

## Dobbel- og trippelbehandling med nye antitrombotika ved koronarsykdom



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Produsent-uavhengig legemiddelinformasjon for helsepersonell



**ANTITROMBOTIKA**

Hvilke typer?      Hvor mange?      Hvor lenge?

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### Avgrensning

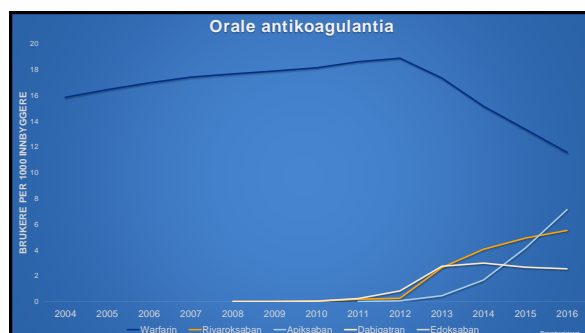
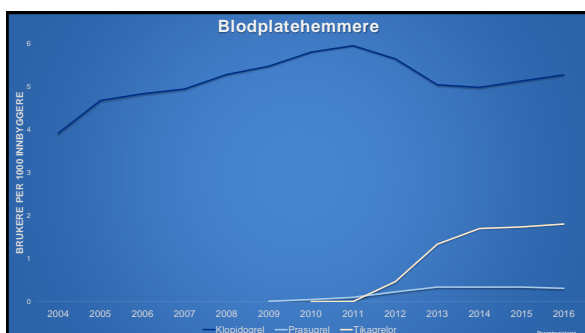
- + Akutt koronarsyndrom (og PCI)
- + PCI med stentimplantasjon
- + PCI og antikoagulasjon
- Kun medikamentell behandling (dvs. uten PCI), unntatt ved ACS
- Bypass (CABG)
- Hjerneslag
- Dyp venetrombose
- Lungeemboli
- Hepariner
- Antitrombotika ved PCI-inngrepet

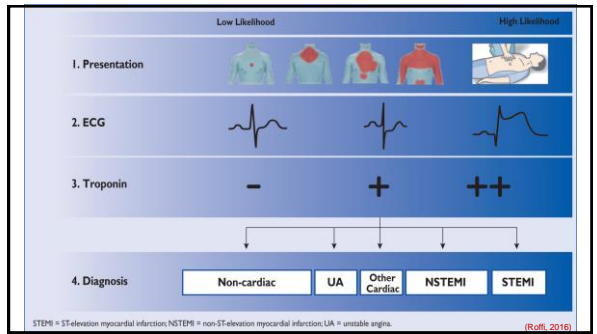
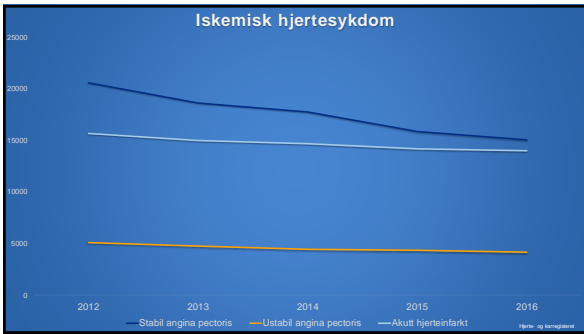
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### Ordforklaringer

- ACS = akutt koronarsyndrom (hjerteinfarkt, ustabil angina pectoris)
- Antitrombotika (her) = blodplatehemmere + orale antikoagulantia (OAK)
- ASA = acetylsalisylsyre
- DAPT = «dual antiplatelet therapy», dobbel blodplatehemming
- DOAK = NOAK = dabigatran, rivaroksaban, apiksaban, edoksaban
- NSTEMI = non-ST-elevasjonshjerteinfarkt
- P2Y<sub>12</sub>-hemmer = klopidogrel, prasugrel, tikagrelor
- PCI = «percutaneous coronary intervention»
- Stabil CAD = stabil koronarsykdom (stabil angina pectoris)
- STEMI = ST-elevasjonshjerteinfarkt
- Klopidogrel: Plavix® + generika
- Prasugrel: Effient®
- Tikagrelor: Brilique®
- Dabigatran: Pradaxa®
- Rivaroksaban: Xarelto®
- Apiksaban: Eliquis®
- Edoksaban: Lixiana®

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**Legemiddelavgivende stent (DES)**

Cytostatika  
↑ Sen stenttrombose

**Metallstent (BMS)**

↑ Restenose  
↑ (Tidlig) stenttrombose

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### NORSTENT

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Drug-Eluting or Bare-Metal Stents for Coronary Artery Disease

K.H. Benaou, J. Mannesverk, R. Wiseth, L. Aaberge, Y. Myrnes, O. Nygård, D.W. Nilsen, N.-E. Klau, M. Uchida, T. Tronvik, B. Bendtz, S. Stavens, R. Bjørnerheim, A.-I. Larsen, M. Slette, T. Steigen, O.J. Jakobsen, Ø. Bleie, E. Fossum, T.A. Hansen, Ø. Dahl-Eriksen, I. Njehstad, K. Rasmussen, T. Willgaard, and J.E. Nordrehaug, for the NORSTENT Investigators\*

**Nye STEMI-retningslinjer går på tvers av norsk studie**

dagensmedisin.no, 10. oktober 2017

- 9013 pasienter
- Offentlig finansiert!
- Ingen forskjell i død/hjerteinfarkt
- BMS: re-revaskularisering, marginalt mer stenttrombose

(Benaou, 2017)

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### DAPT – dobbel blodplatehemming

ASA

Klopidogrel

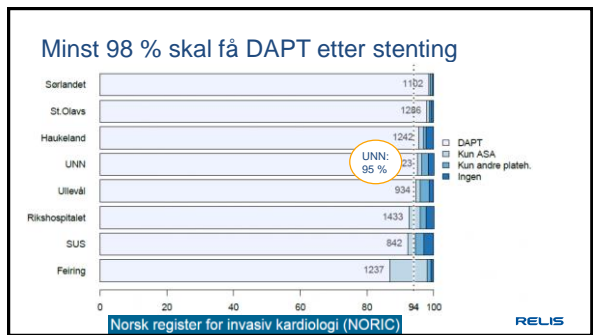
Prasugrel

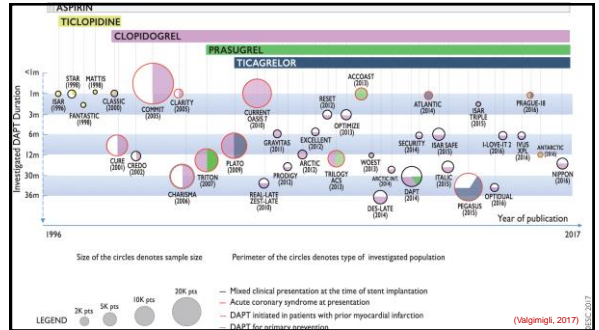
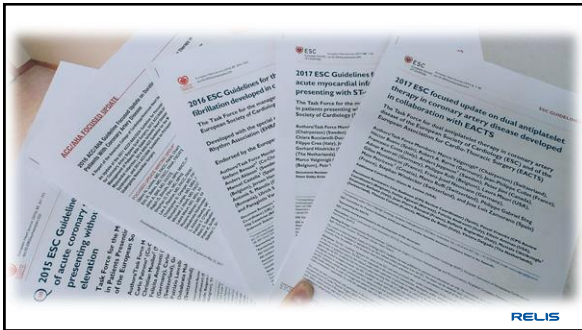
Ticagrelor

(Tiklodipin)

P2Y<sub>12</sub>-hemmere / ADP-reseptorhemmere

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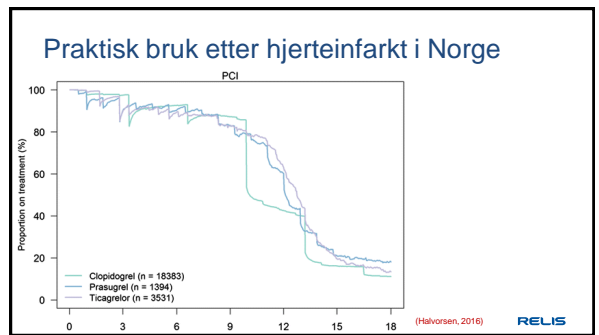
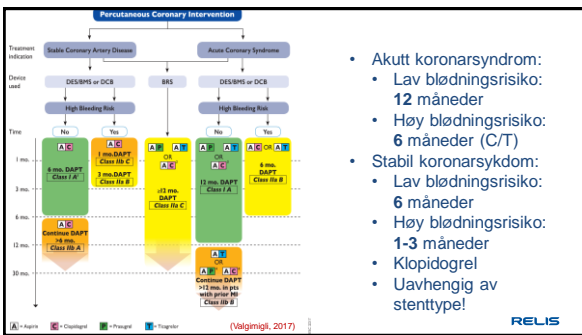
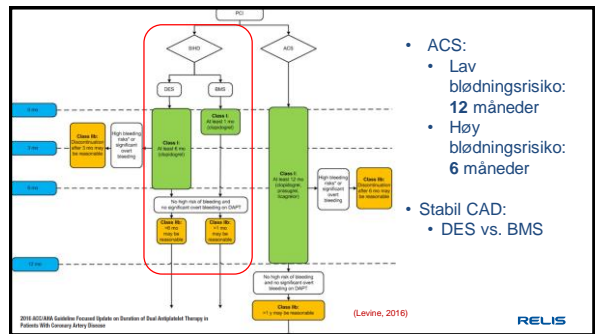


### Tika hva-for-no'? Hvordan velge?

	Klopidogrel	Prasugrel	Tikagrelor
ACS	Ja	Ja*	Ja
Stabil CAD	Ja	Nei	Nei
Trippelterapi	Ja	Nei	Nei
CYP-polymorfisme	Nei*	Ja	Ja
Blødningshistorikk	Ja	Nei	Nei
Hjerneslag/TIA		Nei!	

ASA 75-100 mg      Ikke test blodplatefunksjon      PPI

(Valgmiglit, 2017, Levine 2016)      RELIS



### Risikoscore

- RCT-er
  - DAPT
  - PRECISE-DAPT
- Registre
  - PARIS
  - CALIBER
- Begrenset nytte

DAPT Risk Calculator

Patient Characteristics

Procedure Characteristics

RESULT

Cluster of risk: High

Score Calculated: 33

12 months risk of TIMI major or minor Bleeding: 3.3%

12 months risk of TIMI Major Bleeding: 1.7%

Your patient has a DAPT Score of 0.

### Behandle utover 12 måneder etter PCI?

- ↓ Stenttrombose og MI
- ↑ Død (men ikke kardiovaskulær død)
- Blødninger (Palmeini, 2017)
  - Direkte
  - Indirekte (manglende compliance)
- Men: Ikke ↑ Død (Bavishi, 2017)
- UpToDate: + 18/36 måneder (hvh. stabil CAD/STEMI) (Nåvarese, 2015)

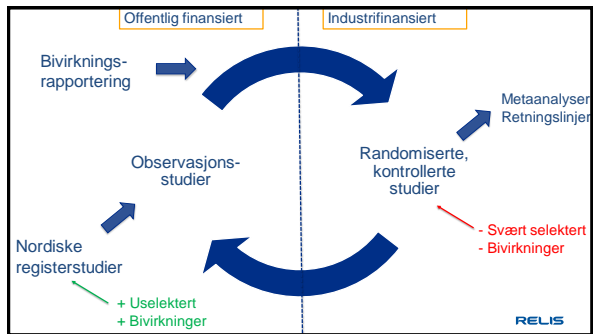
### Rashomon-effekten?

EDITORIAL COMMENT

Bleeding and Mortality With Dual Antiplatelet Therapy: The Rashomon Effect?

Author: S. Kim, MSc, Robert A. Harrington, MD

(Rao, 2017)



### Dobbelterapi, trippelterapi eller DAPT?

A Non-fatal and fatal bleeding

Hazard ratio (95% CI)

(Svenssen, 2009)

- Aspirin alone
- Clopidogrel alone
- Vitamin K antagonist alone
- Aspirin plus clopidogrel
- Aspirin plus vitamin K antagonist
- Clopidogrel plus vitamin K antagonist
- Triple therapy

### Metaanalyser av dobbel/trippel/DAPT

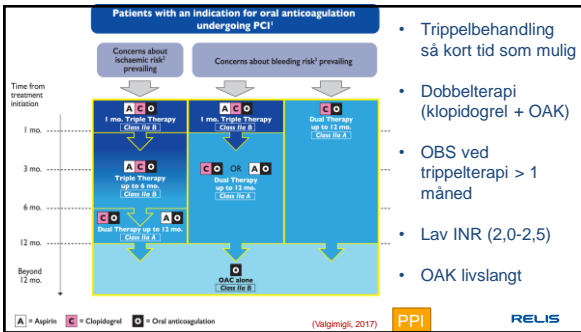
- Blødning:
  - Trippelterapi > Dobbelterapi (blodplatehemmer + OAK)
  - Trippelterapi > DAPT
- Trombotiske hendelser og død:
  - Trippelterapi = Dobbelterapi
  - DAPT er usikkert
- Klopidogrel + OAK er alternativ til trippelterapi
- DOAK, tikagrelor, prasugrel er uavklart

Odds Ratio IV, Random, 95% CI

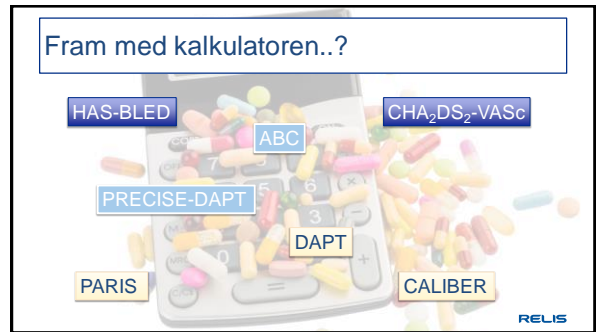
clonidogrel and OAK

Aspirin, clopidogrel and OAK

(D'Ascenzo, 2015, Agarwal 2017)



- Trippelbehandling så kort tid som mulig
- Dobbelterapi (klopidogrel + OAK)
- OBS ved trippelterapi > 1 måned
- Lav INR (2,0-2,5)
- OAK livslangt



### Forskningsfronten

- Kortere og lengere
  - En måned: SENIOR (2018), MASTER DAPT (2019), POEM (2019)
  - > 12 måneder
- Bytte underveis?
  - Tikagrelor/prasugrel → klopidogrel (Cuisset, 2017, TROPICAL-ACS)
  - DAPT → SAPT etter én måned (GLOBAL-LEADERS, 2017)
- It takes two, baby?
  - REDUAL-PCI, RT-AF (2016), AUGUSTUS (2018)
- Er de nye virkelig så gode?
  - Bare brukt i drøyt fem år!

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### Noen råd

- Vær spesielt oppmerksom på behandlingstidspunktet
- Klopidogrel ved høy blødningsrisiko og trippelterapi
- Trippelterapi skal få alle alarmklokker til å ringe
- Pass spesielt på ved trippelterapi utover én måned
- Etterlevelse (adherence) er veldig viktig
- Husk på protonpumphehemmer
- ESC-retningslinjene er relativt pedagogiske og har kortformer og apper: <https://www.escardio.org/Guidelines/>

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www.relis.no

Produktuavhengig legemiddelinformasjon for helsepersonell RELIS

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