

MTN-017: Adverse Events and MedDRA

Ken Ho, MD

Devika Singh, MD

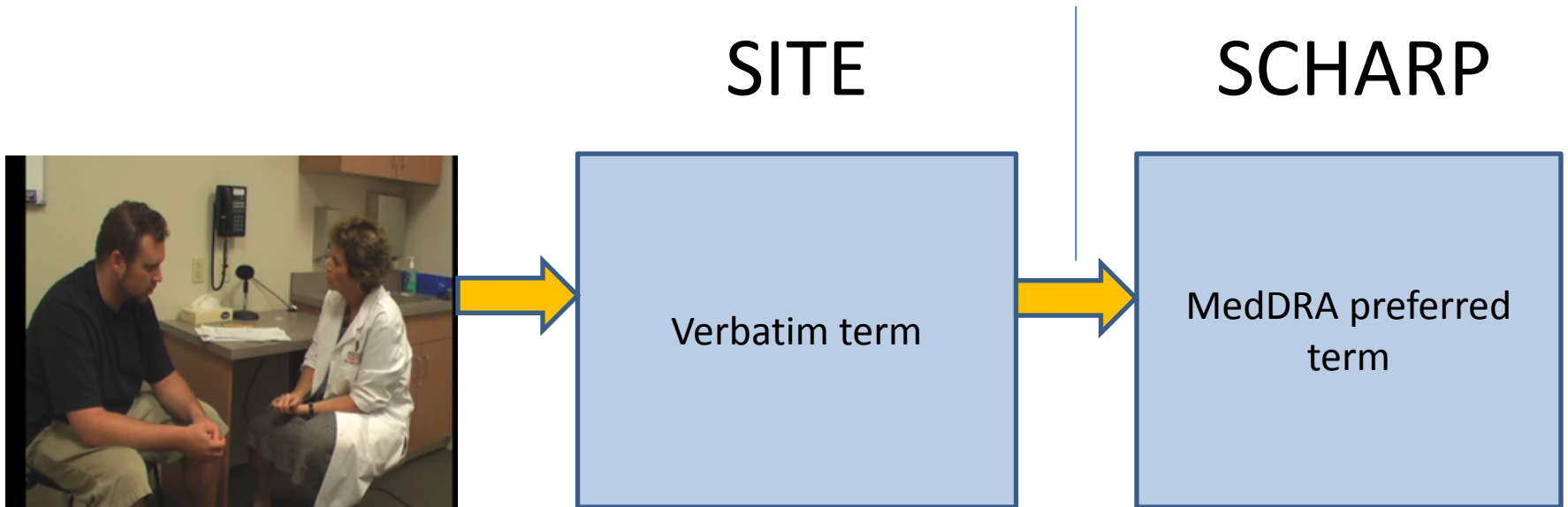
Outline

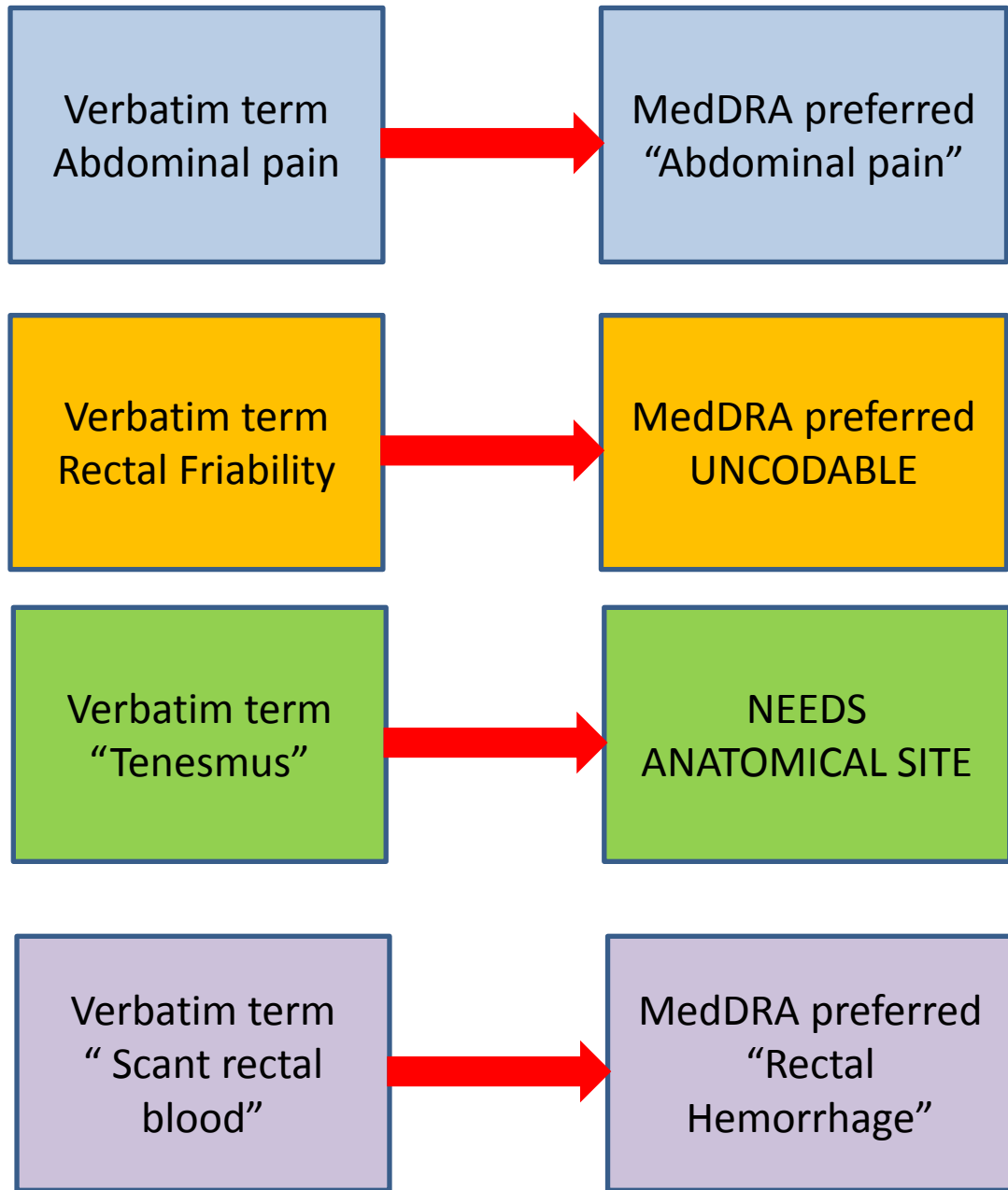
- General description of AE reporting/MedDRA coding process
- Cases
- MTN-017 “Cheat Sheet”

What is MedDRA?

- Extensive and highly specific standardized medical terminology dictionary developed by the ICH
- Facilitate sharing of regulatory information internationally for medical products.
- Most recent version is 16.1

MedDRA terminology





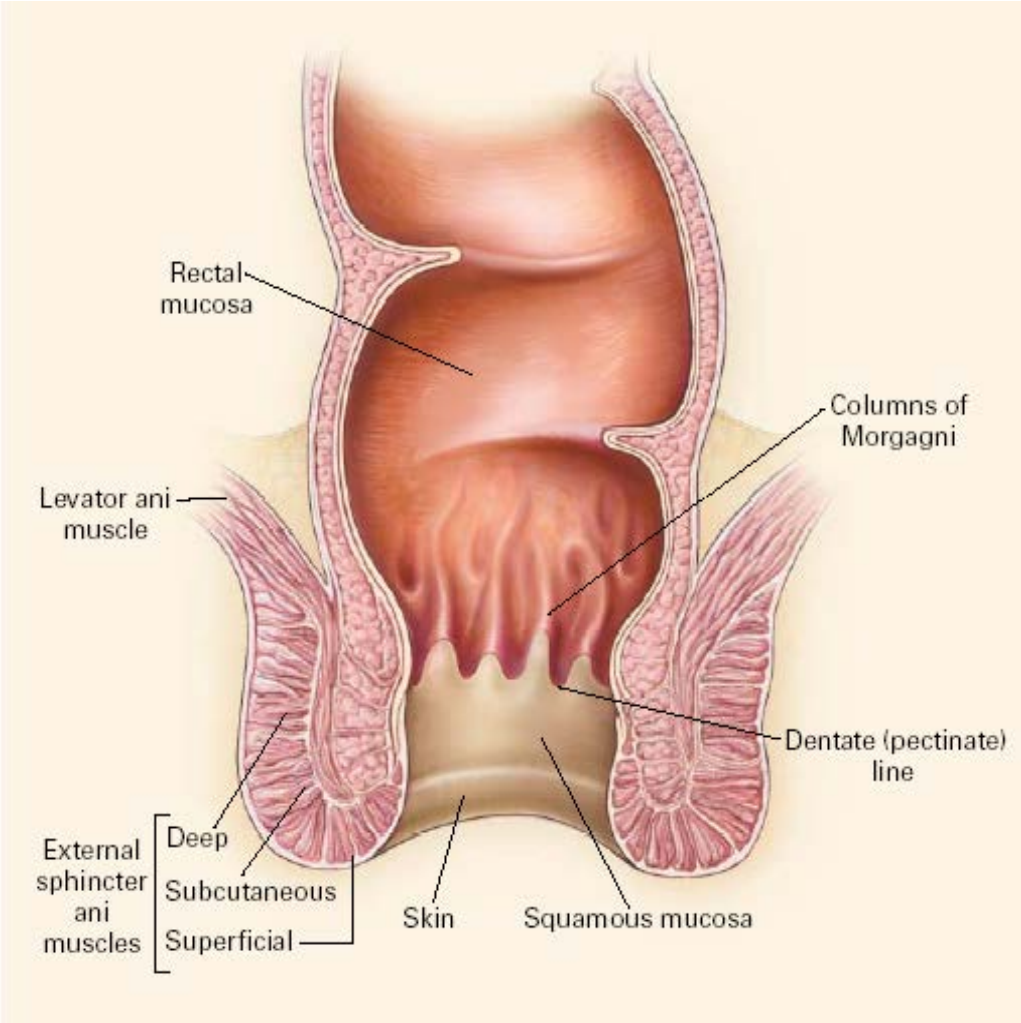
Case 1

- 24 year old male on oral Truvada (Period 1) reports anal pain at his end period visit. It is described as a burning/tingling sensation. He has a prior history of perianal HSV and reports that this is consistent with previous episodes.



- An Grade 2 Adverse Event of “Anal HSV” is reported on the AE CRF and faxed to SCHARP
- Meddra preferred term: Proctitis Herpes

- “Anal HSV”
 - maps to a Meddra preferred term of “Proctitis Herpes”
 - Proctitis - defined as inflammation of rectal mucosa. From the standpoint of MedDRA – also includes anal mucosa.
 - Appropriate if evidence of HSV involving anal mucosa
 - Clinical syndrome of HSV proctitis is a rare entity
- “Perianal HSV”
 - more accurately captures this adverse event
 - Maps to “genital herpes”



Verbatim Term	Meddra Preferred Term
Perianal HSV	Genital Herpes
Anal HSV	Proctitis Herpes
Anal HSV Ulcer	Proctitis Herpes
Rectal HSV	Proctitis Herpes

Take home points

- Important to specify anatomic location
- Distinguish between anal and perianal involvement of HSV

Case 2

- 40 year old male on daily reduced glycerin tenofovir gel presents for his mid-period visit. Reports that his stools are softer and somewhat mushier.

- A verbatim term of “soft stool” is reported
- This maps to a MedDRA preferred term of “Diarrhoea”

- Definition of diarrhea?
 - WHO definition – three or more loose, liquid stools per day
- Alternative is to report as “change in stool consistency” without further detail which will map to “abnormal faeces”
- Any mention of “soft”, “loose”, or “softer” will cause the verbatim term to map to “diarrhoea”
- MedDRA preferred term of “frequent bowel movements” does exist

Take home points

- Certain details will impact MedDRA coding.
- Terms such “loose” or “soft” stool will map to “diarrhoea”
- Diarrhea related to procedure maps to “post procedure diarrhoea”

Verbatim Term	MedDRA Preferred Term
Soft Stools	Diarrhoea
Change in Stool Consistency (Softer)	Diarrhoea
Change in Stool Consistency	Abnormal Faeces
Change in Stool Consistency (mushier)	Abnormal Faeces
Increased stool frequency	Frequent Bowel Movements
Loose stool related to study product application	Post procedural diarrhoea

Case 3

- 34 yo male on RAI associated tenofovir gel.
Reports some “gas pain”

- A verbatim term of “gas pain” is reported
- MedDRA preferred term: Flatulence

What is flatulence?

- The presence of too much air or gas being present in the stomach or intestines
- The process of flatus being passed through the anus

Verbatim Term	MedDRA Preferred Term
Gas pain	Flatulence
Gas	Flatulence
Flatulence	Flatulence
Abdominal Bloating	Abdominal Distension
Abdominal pain	Abdominal pain
Abdominal pain due to bloating	Abdominal Distension

Take Home Points

- Overlap may exist between some medDRA preferred terms
- Opt for the term that captures the underlying cause of the adverse event

Case 4

- 45 yo participant on RAI associated tenofovir gel undergoes anoscopic examination. Reports recent history of receptive anal sex.
- Anoscopy reveals presence of punctate areas of breakdown and disruption involving the rectal mucosa

- A verbatim term of “**rectal mucosal disruption**” is reported
- MedDRA code does not exist for the term “epithelial disruption” and this would most likely generate a query
- DAIDS toxicity table – addendum 3 lists “epithelial disruption” and “endoscopic colorectal mucosal abnormality” but this will likely trigger a query

Anus vs. Rectum



Verbatim Term	Meddra Preferred Term
Rectal mucosal disruption	Not codable
Epithelial disruption	Not codable
Rectal mucosal abrasion	Mucosal excoriation
Anal mucosal abrasion	Anal injury
Anal erosion	Anal erosion
Anal ulcer	Anal ulcer

Take home points

- “Mucosal disruption” or “epithelial disruption” will likely trigger query
- Preference for a more specific terms such as “abrasion”, “excoriation” or “ulcer”
- Specify anatomy/site

MTN-017 Cheat Sheet

- Approximately 136 adverse event verbatim terms obtained from prior gel studies, DAIDS toxicity table – addendum 3, MTN-017, and Anorectal Exam CRF
- Categories mirror rectal DAIDS tox table
 - Anal
 - Colorectal
 - Other GI
 - STI
 - Problem Verbatim terms

MTN-017 Cheat Sheet

Verbatim term	Meddra Preferred Term (PT)
ANAL	
Anal abscess	Anal abscess
Bowen's disease	Bowen's disease
Anal bruising	Contusion
Anal discharge	Rectal discharge
Anal edema	Oedema
Anal erythema	Erythema
Anal fissure	Anal fissure
Anal fistula	Anal fistula
Anal hemorrhoids	Haemorrhoids
Anal intraepithelial neoplasia 1 (biopsy)	Anogenital dysplasia

PROBLEMATIC VERBATIM TERMS		COMMENTS
Tenesmus		The term is missing anatomic location (for example, this could be bladder or rectal tenesmus).
Abdominal pain secondary to abdominal bloating		The reported term should be abdominal bloating. The pain should be listed as a sx of the bloating in the comments field.
Anal carcinoma in situ	Anal cancer stage 0	3" and "Anal carcinoma in situ" are the same. However "anal carcinoma in situ" will map to "anal cancer stage 0" while "anal intraepithelial neoplasia 3" maps to "anogenital dysplasia". Preference would be to report as "anal intraepithelial neoplasia 3" if possible.
Anal HSV	Proctitis herpes	and should be distinguished from "perianal herpes" which maps to "genital herpes".
anal HSV ulcer	Proctitis herpes	Anal ulcer HSV will map to "Proctitis herpes". Alternatively "perianal herpes" maps to "genital herpes".

Future plans

- Spreadsheet will be available soon on www.mtnstopshiv.org website
- Will implement regular updates
- Updates in medDRA coding (new version out next month) may also impact spreadsheet
- Email me at hok2@upmc.edu with questions or suggestions

Acknowledgments

- Ross Cranston
- Javier Lama
- Jeanna Piper
- Karen Patterson
- Yevgeny Grigoriev
- Elaine Dinnie

Questions? Suggestions?