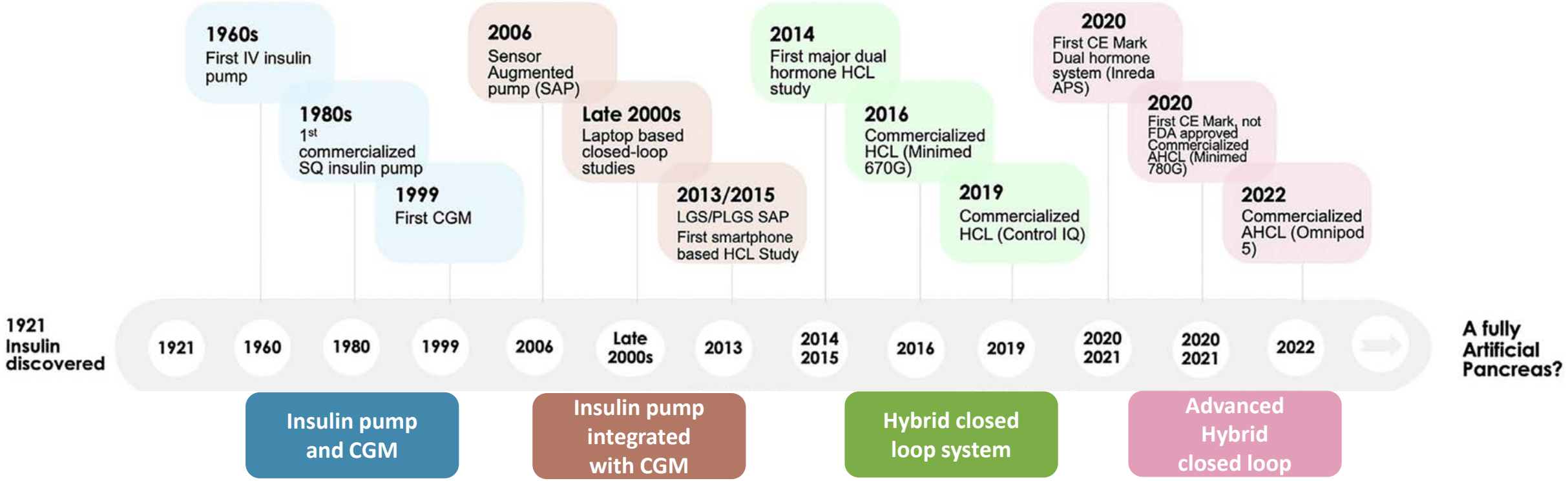
Evolution of diabetes technology

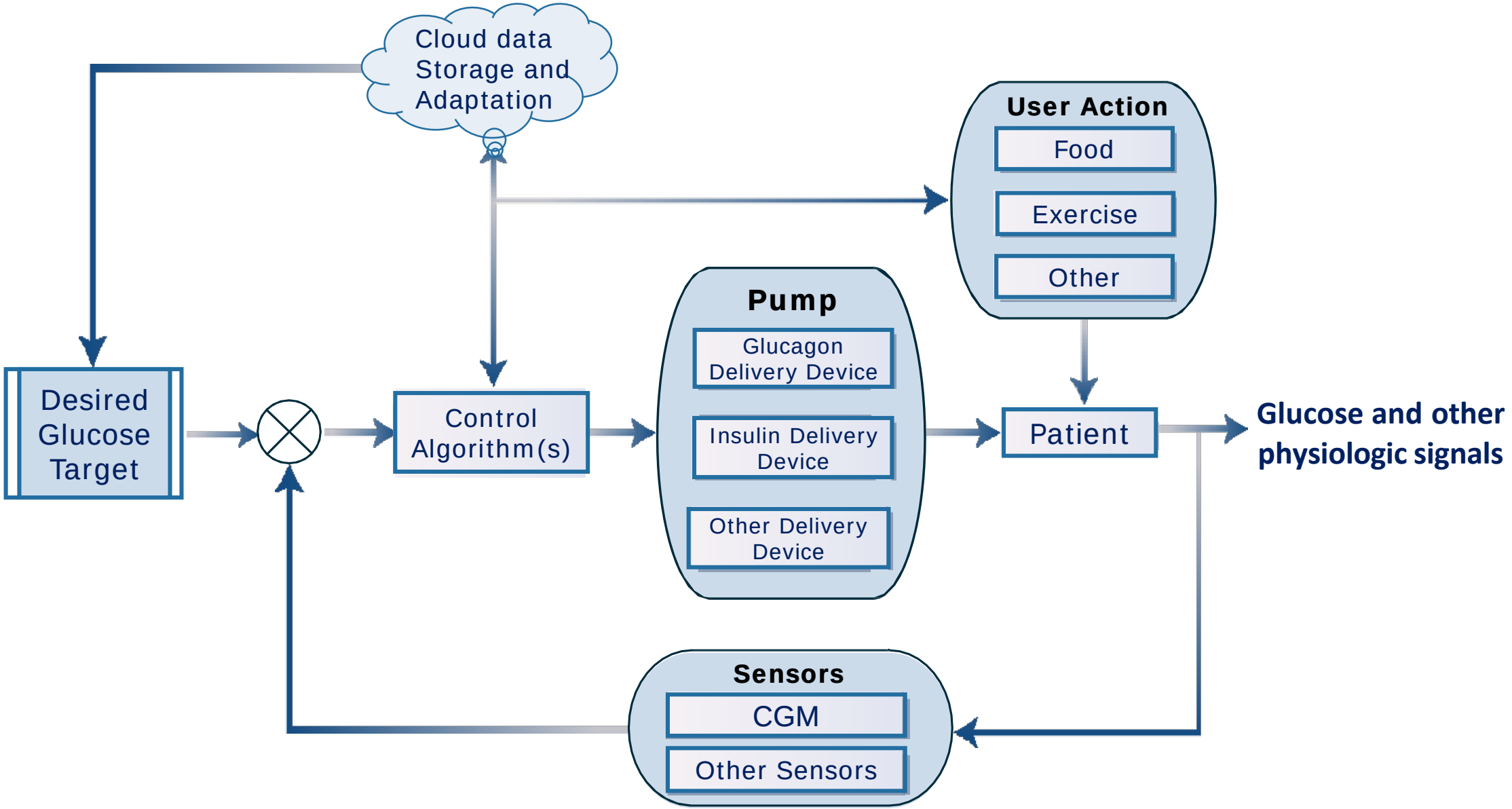
In 1963, Arnold Kadish invented the first insulin pump.

More than 20 years before the first insulin pen was introduced.



Zahid M, et al. *Endo Pract* 2023;29:653-662. doi: 10.1016/j.eprac.2023.04.007

Components of AID



Heile M., et al. *Clin Diabetes* 2020; 38: 474–485. doi 10.2337/cd20-0050

AID systems terminology

Sensor-augmented pump (SAP)	Insulin pump with use of a CGM either on a separate device or displayed directly on the pump. These systems allow for viewing of the sensor data, but insulin delivery is not altered on the basis of sensor glucose values.
Low glucose suspend (LGS) or predictive low glucose suspend (PLGS)	Insulin pump system that suspends insulin delivery for actual hypoglycemia due to sensor glucose value (LGS) or for predicted hypoglycemia (PLGS).
DIY AID (also known as Loop, OPEN APS, Android APS)	**"Do-it-yourself"** AID system using a commercially available CGM system and insulin pump, plus an open-source algorithm; currently not approved by regulatory agencies.

Sher JL., et al. *Diabetes Care* 2022;45:3058–3074. doi:10.2337/dci22-0018

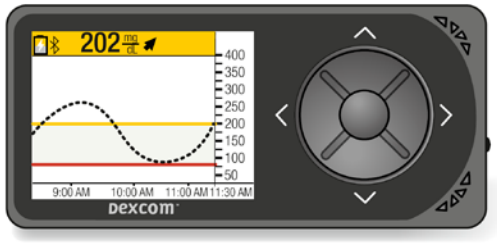
do-it-yourself (DIY) AID systems

OPEN APS

Android APS

Insulin pumps

Continuous glucose monitors



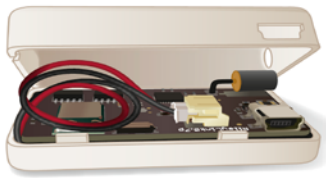
Mobile medical network

Loop

Insulin pump

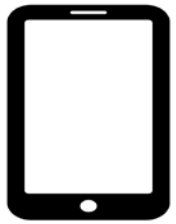
916 MHz wireless

RileyLink



Bluetooth wireless

iPhone



DiAS smartphone

Lal R.A, et al. *Endocrine Reviews* 40: 1521 – 1546, 2019doi: 10.1210/er.2018-00174

Currently Available CGM Devices

Device	iPro2	Guardian Connect	Dexcom G6	Dexcom G7	Freestyle Libre 2	Freestyle Libre 3	Eversense E3
Company	Medtronic	Medtronic	Dexcom	Dexcom	Abbott	Abbott	Senseonics
Classification	Professional CGM	**rtCGM**	**rtCGM**	**rtCGM**	**Flash monitoring**	**rtCGM**	**Implantable CGM**
Accuracy/ MARD	13.6%	8.7%	9%	8.2%	9.2%	7.9%	8.5%
Daily calibration	Yes	Yes	**No**	**No**	**No**	**No**	Yes
Warm-up period	1 h	2 h	2 h	30 min	1 h	1 h	~24 h
Sensor life	7 d	7 d	**10 d**	**10 d**	**14 d**	**14 d**	**180 d**
Alarms and alerts	No	Yes, customizable	Yes, customizable	Yes	No	Yes	Yes
Age	**All ages**	Age **2** and old with insulin pump and age 14 and above as stand-alone CGM	Age **2** and older	Age **2** and older	Ages **4** and up	Ages **4** and up	Age **18** y and older
Inter-operability with an insulin pump	No	**Yes**	**Yes**	**Yes**	**Yes**	**Yes**	No
Interferents	MRI, CT scan, x-ray diathermy, IMRT	MRI, CT scan, x-ray	Hydroxyurea, MRI, CT scan	*	Ascorbic acid, MRI, CT scan, diathermy	Ascorbic acid, MRI, CT scan, diathermy	Mannitol, lithotripsy, diathermy
Downloading software	Yes	Yes	Yes	Yes	**No**	Yes	Yes
System features for patient preferences		***Compatible** with Medtronic 670G/770G And Medtronic 780G	***Compatible** With Tandem t:slim X2 and Omnipod 5	***Compatible** With Tandem t:slim X2 and Omnipod 5 ***Use in pregnancy**	*Want to avoid alarms and alerts ***Use in pregnancy**	***Use in pregnancy**	*Avoid frequent sensor change

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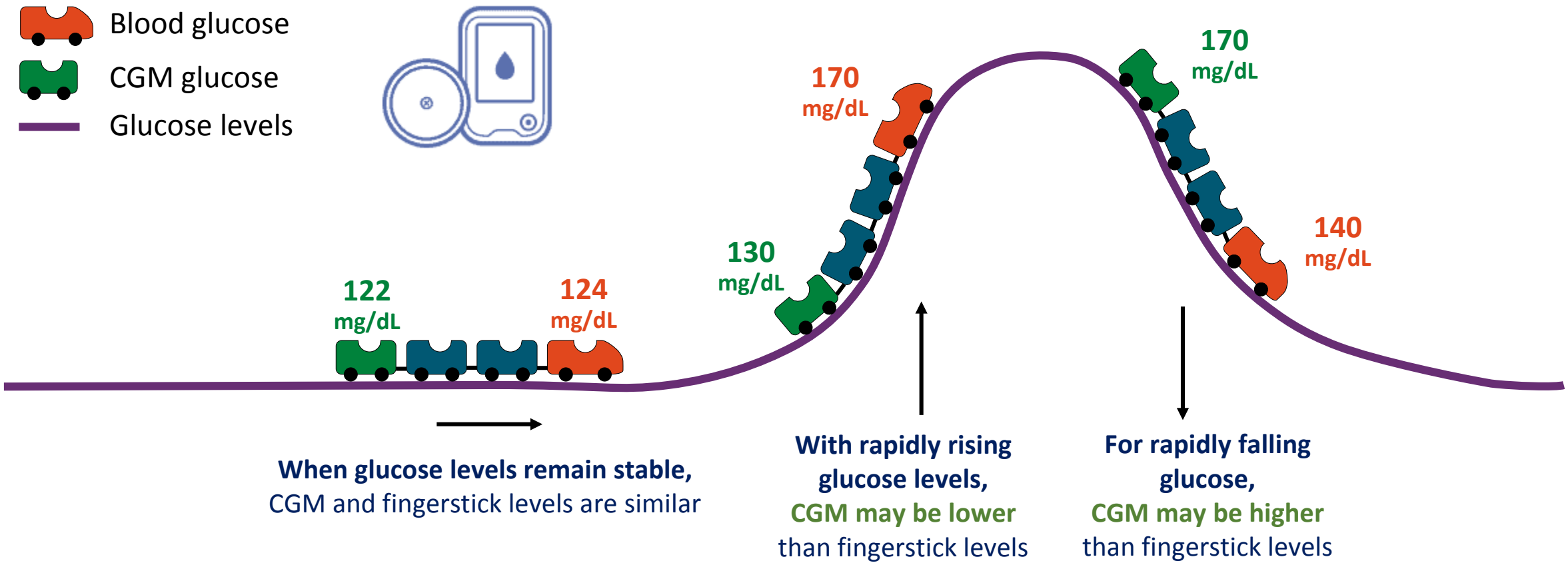
There is a “Lag” Between Fingerstick and CGM Levels



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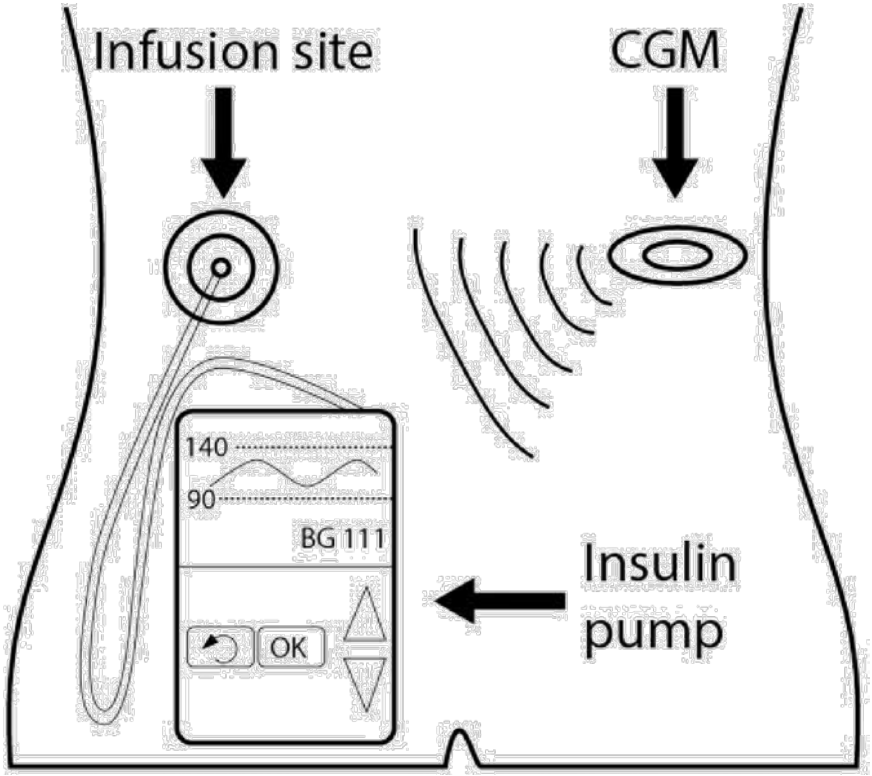
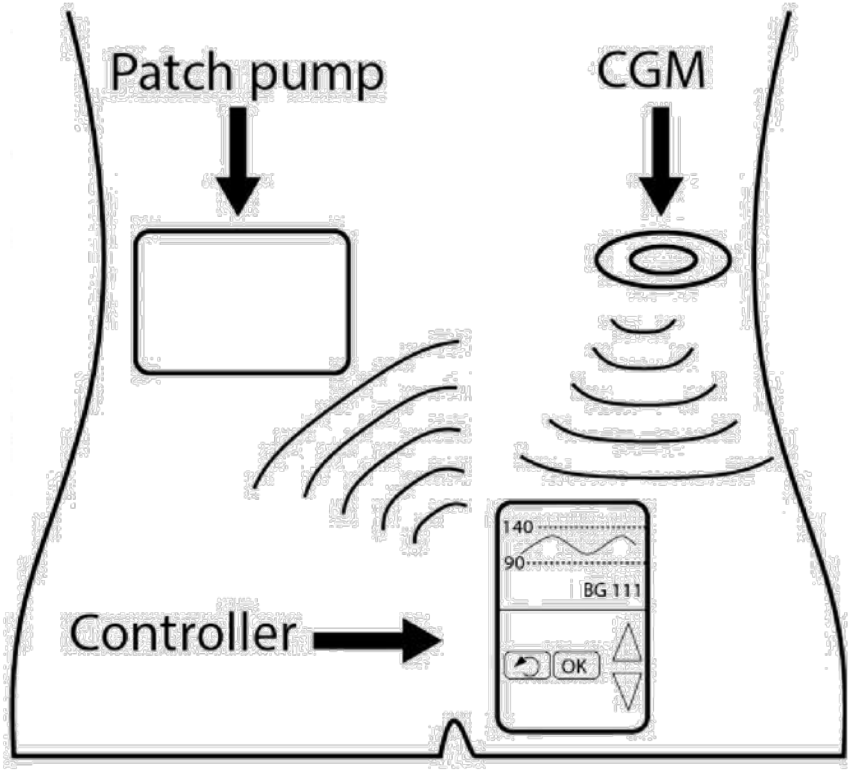
Continuous Subcutaneous Insulin Infusion (CSII)

components and configurations



CSII with tubing with CGM



Patch pump with CGM

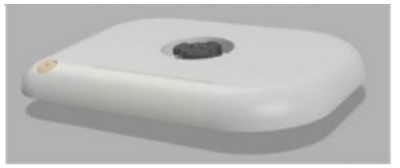
Díaz-Balzac C.A , et al. *J Clinic Endocr Metab* 2023; 108:1019–1033. doi 10.1210/clinem/dgac746

Patch Pumps

- ✓Primarily insulin pen replacements.
- ✓Categorized into:
  - Simplified
    - generally mechanical
    - fully disposable
  - Full-featured
    - generally electromechanical
    - partially disposable (pump and reservoir)

Qforma

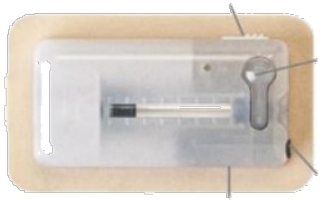
Flexible Patch Pump



Simplicity
Bolus doses only,
2-unit increments;
FDA approved, not launched

https://www.myceqursimplicity.com/
https://www.accu-chek.co.uk/insulin-pumps/solo
https://www.go-vgo.com/

Solo Micropump
FDA approved,
launched in Europe



V-Go, disposable patch pump
Basal rates of 20, 30, 40 units/day
Bolus doses in 2-unit increments
Mostly used in T2D

Barry H. Ginsberg. *Journal of Diabetes Science and Technology* 2019; 13(1) 27–33. doi: 10.1177/19322968187865

Simplified Insulin Delivery Devices

Type	Patch-like insulin pump	Insulin patch
Device	V-Go	CeQur
Company	Mannkind	CeQur Corporation
System features for patient preferences	✓ Daily wear ✓ 3 fixed basal settings available ✓ Holds up to 36 units of bolus insulin ✓ 1 click = 2 units ✓ Total insulin dose of 56 units (V-Go 20), 66 units (V-Go 30) or 76 units (V-Go 40)	✓ 3-d wear ✓ Bolus dosing only ✓ 1-click administers 2 units only ✓ Holds up to 200 units over a 3-day period ✓ Easy to use and learn
Mobile app	No	No

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Evolution of AID Systems

✓AID Algorithms

- Model predictive control (MPC)

Moon S.J, et al. *Diabetes Metab J* 2021;45:813-839. doi: 10.4093/dmj.2021.0177

Evolution of AID Systems

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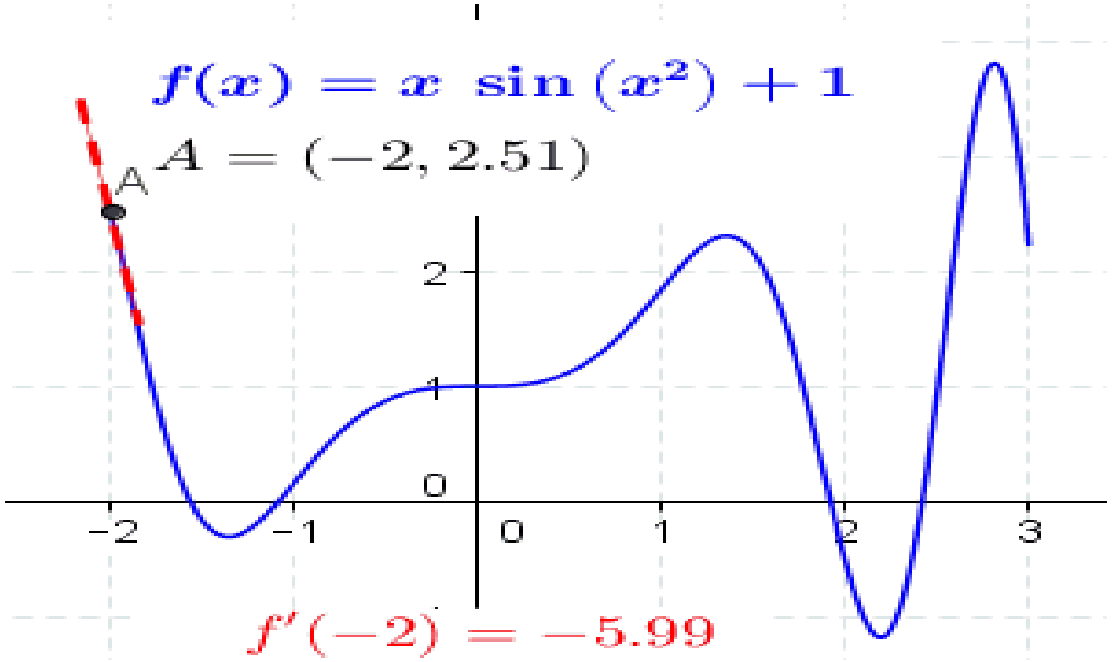
- Model predictive control (MPC)
- Proportional integral derivative (PID)



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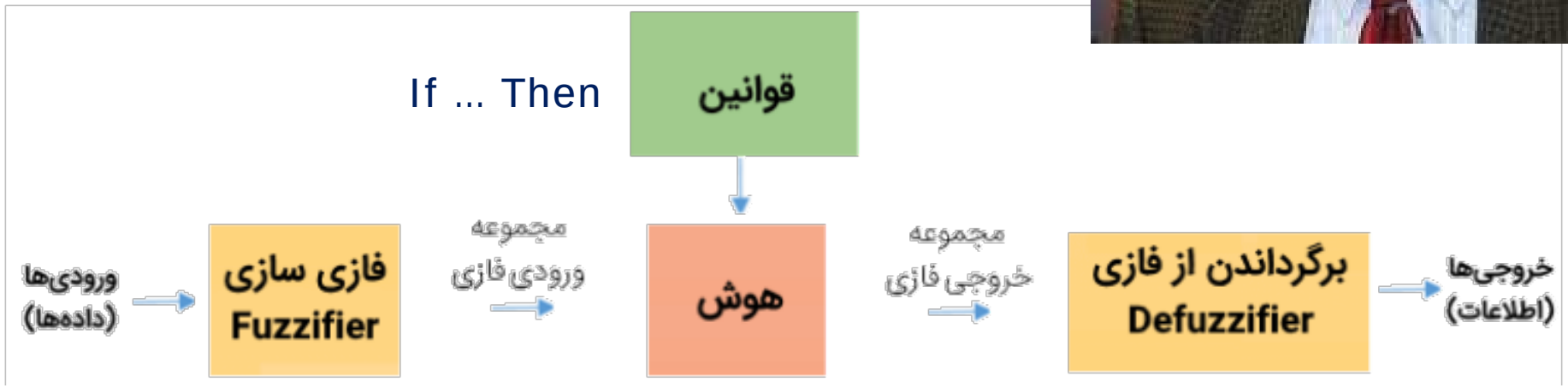
Evolution of AID Systems

✓AID Algorithms

- Model predictive control (MPC)
- Proportional integral derivative (PID)
- Fuzzy logic (FL) controllers



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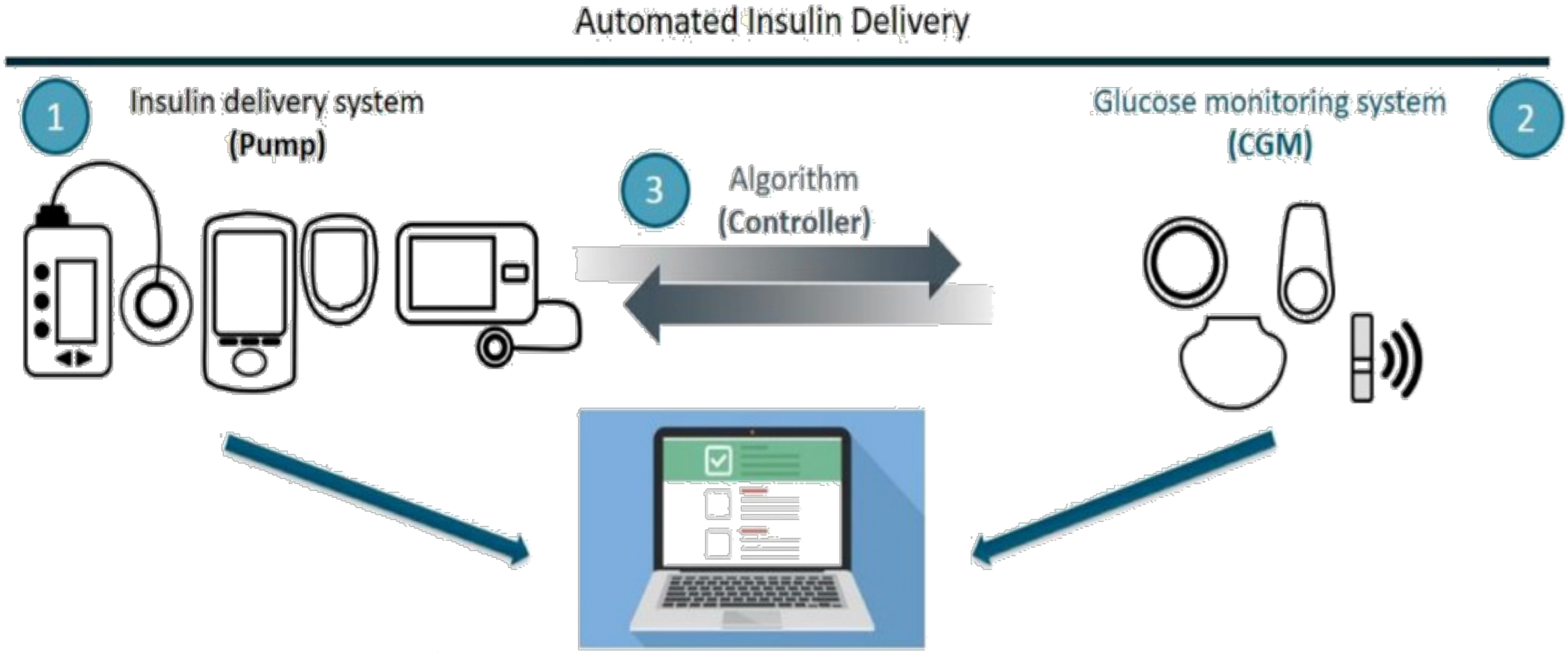
Evolution of AID Systems

✓AID Algorithms

- Model predictive control (MPC)
- Proportional integral derivative (PID)
- Fuzzy logic (FL) controllers

✓Inter-operability and Intra-operability

Steps towards AID and Inter-operability



Heile M., et al. *Clin Diabetes* 2020; 38: 474–485. doi: 10.2337/cd20-0050.

Commercially available AID systems

AID system	Omnipod 5	Tandem t:slim X2 with control IQ	Medtronic 670G/770G	Medtronic 780G (CE mark; not yet FDA approved)
Glucose sensor	Dexcom G6 (anticipated Libre 2), no calibration, 10 d wear	Dexcom G6 (anticipated G7; Libre 2), no calibration, 10 d wear	Guardian 3; **calibration** at least Q 12 h, 7 d wear	Guardian 3 (EU); 4 (US) **calibration** at least Q 12 h, 7 d wear
Algorithm	MPC (in Pod)	MPC (on pump)	PID	PID/Fuzzy Logic/MPC
Age indication (FDA)	**≥ 2 y**	**≥ 6 y**	**≥ 7y / ≥ 2 y**	**≥ 2 y**
System initiation/warm-up	Basal rates, ICR, ISF, Target, No warm-up	TDI, body weight, basal rates, ICR, ISF, Target, no warm-up	Basal rates, ICR, ISF, Target, 48-h warm-up	Basal rates, ICR, ISF, Target, 48-h warm-up
Targets	**Customizable** by 10 mg/dl from 110-150 mg/dl, up to 8 segments per day **Activity mode**: 150 mg/dl	**Fixed** targets depending on time of day: 112.5-160 mg/dl **Sleep mode**: 110-120 mg/dl **Activity mode**: 140-160 mg/dl	**Fixed** target of 120 mg/dl **Temp** target of 150 mg/dl	**Fixed** target 100, 110, and 120 mg/dl **Temp** target 150 mg/dl
Bolus	Required carb entry; incorporates CGM value and trend	Required carb entry; incorporates CGM value	Required carb entry; incorporates CGM value	Required carb entry; incorporates CGM value
Automated correction bolus	Yes	Yes	**No**	Yes

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Commercially available AID systems

AID system	Omnipod 5	Tandem t:slim X2 with control IQ	Medtronic 670G/770G	Medtronic 780G (CE mark; not yet FDA approved)
Basal modulation	Adjusts every 5 min based on target, and prediction of glucose within the next 60 min	Adjusts every 5 min based on the active basal rates, and prediction of glucose within 30 min	Adjusts every 5 min	Adjusts every 5 min
Adaptivity	Based on TDD with every Pod change (72 h)	None, uses actual TDD	TDD-based automation with updates every 6 d	TDD-based automation with updates every 6 d
Mobile application/ cell phone control	Omnipod 5 mobile app/ Yes, full system	T:Connect mobile App/ Yes, bolus only	Minimed Mobile app/ **No**	Minimed Mobile app/ Yes, bolus only
Wireless upload	Yes	Yes	**No**/Yes	Yes
System features for patient preferences	*No tubing minimizes insulin waste *Automated cannula insertion *Only 2 parts, so simple for travel	*2-way Bluetooth (X2)/full integration with multiple Devices *Charges/no disposable Batteries	*Others can view data via sharing app *Slim attachable clip	*Adjusts insulin delivery and corrects glucose levels every 5 min

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Adjustments for physical activity in AID

Type of Exercise	Before Exercise	During Exercise	After Exercise	Overnight
Aerobic	↓ basal rate with 'exercise target' 1–2 hours prior	↓ basal rate with 'exercise target' or suspend insulin delivery[a]	↓ basal rate with 'exercise target' 0– 6 hours after	'Exercise target' overnight (up to 6 hours) as necessary and/or uncovered bedtime snack
Aerobic & Anaerobic	↓ bolus amount by 0%–25% in 1–3 hours prior (may be up to 75% is prolonged exercise is anticipated)	In case glucose level is below 120 mg/ dL, consume 10–20 g carbohydrates at start or 10 min prior[b] Carbohydrates as needed	↓ bolus up to 50% at post-exercise meal	
Anaerobic	May not need insulin adjustments	May not need insulin adjustments	Reduce bolus or cancel exercise target	

[a]Confirm insulin pump suspension.
[b]Avoid consuming carbohydrates 15–60 minutes prior to exercise (can be given as needed during exercise).

Phillip M, et al. *Endocrine Reviews* 2023; 44: 254–280. doi: 10.1210/endrev/bnac022

Summary of Clinical Evidence

- Randomized Controlled Trials

- Real-World Studies

Phillip M, et al. *Endocrine Reviews* 2023; 44: 254–280. doi: 10.1210/endrev/bnac022

Summary of Clinical Evidence: RCTs

- All the AID systems have uniformly demonstrated an increase in TIR and a reduction in mean glucose, time in hyperglycemia, and HbA1c.
- Overall improvement in glycemic control was similar across all age groups and was evident during both day and night.
  - TIR improves more overnight than during the day.
- TIR increased by 9% - 16% for most systems.
- HbA1c decreased by 0.3% - 0.5%, with either no change or a reduction in time in hypoglycemia.
- AID use resulted in reduced rates of both hypoglycemia and hyperglycemia, thus increasing TIR. This contradicts the paradigm that improving glycemic control necessarily leads to an increase in hypoglycemia.

Phillip M, et al. *Endocrine Reviews* 2023; 44: 254–280. doi: 10.1210/endrev/bnac022

Summary of Clinical Evidence: Real World studies

- Outcomes are similar to those of the pivotal studies in the means of TIR and TBR
- HbA1c reduction 0.3% - 0.4%
- Rates of severe hypoglycemia (SH) and DKA were low
- Improved quality of life
- Reduced diabetes burden
- Reduced fear of hypoglycemia
- Return to restful sleep for PwD and family

Phillip M, et al. *Endocrine Reviews* 2023; 44: 254–280. doi: 10.1210/endrev/bnac022

Target Populations for AID Therapy

- Strongly consider to all people with T1D:
  - School-aged children (7–14 years) **A**
  - Adolescents/Adults **A**
- Consider recommending to:
  - Older adults (>65 years) **B**
  - Preschool children (<7 years) **B**
  - People with mod/severe hypoglycemia and hypoglycemia unawareness **C**
  - Pregnancy complicated with T1D **C**
  - People with comorbidities: chronic renal failure and gastroparesis **C**
- Consider recommending appropriate AID systems to people with other types of diabetes treated with intensive insulin therapy (MSII or pump therapy):
  - People with type 2 diabetes **C**
  - People after pancreatectomy **E**
  - People with cystic fibrosis–related diabetes **C**
- Use of AID under supervision should be allowed in hospital settings if not contraindicated by clinical status or treatment needs. **E**

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Summary of recommendations: initiating AID use

- Consider starting “technology naïve” people either an insulin pump and/or CGM before transitioning to AID.
- Advise transitioning from prior insulin pump to AID to use current pump settings if glycemic control is acceptable.
  - However, pump parameters (basal rate, bolus settings) may need reassessment.
- Individualize the approach to AID depending on the AID system.
  - target glucose
  - active insulin time

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Clinical Recommendations for AID Use

- Instead of basal-bolus we suggest using the terms of user-initiated and algorithm modulated insulin delivery.

- All current commercial AID systems still require user-initiated bolusing for carbohydrate intake.

- Pump settings (such as insulin action time, basal rates, etc) are handled differently in the various AID systems, dissimilarities which preclude our ability to provide general recommendations.

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Artificial Intelligence in Diabetes Care

Don't fear Artificial Intelligence

Fear natural stupidity