Quality control program to manage metformin stimulated 18-FDG bowel uptake in PET/CT imaging

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Metformin and Gut

- Metformin ↑ bowel glucose uptake from the bloodstream, ↓ luminal glucose uptake, and ↑ enterocyte glucose consumption.
  - ➢ Metformin ↑ 18-FDG uptake in the bowel (colon > small bowel)
    - ➢ May mimic or mask malignancy in the GI tract

❖ Discontinuing Metformin 48 hours prior to PET/CT scans has been shown to reduce this Metformin effect

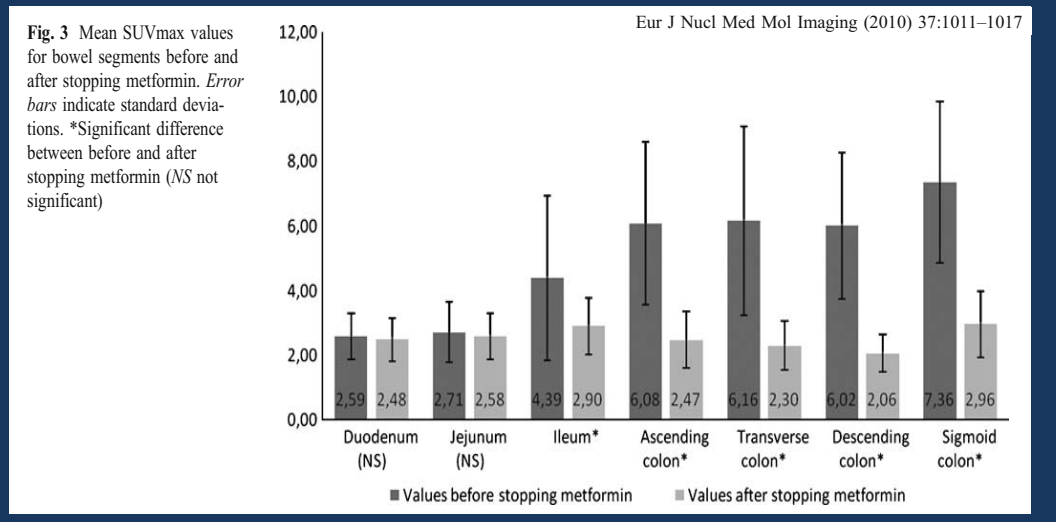
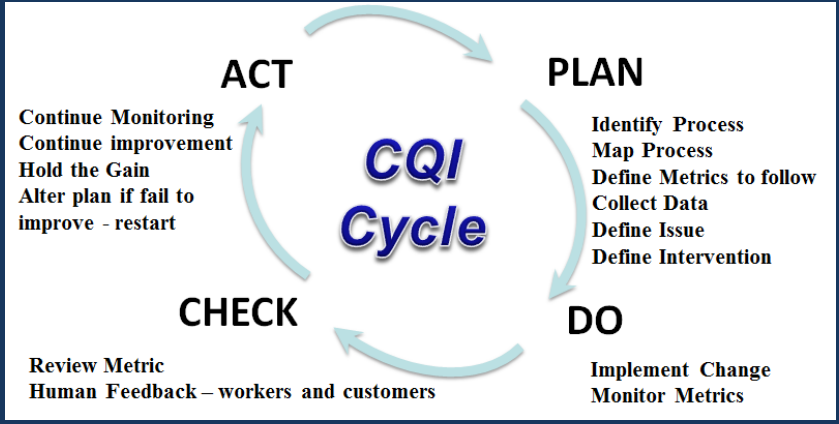


Fig. 3 Mean SUVmax values for bowel segments before and after stopping metformin. *Error bars* indicate standard deviations. *Significant difference between before and after stopping metformin (*NS* not significant)

Addressing the Problem… Quality Improvement



- Adapt the methods from the literature into a viable change in clinical practice
- Use the PDSA or **Deming Wheel** Method to introduce and monitor changes
- Resources from the Institute for Healthcare Improvement
  - http://www.ihi.org/resources/Pages/default.aspx

Planning

- Problem: Metformin ↑ 18-FDG uptake in the bowel (colon > small bowel)
- Aim:
  - Discontinuing metformin should reduce this problem
  - Diabetic patients taking Metformin will have a 90% compliance rate in stopping Metformin 48 hours prior to injection of 18-FDG for PET/CT oncology imaging
- Which of the Institute of Medicine's 6 Quality Aims does this address?
  - Safety

3 Month Baseline Data from Boston Medical Center

- N = 280 oncology patients scanned
- 21% of patients receiving PET/CT scans were diabetic (N= 48)
- 59% of diabetics took Metformin within 24 hours of injection of 18-FDG
- Increased bowel uptake => Bowel/Liver SUVmax ratio >2 (exclude diseased areas)
  - Diabetics taking Metformin: 66%
  - Diabetics not taking Metformin: 17%

Fish Bone Diagram to determine the factors that will affect compliance

Equipment	Process	People	
Phone system functioning Printers functioning	Referring MDs must remember to give patients pre-procedure instructions Complex patient instructions/ misplaced handout Patients referred from site not updated on changes Patients scheduled to receive PET/CT prior to seeing oncologist, so may not receive instruction sheet Unable to contact patient Blood glucose levels increase when not taking Metformin Many patients need rescheduling	Nuclear medicine technicians: * Overworked/ not available to give instructions * Must provide clear instructions * Must record reasoning for glitches in the process Referring physicians: * Must remember to give patients pre-procedure instructions Nuclear Medicine Manager: * Responsible for managing staff & delegating duties Nuclear Medicine schedulers: * Aid in differentiating diabetic patients Nuclear Medicine MDs: * Must decide when to reschedule patients, which could increase the number rescheduled Patients willing to comply	Patient compliance with the discontinuation of Metformin 48 hours prior to PET/CT
Patient instructions Translated instructions Diabetic monitoring sheet Letters for referring MDs and PCPs Script technicians use to deliver patient instructions	Techs properly educated on process and their duties Workload of staff in compliance with union Manager receptive to staff input on workflow/ new duties	Techs aware of new monitoring form and fill it out fully Documentation of why certain steps weren't done Schedulers aware that diabetics must have a different color folder	
Materials	**Environment**	**Measurement**	

Planning

Metrics

- **Outcome measure:**
  - **% of patients discontinuing Metformin 48 hrs prior to PET/CT**
- Process measures:
  - % patients receiving telephone reminders at 72 hrs and 24 hrs prior to PET/CT scan
  - % technicians recording whether Metformin was discontinued 48 hrs prior to scan, & if it wasn't, the reasoning for that
  - % of patients receiving print-outs of pre-procedure instructions
- **Balancing measures:**
  - **Blood glucose level on day of scan**
  - **Bowel uptake of 18-FDG→ bowel/liver SUVmax ratio**
  - Extra hours per week to make phone calls to patients

Sample of the Technologist's Worksheet

BOSTON MEDICAL
EXCEPTIONAL CARE. WITHOUT EXCEPTION.

PET/CT: DIABETIC PATIENTS

PATIENT NAME: _____ MRN: _____ Phone #: _____

Diagnosis or reason for ordering scan: _____

ORDERING MD: Name: _____ Dpmt: _____ Phone #: _____

	DATE	INITIALS
☐ Patient received pre-procedure instructions from PET/CT technician in our department If no, reason _____ Is the PET/CT scheduled **before** or **after** an oncology appointment? (please circle)	_____	_____
☐ **72 hours** prior to scan, patient received reminder phone call If no, reason_____	_____	_____

☐ Patient received pre-procedure instruction sheet: ☐ No ☐ Yes – where (mail, onc, nuc med)? _____

☐ Diabetic Meds (please circle): Metformin Glipizide Gliburide Insulin Other:_____

☐ Reminded patients taking Metformin to stop it 48 hours prior to PET/CT

- AM Fasting Blood Glucose (*Note if patient doesn't have a glucometer):

	Date	Time checked	Time ate	Blood glucose
1)				
2)				

	DATE	INITIALS
☐ The **day before** the scan, patient received reminder phone call	_____	_____

☐ Yes ☐ No ☐ N/A Patient discontinued Metformin 48 hours prior to scan time _____
Date/Time Stopped

☐ Reminded patient to fast for ≥6 hours prior to scan & consume a low carb/high fat diet as the last meal

☐ Reminded patient to discontinue exercise 24 hours prior to scan

- AM Fasting Blood Glucose (today and yesterday):

	Date	Time checked	Time ate	Blood glucose
1)				
2)				

DAY OF SCAN: Date _____ Time_____ Tech name _____

Glucose: _____mg/dl Last Meal: date/time:_____ content: _____

☐ Yes ☐ No ☐ N/A Patient discontinued Metformin 48 hours prior to scan time _____
Date/Time Stopped

****IF NO** please provide reason:

☐ Didn't receive instructions from tech ☐ Didn't receive written instructions ☐ Language barrier
☐ Didn't receive reminder phone call ☐ Didn't understand instructions ☐ Forgot
☐ Nervous glucose would increase ☐ Lost instructions
☐ Other_____

- Patients must be rescheduled if blood glucose >200 mg/dl, or if Metformin was not discontinued 48 hours prior to scans in patients with pelvic (ovarian, uterine, cervical) cancer, GI cancer, or lymphoma

☐ Yes ☐ No Had to be rescheduled. If yes, reason _____

PDSA Cycle #1

- Interventions
  - Implemented policy to discontinue Metformin 48 hours prior to PET/CT scan
  - Staff education
  - **Head technician calls diabetics 72 and 24 hours prior to scan to give instructions**

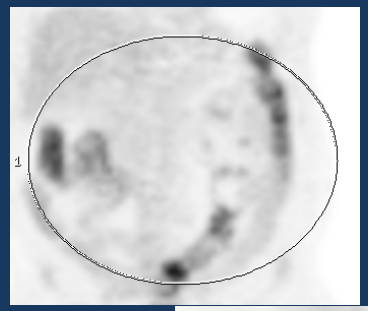
- Outcomes
  - Number of diabetics taking Metformin each month after intervention:
    - N = 12 → 9 → 9 → 9
  - **Monthly compliance rates with instructions to discontinue metformin:**
    - 83%→ 89%→ 80%→ 67%
  - **Bowel/liver SUV ratio >2 = 15% of compliant patients**
    - **Similar to diabetics not on Metformin**
  - No significant increase in blood glucose

PDSA Cycle #2

- Changes:
  - Updated Patient Preparation Instructions
    - Simplify language and steps
  - **Have referring physicians from oncology clinics distribute patient instructions when ordering a PET/CT scan**
  - Re-educate Staff – continue technologist phone calls with repeat verbal instructions.

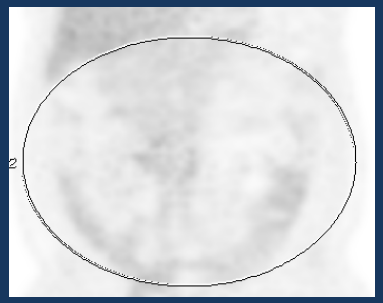
- Outcomes:
  - **Compliance rate: 100% in first month (N = 6)**
  - Bowel/liver SUV ratio >2 = 15% (same levels as those not taking metformin)
  - No patient had blood glucose over 200mg/dl

Bowel Activity: On vs. Off Metformin



SUVmax 8.6

SUVmax 2.9



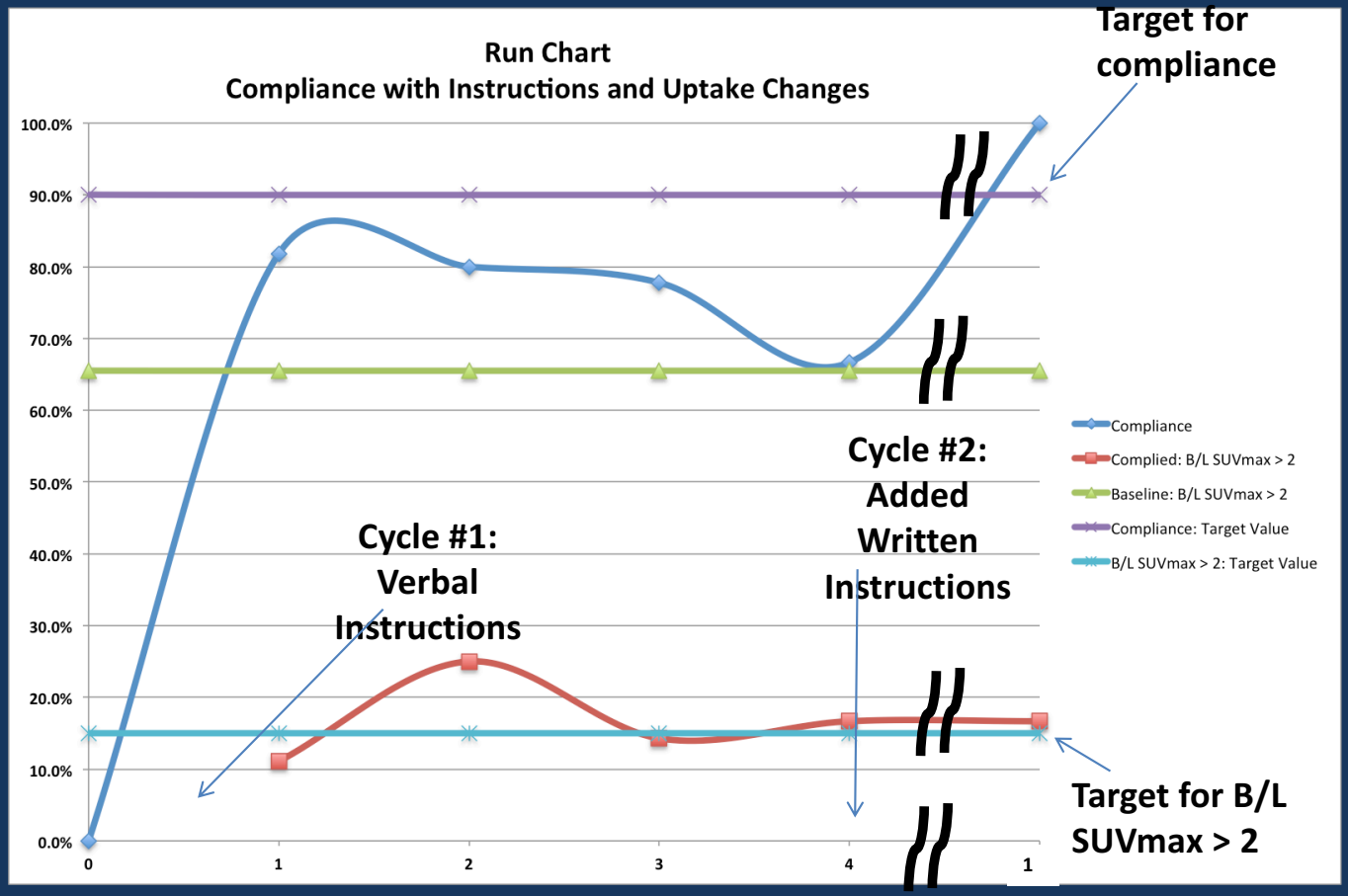
MIP Images

ON METFORMIN

OFF METFORMIN

	Bowel SUVmax (gm/ml)				
	Baseline		After Interventions		
	On Metformin	No Metformin Prescription	Complied with Instructions	Did not Comply	No Meformin Prescription
Mean	6.9	3.7	3.9	6.5	2.9

***Discontinuing Metformin for at least 48 hours reduced bowel activity while liver activity was unchanged**



B/L = Bowel to Liver SUVmax Ratio

Green line is fraction of diabetics taking Metformin in the baseline period and with B/L SUVmax > 2

Compliance with instructions to discontinue Metformin for 48 hours before injection:

- Cycle #1: almost reached target (90%) but fell 3 months later.
- Cycle #2: improved after 1st month

Fraction of patients with **Bowel to Liver SUVmax ratio > 2** dropped to target level in compliant patients (See Green line vs. Orange curve)

*** Month 5 after cycle #1 not included due to only 2 patients taking metformin and one with incomplete data**

Lessons Learned

- **Metformin effect on the bowel results from increased uptake from the blood stream.**

- **Withholding Metformin for at least 48 hours before injection of 18-FDG reduces bowel activity to levels seen in diabetics not using metformin.**
  - This improves scan quality, and should improve diagnostic accuracy.
  - In our facility this change had no ill side effects in blood glucose levels at the time of injecting 18-FDG

- **This quality improvement was achieved using the Deming Wheel methodology, an accepted tool for quality improvement.**
  - Improvement required progressive interventions from verbal instructions to written instructions
  - It also required continued monitoring for compliance and effect on image quality

- **Additional lessons in the implementation of this project included**:
  - Small system changes are challenging
  - Buy-in of key stakeholders is essential
  - Multi-disciplinary team approach is critical to the success
  - Determining the best contacts and leaders is helpful
  - Having a clear goal and a direct outcome measurement helped focus our efforts and track progress

References:

- Pernicova, Ida, and Márta Korbonits. “Metformin--Mode of Action and Clinical Implications for Diabetes and Cancer.” Nature Reviews. Endocrinology 10, no. 3 (March 2014): 143–56. doi:10.1038/nrendo.2013.256.
- Aldea, Mihaela, Lucian Craciun, Ciprian Tomuleasa, Ioana Berindan-Neagoe, Gabriel Kacso, Ioan Stefan Florian, and Carmen Crivii. “Repositioning Metformin in Cancer: Genetics, Drug Targets, and New Ways of Delivery.” *Tumour Biology: The Journal of the International Society for Oncodevelopmental Biology and Medicine* 35, no. 6 (June 2014): 5101–10. doi:10.1007/s13277-014-1676-8.
- Gontier, Eric, Emmanuelle Fourme, Myriam Wartski, Cyrille Blondet, Gerald Bonardel, Elise Le Stanc, Marina Mantzarides, Herve Foehrenbach, Alain-Paul Pecking, and Jean-Louis Alberini. “High and Typical 18F-FDG Bowel Uptake in Patients Treated with Metformin.” *European Journal of Nuclear Medicine and Molecular Imaging* 35, no. 1 (January 1, 2008): 95–99. doi:10.1007/s00259-007-0563-6.
- Oh, Jong-Ryool, Ho-Chun Song, Ari Chong, Jung-Min Ha, Shin-Young Jeong, Jung-Joon Min, and Hee-Seung Bom. “Impact of Medication Discontinuation on Increased Intestinal FDG Accumulation in Diabetic Patients Treated With Metformin.” *American Journal of Roentgenology* 195, no. 6 (December 1, 2010): 1404–10. doi:10.2214/AJR.10.4663.
- Özülker, Tamer, Filiz Özülker, Meral Mert, and Tevfik Özpaçacı. “Clearance of the High Intestinal 18F-FDG Uptake Associated with Metformin after Stopping the Drug.” *European Journal of Nuclear Medicine and Molecular Imaging* 37, no. 5 (May 1, 2010): 1011–17. doi:10.1007/s00259-009-1330-7.
- Steenkamp, Devin W., Marie E. McDonnell, and Sara Meibom. “Metformin May Be Associated with False-Negative Cancer Detection in the Gastrointestinal Tract on PET/CT.” *Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists* 20, no. 10 (October 2014): 1079–83. doi:10.4158/EP14127.RA.